ID: 6  
TITLE: Nursing interventions to reduce the incidence of intraventricular hemorrhage in preterm infants: a multicenter cohort study.  
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CONTENT:  
Germinal matrix-intraventricular hemorrhage (GMH-IVH) is a major, frequently occurring complication of preterm birth. Nursing interventions aimed at maintaining a more stable cerebral blood flow and decreasing cerebral venous congestion have been suggested to reduce the risk of GMH-IVH in preterm infants. The objective of the present study was to investigate the effect of a nursing intervention bundle (NIB) on the incidence of GMH-IVH in very preterm infants (gestational age, GA, <30 weeks).  
Two Dutch tertiary neonatal intensive care units participated in this cohort study. The intervention group consisted of 140 neonates per center, whereas 140 infants per center served as historical controls (GA<30 weeks). The NIB was implemented and applied during the first 72 hours after birth. The NIB consisted of maintaining the head in the midline, tilting the head of the incubator and avoidance of flushing/rapid withdrawal of blood and sudden elevation of the legs. The incidence of GMH-IVH occurring after the first ultrasound (but within 72 hours), progressive GMH-IVH, cystic periventricular leukomalacia (cPVL) and/or in-hospital death was the primary composite outcome measure. Logistic regression analysis was used to explore statistically significant differences between groups.  
The NIB was associated with a lower risk of developing a GMH-IVH (any degree), cPVL and/or mortality (OR 0.42, 95%CI 0.28-0.65). In the group receiving the NIB, severe GMH-IVH, cPVL and/or death were less often observed (OR 0.55, 95% CI 0.33-0.91). There was a more pronounced effect on the incidence of severe GMH-IVH compared to low grade hemorrhages. In addition: the beneficial effect of the NIB was greater in extreme premature infants (GA<27 weeks). No disadvantages of the NIB were observed.  
The application of a bundle of nursing interventions reduces the risk of a new/progressive (severe) GMH-IVH, cPVL and/or mortality in preterm infants when applied during the first 72 hours after birth. Since it is relatively easy and cheap to apply and no disadvantages of the NIB were observed, we advise the routine use of this NIB in all preterm neonates during the first 72 postnatal hours, especially in those born extremely prematurely.

IMAGE / TAB:  

IMAGE / TAB CAPTION:  

COI: None declared
ID: 12

TITLE: WHAT HAPPENS NOW AND WHAT DO PARENTS WANT? A QUALITY IMPROVEMENT APPROACH TO UNDERSTAND PARENT INFORMATION NEEDS IN NEONATAL CARE.

AUTHORS: Susanna Sakonidou 1; Sophia Kotzmanis 2,3; Izabela Andrzejewska 1; Wendy Carnegie 2; Neena Modi 1; Derek Bell 2; Christopher Gale 1

AFFILIATIONS: 1 Imperial College London, Neonatal Medicine, London, United Kingdom.
3 Neonatal parent representative

CONTENT:

1 in 8 babies born in the UK require neonatal care. This is stressful for parents, who are often dissatisfied with the information provided by neonatal staff. Our aim was to map and describe the current information exchange in neonatal care, elicit the key information themes that are exchanged between parents and neonatal staff members and explore parents’ needs regarding the optimal content, format and delivery of information.

A prospective process-mapping study to explore information exchange with staff at a UK tertiary neonatal unit, and with parents whose babies had received UK neonatal care. We approached parents nationwide using social media. We held an interactive session with staff to temporally map information transfer on the neonatal unit; for parents we held a focus group which was audio-recorded and for parents unable to attend we developed an online survey and collated free text entries. We used a grounded theory approach to code feedback and group it into information themes. We plotted themes temporally in relation to an infant’s journey, creating a virtual map of information flow. We examined the themes most important to parents and their preferred way of receiving information.

Staff: 47 staff members reported discussing 20 themes with parents (Figure 1). Verbal clinical updates were shared with parents throughout the neonatal journey; written information was provided only at the beginning, middle and end. Parent involvement information was not shared during clinical deteriorations, infant transfers and when making clinical decisions. Parents: 76 engaged online, 4 participated in the focus group and 50 completed the online survey. Parents reported discussing 10 themes with staff, 8 matching with staff and 2 new (Figure 1). Parents identified 7 themes as most important, prioritising clinical updates; we categorised these into infant-specific and unit-specific information. Overall, parents agreed with staff on the type of information shared, but wanted it communicated in a different way: more objective, consistent, readily available and jargon-free.

Communication with parents in neonatal care predominantly involves verbal updates. Written information is inconsistent through an infant’s journey. Parents and staff agree on the type of information shared between them but parents want it delivered more consistently, in easily understandable language. A communication tool providing written information in a parent-centred way could be a valuable adjunct to verbal communication in neonatal care.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=58e3b058e09a4c55f97d31d36651af22-MjAxOS0wNSM1Y2UyNyYmI1M2RI

IMAGE / TAB CAPTION: Figure 1. Information themes discussed in neonatal care, as they emerge temporally in infant journeys: 20 themes reported by staff (all shown), 8 of them were also reported by parents (highlighted in red). 2 themes were only reported by parents (in blue boxes).
COI: SS has received research grants from the National Institute of Health Research (NIHR), the NIHR CLAHRC NWL, Rosetrees Trust and CW+ charity. NM is Director of the Neonatal Data Analysis Unit at Imperial College London. In the last five years NM has served on the Board of Trustees of the Royal College of Paediatrics and Child Health, David Harvey Trust, Medical Women’s Federation and Medact; and is a member of the Nestle Scientific Advisory Board. NM has received research grants from the British Heart Foundation, Medical Research Council, National Institute of Health Research, Westminster Research Fund, Collaboration for Leadership in Applied Health and Care Northwest London, Healthcare Quality Improvement Partnership, Bliss, Prolacta Life Sciences, Chiesi, Shire and HCA International; travel and accommodation expenses from, Nutricia, Prolacta, Nestle and Chiesi; honoraria from Ferring Pharmaceuticals and Alexion Pharmaceuticals for contributions to expert advisory boards, and Chiesi for contributing to a lecture programme. CG is funded by the United Kingdom Medical Research Council (MRC) through a Clinician Scientist Fellowship award. He has received support from Chiesi Pharmaceuticals to attend an educational conference; in the past 5 years he has been investigator on received research grants from Medical Research Council, National Institute of Health Research, Canadian Institute of Health Research, Department of Health in England, Mason Medical Research Foundation, Westminster Medical School Research Trust and Chiesi Pharmaceuticals. SK, IA, WC, DB: none declared.
ID: 23
TITLE: INHIBITION OF HMGB1 IMPROVES NECROTIZING ENTEROCOLITIS BY INHIBITING NLRP3 VIA TLR4 AND NF-κB SIGNALING PATHWAYS
AUTHORS: Renqiang Yu, Shanyu Jiang, Yaqin Tao, Ping Li, Qin Zhou
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CONTENT:

Necrotizing enterocolitis (NEC) is an acquired gastrointestinal disease which primarily affects premature babies. It is the most common gastrointestinal emergency in the newborn and may lead to death in severely affected infants. Although the exact cause is unknown, the critical elements are thought to be prematurity, enteral feeding, an inappropriate pro-inflammatory response and bacterial colonization. The current rodent models of NEC aim at mimicking these factors by feeding animals with lipopolysaccharide (LPS)-supplemented formula milk in combination with repeated exposure to hypoxia and/or hypothermia. There is strong evidence that the initial bacterial colonization of the newborn intestine plays a pivotal role in the development of NEC. NEC is characterized by an extensive hemorrhagic inflammatory necrosis of the distal small bowel and proximal colon with extensive infiltration of neutrophils. Intestinal epithelial cell lines constitutively express several members of a novel family of transmembrane receptors designated toll-like receptors (TLRs) that may serve as major links between the innate and adaptive mucosal immune responses. TLR4 is the primary receptor needed for the promotion of macrophage activation, cytokine release, and tissue damage. It mediates the recognition of antigens in the intestinal lumen as LPS due to the activation of NF-κB via increasing the production of proinflammatory cytokines. Extracellular high mobility group box 1 (HMGB1) induces inflammatory responses by directly acting on pattern recognition receptors, including TLR2 and 4. HMGB1, a ubiquitous and abundant nuclear protein, can either be passively released into the extracellular milieu in response to necrotic signals or actively secreted in response to inflammatory signals. When releases from cells, HMGB1 can elicit proinflammatory responses in different cell types, such as endothelial cells, macrophages, and neutrophils. Activated NLRP3 couples adaptor protein apoptosis-associated speck like protein (ASC) and caspase-1 to form a multiprotein cytosolic complex, NLRP3 inflammasome. NLRP3 inflammasome plays a crucial role in the innate immune system. Recent studies have shown that the NLRP3 inflammasome is involved in several adaptive immune diseases. Mutations in NLRP3 lead to chronic autoinflammatory syndromes.

Even studies have shown the role of HMGB1 and NLRP3 in animal models of acute colitis has been reported. However, the contribution of HMGB1 to NLRP3 inflammasome activation has not been explored in NEC. In this study, we studied the effect of HMGB1 expression on NLRP3 expression and some inflammatory factor to explore the relationship between HMGB1 and NLRP3 in NEC.

NEC rat models were constructed and treated with HMGB1 inhibitor Glycyrrhizin (GL) with different concentration. Inflammatory condition of intestinal tissue in newborn NEC rats was observed by H&E staining. The mRNA and protein expression of HMGB1, NLRP3, TLR4, NF-κB and Caspase-1 were determined by real-time PCR and western blot, respectively. Content of IL-1β and TNF-α was determined by ELISA assay. Human intestinal epithelial cell lines were induced to NEC by LPS. LPS-induced cells were transfected with siRNA-HMGB1 and NLRP3 plasmid vector. The mRNA and protein expression of HMGB1, NLRP3, TLR4, NF-κB, Caspase-1, IL-1β and TNF-α were determined by real-time PCR and western blot, respectively.

The mRNA and protein expression of HMGB1 and NLRP3 in NEC group was significantly higher than the control group. Inhibition of HMGB1 expression improved intestinal inflammation in newborn NEC rats. The expression of HMGB1, NLRP3, TLR4, NF-κB and Caspase-1 was up-regulated in NEC and was weakened after treating with GL. LPS induction to intestinal epithelial cells markedly increased the expression of HMGB1, NLRP3, TLR4, NF-κB, Caspase-1, IL-1β and TNF-α. Knockdown
of HMGB1 abolished the increase of expression, while further transfection with NLRP3 plasmid vector recovered the increase.

HMGB1 and NLRP3 were all up-regulated in the development of NEC. Inhibition on HMGB1 could improve the intestinal inflammation in NEC by inhibiting NLRP3 via TLR4 and NF-κB signaling pathways

**IMAGE / TAB:**

**IMAGE / TAB CAPTION:**

**COI:** None declared
ID: 24

TITLE: EARLY DIAGNOSIS OF NEONATAL SEPSIS BY PROCALCITONIN COMBINED WITH 16s rRNA

AUTHORS: Renqiang Yu

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CONTENT:

Neonatal septicemia (NS) is characterized by high morbidity and high mortality. Pathogens in newborns can grow rapidly in the blood and cause inflammatory reaction, leading to multiple organ damage or even death. However, early stages of NS often exhibit no obvious symptoms. Therefore, it is of great significance of early diagnosis for NS treatment. It was found that procalcitonin (PCT) and bacterial 16s rRNA have a good diagnostic value for early NS. However, their combined application has not been reported for the early diagnosis of NS.

92 patients admitted to the neonatology department from October 2016 to February 2018 were enrolled, including 50 NS patients and 42 non-infected neonates. The PCT content in serum was detected by immunofluorescence (IFAT). The 16s rRNA content in blood was detected by fluorescence quantitative PCR (FQ-PCR). The sensitivity and specificity of combined diagnosis were analyzed.

Serum PCT levels were significantly higher in the sepsis group compared with control (P<0.05). In the sepsis group, the positive rate of 16s rRNA was 98% (49/50) and the positive rate of blood culture was 72% (36/50) (P<0.05). In the control group, the blood samples were negative for 16s rRNA detection and bacterial culture. The sensitivity and the specificity of the combined diagnosis were 100% and 98.2%, respectively.

The combination of PCT and 16s rRNA can improve the diagnostic efficiency of NS. Their combination is simple and rapid, and can provide early sensitive diagnostic methods for NS, which can help to evaluate the therapeutic effect of the disease.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 37


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CONTENT:

Fat is very important for human nutrition. Fatty acids can be divided into saturated fatty acids and unsaturated fatty acids according to their different structures. Among them, unsaturated fatty acids can also be divided into monounsaturated fatty acids and polyunsaturated fatty acids (PUFA). PUFA is a biologically active fatty acid. As an important component of cell membrane phospholipids, PUFA directly affects the function of cell membrane and the fluidity and permeability of cell membrane [1]. The precursors of long chain polyunsaturated fatty acids (LCPUFA), linoleic acid (LA) and linolenic acid (ALA), cannot be synthesized in human body and must be obtained from food. The fetus receives nutrition from the mother through the placenta. The fatty acids obtained from the mother are influenced by the dietary composition of the mother. At the same time, the placenta plays a very important role in the transfer of fatty acids from the mother to the fetus [2,3]. Preeclampsia in pregnant women is often associated with fetal growth restriction and early placental development defects. Placenta is one of the main sources of lipid peroxidation. LCPUFA plays a potentially important role in regulating the fat metabolism of placenta and fetus. Studies have shown that arachidonic acid (AA) can up-regulate inflammation, while Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) can up-regulate inflammation. It has the effect of down-regulating inflammatory reaction [4]. We hope to find out the changes of fat metabolism in preeclampsia and its possible influence on fetus by measuring the fatty acid content in blood, placenta and umbilical cord blood of preeclampsia and normal pregnant women.

The composition of polyunsaturated fatty acids (PUFA) in the blood, placenta and umbilical cord blood was compared between normal pregnancy women and preeclampsia women. Thirty cases including maternal blood, placenta and umbilical cord blood in normal pregnancy women and preeclampsia women were collected. Fatty acid contents of maternal blood, placenta and umbilical cord blood were determined by gas chromatography. The absolute content and percentage content of 5 kinds of PUFA between the two groups were compared.

The contents of arachidonic acid (AA) and docosahexenoic acid (DHA) in the blood of preeclampsia women were higher than that of the normal pregnancy women. The content of linoleic acid (LA) in the blood of preeclampsia women was lower than that of the normal pregnant women (P<0.05). The ratio of AA/DHA in the placenta of the preeclampsia group was higher than that of the normal parturient group; The content of linolenic acid (ALA) in the placental was increased significantly in the preeclampsia group (P<0.05). The content of LA in the umbilical cord blood of the preeclampsia group was higher than that of the normal parturient group (P<0.05).

The components of PUFA in the blood, placenta and the cord blood of preeclampsia women were changed. These changes may relate to preeclampsia and need further research.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 40

TITLE: ULTRASONOGRAPHY FOR UMBILICAL CATHETER PLACEMENT; eLEARNING FOR NEONATOLOGISTS

AUTHORS: Rikke Kaae 1; Jette Led Sørensen 2; Simon Trautner 3; Christian A. Frederiksen 4; Kasper Jacobsen Kyng 1; Tine Brink Henriksen 1

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4: Department of Cardiology, Aarhus University Hospital, Denmark

CONTENT:

Several studies have documented that ultrasonography (US) performed by experienced ultrasound examiners may be superior to X-ray in accurately detecting the position of umbilical catheter tips. However, prior to introduction of US for this application in the neonatal intensive care unit (NICU), sufficient US skills need to be established for all “on-call” neonatologists when conducting the US task as the overall procedural quality will depend on the ultimate US skill of each of the physicians involved. A national survey of Canadian neonatologists (2010) and a survey among neonatal-perinatal United States residents (2015) have indicated, that the obstacles in the use of point-of-care US, were the lack of instructors and standardized teaching. A challenge is that neonatologists are learners with a high degree of mobility, with busy day-to-day schedules, day and night shifts and who may have different levels of previous US experience and competences.

eLearning may be a solution for overcoming some of these obstacles. eLearning has been shown to impact knowledge and skill acquisition compared to more traditional teaching methods. In addition it provides a flexible, standardized, teacher-independent educational tool. However, the feasibility and learning outcome of eLearning in neonatology related to point-of-care US has not been studied.

We aimed to investigate the change in knowledge related to neonatologists’ US skills from before to after a 1.5-hour eLearning program in ultrasonography-based examination of umbilical catheter placement stratified by a priori experience in point-of-care US.

All 48 neonatologists employed at the four university based tertiary NICUs in Denmark were included. Based on their self-reported practical experience with point-of-care US, the neonatologists were categorized into one of the following three groups; 1) perform less than one US examination per month, 2) perform one or more US examinations per month but less than one per week, 3) perform one or more US examinations per week but less than one per day and 4) perform one or more US examination per day. The eLearning comprised video examples with voiceover. The effect of eLearning was tested with a validated 25-item Multiple Choice Questionnaire (MCQ). Range in MCQ score 1 to 25. The learning outcome was measured as the changes in MCQ score from before to after the eLearning.

The characteristics of the 48 neonatologists are presented in Table 1. The average MCQ scores before and after completing the eLearning were 18 (95% confidence interval (CI) 17; 19) and 24 (95% CI 23; 24), respectively. The mean MCQ score difference between the pre- and post-MCQ score was 5 (95% CI 5; 6). Prior to eLearning the neonatologists’ mean pre-MCQ score varied by their self-reported level of US experience prior to the study. A relationship between US experience and performance in the pre-MCQ score was identified; the more US experience the higher pre-MCQ performance. After eLearning exposure the difference in MCQ score performance between neonatologists with different prior US experience was no longer detectable. The change in MCQ score for neonatologists by differences in their clinical use of point-of-care US are presented in Table 2.
The use of a short dedicated eLearning program was a feasible educational strategy to provide all Danish neonatologists employed in tertiary NICUs the knowledge of skills concerning the US task for examination of umbilical catheter placement. eLearning homogenized and increased the knowledge of the US skill in the overall group of neonatologists.

**IMAGE / TAB:**
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**IMAGE / TAB CAPTION:** Table 1. Characteristics of all neonatologists (n=48) employed in the four tertiary Neonatal Intensive Care Units in Denmark by January 2019.
Table 2. Mean multiple-choice questionnaire (MCQ)-score and changes in score from before to after eLearning in 48 neonatologists with different self-reported levels of ultrasound experience prior to the study.

**COI:** None declared
ID: 43

TITLE: EARLY ASYMPTOMATIC VERSUS LATE SYMPTOMATIC TREATMENT OF PATENT DUCTUS ARTERIOSUS ON SHORT AND LONG-TERM OUTCOMES IN PREMATURELY BORN INFANTS LESS THAN 28 WEEKS GESTATION

AUTHORS: Louise Francis1; Dominique James 2; Ramon Fernandez 1,2; Neil Aiton 2; Nikolay Drenchev 2; Cassie Lawn 2; Ryan Watkins 2; Bettina Reulecke 2 and Prashanth Bhat 1,2

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CONTENT:
A patent ductus arteriosus (PDA) complicates the clinical course of prematurely born infants, increasing their risks of developing pulmonary haemorrhage (PH), intraventricular haemorrhage (IVH) necrotizing enterocolitis (NEC) and chronic lung disease (CLD). The risk of developing the above complications is inversely related to the gestational age. A PDA can be treated pharmacologically with Indomethacin, Ibuprofen or Paracetamol, or surgically ligated. PDA treatment with pharmacotherapy could either be early asymptomatic (EA) (treatment within the first 72 hours of life, before the infant develops signs and symptoms) or late asymptomatic (LS) (after the first 72 hours of life when there are clinical signs and symptoms). It is still unclear when the best time to treat a premature newborn with PDA is – early asymptomatic or late symptomatic. The aim of this study was to compare the short and long-term outcomes of prematurely born infants less than 28 weeks gestation treated for early asymptomatic and late symptomatic patent ductus arteriosus.

A retrospective analysis of patient data over a four year period was undertaken. Preterm infants less than 28 weeks gestation admitted to a tertiary neonatal unit with PDA diagnosed on echocardiogram and treated pharmacologically either early (> 72 hours of age) or late (> 72 hours of age) were included. Those infants who developed pulmonary haemorrhage (PH), IVH (grade 2 and above) or spontaneous intestinal perforation before an echocardiogram was undertaken were excluded. Short term (PH, IVH) and long-term (NEC, duration of ventilation and CLD) outcomes were noted. SPSS Statistics version 25 was used to analyse the data that was collected. Non-parametric test (Mann Whitney U) was used to compare the outcomes between the groups. A p value < 0.05 was considered statistically significant.

A total of 70 infants were enrolled into the study (34 infants in EA group and 36 infants in LS group). The median age of treatment in the EA group and LS group were 28 hours of age and 10 days of life respectively. 8 infants (22%) developed PH during their clinical course in the LS group when compared to two infants (5.8%) in the EA group. However, this was not statistically significant (p=0.053). There were no significant differences between the two groups with regards to IVH (p=0.51); further medical PDA treatment (p=0.147); PDA needing surgical ligation (p=0.881); NEC Bell’s stage 2 and above (p=0.792); NEC with intestinal perforation (0.561); duration of invasive ventilation (p=0.190); BPD (p=0.601) or death (p=0.400). However, infants in the EA group when compared to the infants in the LS group had significantly shorter duration of non-invasive ventilation (p=0.021).

Although there were no statistically significant differences between the two groups with regards to important outcomes especially PH and IVH, there were fewer incidences of pulmonary haemorrhage and shorter duration of non-invasive ventilation in the EA group. EA treatment is a promising approach but large multi-centre randomised controlled trials amongst high risk premature neonates are needed to evaluate the effectiveness of such an approach.

IMAGE / TAB: https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=33345b9240fa7dbd9b7ec70de7d4cb1c-MjAxOS0wNSM1Y2UyNjJyYmJzMDEx

IMAGE / TAB CAPTION: Results

COI: None declared
ID: 45

TITLE: THE RELATIONSHIP BETWEEN LEFT VENTRICULAR SYSTOLIC LONGITUDINAL DEFORMATION MEASUREMENTS AND PRELOAD IN PREMATURE INFANTS

AUTHORS: Neidin Bussmann1; Aisling Smith1; Alessia Cappelleri1; Naomi McCallion1,2; Orla Franklin3; Afif EL-Khuffash1,2.

AFFILIATIONS: 1 Department of Neonatology, The Rotunda Hospital, Dublin, Ireland.
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3 Department of Paediatric Cardiology, Our Lady’s Children’s Hospital Crumlin, Dublin, Ireland.

CONTENT:

Longitudinal deformation imaging including Strain and Strain rate (SR) is gaining interest in the neonatal field. Reference ranges in extremely low birthweight infants are emerging. However, the relationship between deformation parameters and loading conditions are still being debated. Strain is thought to be influenced by loading conditions and therefore is not reflective of intrinsic contractility. Systolic SR may be less load dependent offering a better reflection of intrinsic contractility. We aimed to assess the influence of preload on left ventricular (LV) global longitudinal strain (GLS) and SR.

We recruited three groups of premature infants < 29 weeks gestation who are enrolled in the PDA RCT (ISRCTN:13281214) over two time points (Day 2 & Day 8) to reflect different preload conditions. Group 1 (RCT-OPEN, n=22) are preterm infants with a large patent ductus arteriosus (PDA) that remains open over the two time points; Group 2 (RCT-CLOSED, n=10) are infants with a large PDA on Day 2 that closed on Day 8; and Group 3 (OBSERVED, n=11) are infants with a small or no PDA on both days. PDA diameter, left atrial to aortic root ratio (LA:Ao), LV GLS and SR (measured using speckle tracking echocardiography) were assessed on Days 2 and 8. Changes in those measurements were examined overtime.

Forty three infants with a mean ± SD gestation and birthweight of 26.7 ± 1.4 weeks and 919 ± 227 grams respectively were included. LA:Ao remained high in the RCT-OPEN Group (2.0 ± 0.3 vs. 2.1 ± 0.4, p=0.24) but decreased in the RCT-CLOSED Group (2.0 ± 0.4 vs. 1.6 ± 0.4, p=0.05) and remained low in the OBSERVED Group (1.7 ± 0.5 vs. 1.6 ± 0.6, p=0.3) over the study period (Figure). LV GLS remained high in the RCT-OPEN group, decreased in the RCT-CLOSED group, and remained low in the OBSERVED group (Figure). There were no differences in SR between the groups or over time (Figure).

Longitudinal strain is highly influenced by preload and mirrors changes in LV preload overtime. Therefore, it is not reflective of intrinsic contractility. There was no relationship between changes in preload in this cohort and longitudinal strain rate suggesting a lack of influence of preload. Strain rate is more likely to reflect intrinsic contractility in extremely premature infants.

IMAGE / TAB:
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IMAGE / TAB CAPTION: Figure: PDA diameter, LA:Ao, Strain and Strain Rate in the cohort over the 2 days. Values are presenting as means and Standard Error. *=p<0.05 within that time point.

COI: None Declared
ID: 46

TITLE: CIRCUMFERENTIAL AND RADIAL DEFORMATION ASSESSMENT IN PREMATURE INFANTS: READY FOR PRIMETIME?

AUTHORS: Neidin Bussmann1; Aisling Smith1; Alessia Cappelleri1; Naomi McCallion1,2; Orla Franklin3; Afif EL-Khuffash1,2.

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3 Department of Paediatric Cardiology, Our Lady’s Children’s Hospital Crumlin, Dublin, Ireland.

CONTENT:

The utility of longitudinal deformation measurements (longitudinal strain and strain rate) in in premature infants is becoming well established. However, more studies are needed to demonstrate feasibility and reproducibility of left ventricular (LV) circumferential (circ) and radial strain and strain rate (SR) in this population. We aimed to assess feasibility and reproducibility of circ and radial deformation measurements in preterm infants < 29 weeks gestation, and study the impact of a haemodynamically significant patent ductus arteriosus (hsPDA) on those measurements.

We recruited premature infants < 29 weeks gestation who are enrolled in the PDA RCT (ISRCTN:13281214) over two time points (Day 2 & Day 8). The cohort was divided on the basis of the presence of a hsPDA on Day 8 (defined using a previously published PDA risk score). Circ and radial strain, systolic strain rate (SRs), early diastolic strain rate (SRe) and late diastolic strain rate (SRa) were measured on Days 2 and 8 using speckle tracking echocardiography. Intra- and inter-rater reproducibility were determined using Bland Altman analysis, intraclass correlation coefficient (ICC) and the coefficient of variation (COV). The impact of a hsPDA on all those measurements was also assessed.

40 infants with a mean ± SD gestation and birthweight of 26.9 ± 1.1 weeks and 985 ± 211 grams respectively were recruited. Imaging and offline analysis was possible in all scans. Circ parameters demonstrated excellent intra- and interrater reproducibility with minimal bias, an ICC range between 0.89 – 0.99 (all p<0.001) and a COV between 4 – 13%. Radial parameters demonstrated acceptable intra- and interrater reproducibility with minimal bias, an ICC range between 0.73 – 0.96 (all p<0.001) and a COV between 14 – 27%. Day 2 and Day 8 reference values are presented in the Table. On Day 8, infants with a hsPDA (n=21, 53%) demonstrated higher Radial strain, SRs and SRe but not SRa (Figure). There were no differences in circ parameters between those with and without hsPDA at either time point.

Measurements of circumferential and radial deformation in premature infants are feasible and reproducible. A haemodynamically significant PDA increases radial (but not circumferential) systolic strain, systolic SR and early diastolic SR. This novel information suggests that increased LV preload secondary to a hsPDA may increase intrinsic contractility in the radial but not circumferential plane.

IMAGE / TAB:
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IMAGE / TAB CAPTION:

COI: None declared
ID: 49

**TITLE:** Examining the association of right ventricular dysfunction with moderate to severe bronchopulmonary dysplasia in preterm infants

**AUTHORS:** Wisam Muhsen 1

**AFFILIATIONS:** Neonatal Unit, University Hospital Plymouth, Plymouth, UK

**CONTENT:**

Over the last three-and-a-half decades, many advances have been made in the care of preterm infants. Some of the most important developments have been in hemodynamic management, including the use of functional echocardiography exams. The Right Ventricle (RV) functional assessment has enabled investigators to track cardiac maturational changes in the first few months of life of Very and Extremely Preterm Infants (VEPIs). The present review investigates whether early RV dysfunction can be used to identify preterm infants with early Significant Bronchopulmonary Dysplasia (sBPD), that is, moderate to severe BPD.

A systematic electronic search of several bibliographic databases (Medline, PubMed, CINAHL, Web of Science, Embase, Google Scholar, Cochrane Library and DelphiS indexes) was performed, and e-journals were examined through ProQuest. Medical subject headings were applied. Out of the 23 initially identified studies, only 6 met the eligibility criteria. The other 17 were rejected because they did not examine any subgroups of BPD (4), performed ECHO outside this review’s target age range (4), had a different focus (3), were designed as case-series or overly small case-control studies (2), only studied the link between PH & BPD (1), investigated new ECHO methods (1) or consisted of a device review (1) or an animal study (1).

Each study indicated that one or more of the measured ECHO parameters was or were negatively affected by sBPD. For example, S1 detected a reduction of the RV-Fraction Area Change (RV-FAC) among the VEPIs affected with sBPD. S5 showed that the RV-Myocardial Performance (RV-MPI) via the Pulsed-Wave Doppler (PWD) was higher in earlier development stages among VEPIs (i.e., when the infants were four weeks old). However, this result was only statistically significant when measured on the 28th DOL. In contrast, S2–4 found significant increases in RV-MPI but via Tissue Doppler imaging (TDI) rather than PWD; these studies also measured it at a later age (35-37 weeks of PMA). Meanwhile, S6 examined the strain rate of the RV using the speckle tracking method and found that the regional peak systolic strain in the free wall middle segment (1/6 total segments) was lower in patients with sBPD.

This literature review serves as an impetus for further research into the early detection of progressing sBPD by using RV functional assessments in the first 28 DOL. Paediatric cardiology support and the utilization of a wide combination of RV functional ECHO tests by trained clinicians are recommended.

**IMAGE / TAB:**
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=3a2a629658dcff278572e46d908db15a-MjAxOS0wNSM1Y2UyNjY2YmJYWM4

**IMAGE / TAB CAPTION:** Reviewed Studies Echo details and results

**COI:** None declared.
ID: 50

TITLE: ACTIVE MANAGEMENT OF INBORN VERSUS OUTBORN LIVEBIRTHS AT 22-24 WEEKS' GESTATION

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CONTENT:

Management of periviable births at 22-24 weeks' gestation requires important clinical decisions that affect survival chances for the infant, including antenatal corticosteroid administration, in-utero transfer to a tertiary centre, mode of delivery, resuscitation at birth and provision of neonatal intensive care. There are wide variations in approaches to 'active management' of periviable births internationally. Our aim was to report rates of active management of births at 22-24 weeks' gestation in Victoria, Australia, comparing rates in tertiary centre (inborn) births with non-tertiary (outborn) births. We also aimed to report temporal changes in rates of active management.

We conducted a population-based cohort study of all 22-24 weeks' gestation births in Victoria, Australia from 1/1/2009 to 31/12/2016 (8 years). Perinatal data and infant mortality data were obtained from the Department of Health and Human Services, Victoria. 'Active management' was defined as delivery room resuscitation, comprising any of positive pressure ventilation, CPAP, intubation, external chest compressions and/or administration of adrenaline and/or volume expanders. Active management rates comparing inborn with outborn infants were analysed by logistic regression, adjusted for gestational age, birth weight and sex. Adjusted odds ratios (aOR), 95% confidence intervals (CI) and p-values for each intervention were calculated. Temporal changes were analysed by logistic regression.

In 2009-2016, there were 1,266 births recorded at 22-24 weeks' gestation: 705 (56%) were liveborn. Livebirth rates were 42%, 54% and 68% at 22, 23, and 24 weeks' gestation respectively. Overall, 70% (n=492) of livebirths occurred in a tertiary centre. Active management rates increased with increasing gestational age: 10/169 (6%) at 22 weeks, 94/224 (42%) at 23 weeks and 277/312 (89%) at 24 weeks. Inborn infants were more likely to be resuscitated compared with outborn infants: 64% versus 31%. A total of 381 (54%) infants were resuscitated and of these, 356 (93%) survived to nursery admission. At one year, 231 (61%) actively managed infants were alive: 67% (209/314) inborn versus 33% (22/66) outborn infants (aOR 1.94, 95% CI 1.10, 3.39, p=0.02). Survival rates were 0% at 22 weeks, 52% at 23 weeks and 66% at 24 weeks. There were no significant changes in active management rates over time.

Active management is rare at 22 weeks' gestation in Victoria, but by 24 weeks' gestation, nearly 90% of livebirths are actively managed. Infants born in tertiary perinatal centres are significantly more likely to be offered active management, especially at 23 weeks' gestation. As a result, survival rates at one year are higher in inborn infants. Further research is required to identify barriers to active management of outborn periviable infants.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 51
TITLE: MALPOSITIONED UMBILICAL VENOUS CATHETERS AND PERIPHERALLY INSERTED CENTRAL LINES AS INCIDENTAL FINDINGS ON NEONATOLOGIST PERFORMED ECHOCARDIOGRAPHY IN PRETERM INFANTS
AUTHORS: María Carmen Bravo, Rebeca Sánchez, Ana Isabel Blanco, Adelina Pellicer.
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CONTENT:

Umbilical venous catheters (UVC) and peripherally inserted central lines (PICL) are routinely used in the NICU. X-ray confirmation of the catheter tip in the vena cava next to the cavo-atrial junction is considered optimal and carries the lowest rate of complications. We aim to analyse the incidence of incidental malposition of UVC and PICL by routine Neonatologist Performed Echocardiography (NPE).

Retrospective analysis on a cohort of infants recruited at our institution for a multicenter randomized trial comparing ibuprofen bolus vs ibuprofen continuous infusion for the treatment of PDA (EudraCT:2016-002974-11). Serial NPE, as per study protocol, was conducted. Catheter insertion was always followed by x-ray to confirm adequacy of tip position. The incidence of malposition of the UVC/PICL according to the PDA screening scans was assessed.

During 19 months, 61 infants [mean GA 26.4 (2.1) weeks; mean BW 883 (298) gr] enrolled in the study underwent screening NPE at a mean postnatal age of 77 (64) hours. Among those with UVC or PICL (56 infants), catheter malposition was found to be more prevalent in the UVC group (18/36) than in the PICL group (8/20), p=0.04. The most common localisation was the left atrium (26% of malposition). Prevalence of catheter tip malposition was not associated with GA or BW.

Malposition of central venous catheters is common in the preterm infant, particularly in UVC. Echocardiography, as compare to x-ray, better defines the catheter tip therefore reducing the likelihood of catheter-related complications.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: The authors acknowledge the Instituto de Salud Carlos III (PI16/00644 grant), Mutua Madrileña Foundation (AP163272016 grant) and the SAMID (Salud Materno Infantil y Desarrollo) Network [RETICS funded by the PN 2018-2011 (Spain), ISCIII- Sub-Directorate General for Research Assessment and Promotion and the European Regional Development Fund (FEDER), ref. RD12/0026], for their scientific support.
TITLE: Dose-response investigation on poractant alfa nebulization treatment during nCPAP ventilation in spontaneously-breathing surfactant-deficient newborn piglets

AUTHORS: Rey-Santano C1, Mielgo V1, Gomez MA1, Salomone F2, Bianco F2, Ricci F2, Loureiro B3

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CONTENT:

The current clinical treatment of neonate with respiratory distress syndrome (RDS) includes endotracheal intubation and rapid intratracheal instillation of exogenous surfactant. Nebulization of surfactant offers an attractive alternative. The aim of this study was to test the nebulization as noninvasive method of administering surfactant, and to determine the optimal dose for the treatment of neonatal RDS.

Thirty-six spontaneously breathing newborn piglets with surfactant-deficiency were assigned to one of six treatment groups (n=6/group): poractant alfa (100, 200, 400 or 600 mg/kg) nebulized via a customized eFlow Neos vibrating-membrane nebulizer system, bolus administration using InSurE technique (200 mg/kg), or no surfactant treatment during nCPAP ventilation (180 min). Pulmonary (gas exchange, lung mechanics), hemodynamic (arterial blood pressure, heart rate) and cerebral effects (carotid blood flow) were evaluated. Lung and brain histological analysis were also performed.

After bronchoalveolar lavages, newborn piglets developed mild respiratory distress syndrome (FiO2: 1, pH: 70 mmHg, PaO2<70 mmHg, Cdyn<0.5 ml/cmH2O/kg). Rapid improvement in pulmonary status was observed in the InSurE group, while a dose-related effect was observed in nebulized groups. Nebulized poractant alfa was effective at a dose higher than 100 mg/kg, showing pulmonary, hemodynamic and cerebral behavior similar to the InSurE group (and significantly better than no surfactant treatment group), but showing lower lung injury score.

In newborn piglets with mild RDS, our results indicate that the administration of nebulized poractant alfa using a customized eFlow Neos nebulizer system is an effective and safe way of non-invasive surfactant administration technique. Supported by: ISCIII-PI18/00166-FEDER/FSE, IT583-13 and Chiesi-Farmaceutici S.p.A.

Supported by: ISCIII-PI14/00166-FEDER/FSE, IT583-13 and Chiesi-Farmaceutici S.p.A.
ID: 71
TITLE: ENDOCAN, A POTENTIAL NEW MARKER FOR NEONATAL INFECTION
AUTHORS: Gabriela I. Zonda1,2, Radu Zonda3, Andrei T. Cernoma24, Andreea L. Avasiloaiei1,2, Bogdan D. Grigoriu4, Luminița Păduraru1,2
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2Regional Centre of Neonatal Intensive Care Unit, “Cuza-Vodă” Hospital of Obstetrics and Gynecology, Iași, Romania
3"Petru Poni” Institute of Macromolecular Chemistry, Iași, Romania
4Division of Pneumology, Department of Medical Specialties III, “Grigore T. Popa” University of Medicine and Pharmacy, Iași, Romania
CONTENT:

Early onset sepsis is a major cause of mortality in neonates and the diagnosis is challenging, as accurate biochemical markers are lacking and culture results usually become available after 24 hours. Endocan is one of the specific endothelial mediators involved in the inflammatory response. Its role in the diagnosis of sepsis has been proven in adult patients and studied in neonates with late onset sepsis. The purpose of our study was to assess the potential use of endocan as a biomarker for early onset neonatal sepsis.

We conducted a prospective study that included 24 term and 35 preterm newborns admitted within 24 hours since birth in the Neonatology Intensive Care Unit of a level III center based on the presence of risk factors and clinical signs of sepsis. The newborns were split into 2 groups: group I, septic (32 newborns with confirmed infection by positive blood culture, and probable infection, with negative blood cultures but with clinical and laboratory evidence of sepsis) and group II, non-septic (27 neonates assessed for clinically suspected sepsis at admission that was not confirmed by laboratory findings). The serum concentration of endocan was determined by a sandwich-type enzyme-linked immunosorbent assay using anti-Endocan monoclonal antibodies; values are expressed in ng/mL.

Mean serum concentration (ng/mL) of endocan was significantly higher at admission in group I compared to group II (2.43 +/- 0.95 vs. 1.77 +/- 0.57, p = 0.004 (95%CI of mean difference = 0.22-1.1)). In both groups mean endocan levels continued to rise on day 3, with higher concentration in septic patients, but the difference was no longer statistically significant. On day 7 endocan level was lower compared to day 3 in both groups, with a statistically significant decrease only in septic newborns (2.04 vs. 2.92, p=0.01). ROC curve analysis for the utility of endocan in differentiating between septic and non-septic newborns returned an area under the curve of 0.73 (p=0.004, 95% CI = 0.597 - 0.871). An optimum threshold value of 1.62 ng/mL (based on max Youden index) has a sensitivity of 88% and a specificity of 50%.

The variation pattern of serum endocan levels in neonates with suspected EOS suggests that this biomarker could probably be integrated with other inflammatory markers and clinical elements in order to develop a composite diagnostic tool. Further studies on a larger number of cases are needed in order to establish the diagnostic role of this molecule in practice.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: This results are a part of a larger study funded by grant 30885/30/12/2014 awarded by "Grigore T. Popa" University of Medicine and Pharmacy Iasi to Dr. Gabriela Ildiko Zonda, accepted for publication in Journal of Infections in Developing Countries.
ID: 74

**TITLE:** The population of circulating extracellular vesicles dramatically alters after very premature delivery- a previously unrecognised postnatal adaptation process?

**AUTHORS:** Daniel O’Reilly1,6, Karl Egan1,2, Oscar Burke1, Angharad Griffiths3, Elaine Neary3, Alfonso Blanco1, Paulina Szkłanna1, Patricia Maguire1, Naomi McCallion3,5, Fionnuala Ni Áinle1,2,4

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**CONTENT:**

Following birth, the transition from intrauterine to extraterine life is associated with major physiological changes, including the clearance of lung liquid and the closure of the ductus arteriosus. Many pathological processes linked with mortality and serious morbidity in preterm infants start at this time. Extracellular vesicles (EVs) are small subcellular particles released by all known cell types and readily detectable in large numbers in all biological fluids. EVs are heterogeneous in size and origin, consisting of exosomes (endosomal origin, 30-150 nm), microvesicles (plasma membrane-derived, 50-1000nm), and apoptotic bodies (500-2000 nm). They are linked with a wide variety of processes including coagulation and cell-cell communication, and it has been hypothesized that they may affect lung disease and other preterm morbidities. It is however unknown whether circulating EVs can change during this extraterine transition period.

Preterm neonates were recruited through the Department of Neonatology at the Rotunda Hospital, Dublin, Ireland. Written informed consent was obtained from the parents of all participants. Blood collection was performed during routine phlebotomy. Platelet free plasma was prepared by double centrifugation at 3000g for 10 minutes. 15x Day 1 of life and 14x days 3 of life plasma samples were available from preterm neonates, 8 of which were matched Day 1 (D1) and Day 3 (D3) samples. EVs were quantified and characterised by both nanoparticle tracking analysis (NTA) and flow cytometry.

NTA and Flow Cytometry were utilised to demonstrate significant difference in EV populations between D1 and D3 of life with differences in size and concentration with EVs in both 0-200nm range (D1; 4.0 ± 2.5 x 107/µl vs. D3; 7.2 ± 4.4 x 107/µl; p = 0.03) and the 100-900nm range (D1; 1.1 ± 0.3 X 106/µl vs. D3; 4.2 ± 3.2 x 106/µl, p = 0.0009) becoming significantly different. D3 samples were characterised by a unique population of homogenous particles 100-300nm in size with unique side scatter properties suggesting a potential change in membrane or internal composition of EVs during the transition period. We assessed the levels of platelet EVs (CD41+/Annexin V+), a marker of platelet activation. The percentage of CD41+/Annexin V+ EVs significantly decreased from D1 to D3 (D1; 6.5 ± 4.9 % vs. D3; 2.4 ± 1.9 %, p = 0.007), suggestive of a platelet activation event during transition.

In this study, we clearly demonstrate that the extraterine transition period is characterised by major changes in plasma EVs. These changes include an increase in the levels of EVs, a change in the composition of EVs, and a reduction in the percentage of platelet-derived EVs. The physiological or pathophysiological causes of the changes need to be further elucidated.

**COI:** None Declared
ID: 79
TITLE: DIAGNOSTIC VALUE OF CYTOMEGALOVIRUS IGM ANTIBODY IN PCR-CONFIRMED CONGENITAL CYTOMEGALOVIRUS INFECTION
AUTHORS: Shohei Ohyama 1; Kazumichi Fujioka 1; Sachiyu Fukushima 1; Shinya Abe 1; Mariko Ashina 1; Toshihiko Ikuta 1; Kosuke Nishida 1; Hisayuki Matsumoto 2; Yuji Nakamachi 2; Kenji Tanimura 3; Hideto Yamada 3; Kazumoto Iijima 1
AFFILIATIONS: 1 Department of Pediatrics, Kobe University Graduate School of Medicine, Kobe, Japan
2 Department of Clinical Laboratory, Kobe University Hospital, Kobe, Japan
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CONTENT:

Cytomegalovirus (CMV) is a virus that causes mother-to-child infections, and congenital CMV infection (CCMVI) can result in non-hereditary hearing impairment and severe developmental disorders. In recent years, detection of CMV DNA in urine within 3 weeks after birth has become the standard for diagnosis of CCMVI; however, PCR technique is not comprehensively available in general obstetric clinics and is therefore not clinically convenient. No previous studies have reported the efficacy of CMV-specific IgM (CMV IgM) and CMV-specific IgG (CMV IgG) in the diagnosis of CCMVI, using infants with a PCR-confirmed CCMVI cases and non-CCMVI controls.

We examined CMV-specific antibody, and urine viral load was measured using quantitative real-time PCR (qRT-PCR) in 177 neonates suspected of CCMVI during 2014–2018. Diagnosis of CCMVI was confirmed by positive qRT-PCR results for urine taken within 3 weeks after birth. A CMV IgM-positive result was defined as an antibody index value ≥0.8, and a CMV IgG-positive result was defined as an EIA value ≥2.0. Based on the presence or absence of CCMVI and the timing of antibody testing, we classified participants into the CCMVI-standard group (n=20, first antibody test ≤2 weeks), CCMVI-delayed group (n=14, first test >2 weeks), and non-CCMVI group (n=143, first test ≤2 weeks). We then compared the positive rates of CMV IgM and IgG antibody among the groups.

The gestational age of infants in the CCMVI-standard group [37 (24–40) weeks] was significantly lower than those in the CCMVI-delayed group [39 (32–40) weeks, p=0.04] and those in the non-CCMVI group [38 (28–42) weeks, p<0.01]. The incidence of symptomatic CCMVI was significantly higher in the CCMVI-standard group than in the CCMVI-delayed group (70% versus 14%, p=0.02). CMV IgM-positive rates were 17/20 (85%) in the CCMVI-standard, 7/14 (50%) in the CCMVI-delayed, and 1/143 (0.7%) in the non-CCMVI group. Positive CMV IgG rates were 20/20 (100%) in the CCMVI-standard, 14/14 (100%) in the CCMVI-delayed, and 142/143 (99.3%) in the non-CCMVI group. CMV IgM-positive rates were significantly higher in the CCMVI-standard than in the CCMVI-delayed (85% vs. 50%, p=0.03) and non-CCMVI groups (85% vs. 0.7%, p<0.001). There was no difference in CMV IgG-positive rates among groups.

In conclusion, the sensitivity of CMV IgM was sufficient for the diagnosis of CCMVI in suspicious cases; however, a combination of other laboratory tests might be required for exclusion diagnosis of CCMVI. To maintain accurate diagnostic value, CMV IgM testing should be performed within 2 weeks after birth.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 81

TITLE: CARDIORESPIRATORY EVENTS IN PRETERM INFANTS IN NICU: EFFECTS OF SLEEP POSITION, STATE AND AGE

AUTHORS: Kelsee L Shepherd 1; Stephanie R Yiallourou 1,2; Alexandria Odoi 1; Emma Yeomans 3; Rosemary SC Horne 1; Flora Y Wong 1,3

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CONTENT:

Preterm infants in NICU are often placed prone to improve respiratory function. Clinical guidelines recommend preterm infants are slept supine from 32 weeks of postmenstrual age (PMA), regardless of gestational age (GA) at birth. However, respiratory dysfunction is related to GA and chronological age after birth rather than PMA. Respiratory function is also affected by the sleep state. Currently, the effects of the prone position on cardiorespiratory function in preterm infants in relation to age and sleep states remain unknown. We assessed the effects of position and sleep state on bradycardias, apnoeas and desaturations in preterm infants longitudinally, in relation to GA at birth and PMA.

Twenty-three extremely (24-28 weeks’ GA) and 33 very preterm (29-34 weeks’ GA) infants were studied weekly from birth until discharge, in prone and supine positions, and in quiet sleep (QS) and active sleep (AS). Cardiorespiratory events were defined as episodes of bradycardia (heart rate≤100 bpm), apnoea (pause in respiratory rate ≥10s), desaturation (oxygen saturation ≤80%) and percentages of time spent in each sleep states (QS% and AS%) were analysed. Frequency, duration and associated physiological data of the cardiorespiratory events, and %QS and %AS were analysed using a linear mixed model approach.

In extremely preterm, the prone position infants reduced the frequency of bradycardias and desaturations, and desaturation duration. The %QS was higher in prone compared to supine position. In contrast, in very preterm infants, prone positioning only reduced the frequency of desaturations. In the prone position, the very preterm infants had higher %QS and lower %AS compared to the supine position. The position-related effects in both groups of infants were not related to PMA or chronological age. QS reduced bradycardias and desaturations in both extremely and very preterm infants, but the effects are more marked in the very preterm infants. In the extremely preterm infants only, cardiorespiratory events reduced with increasing PMA rather than chronological age.

Prone-position-related benefits in cardiorespiratory function are dependent on GA but not PMA. Cardiorespiratory stability was improved by the prone position only in extremely preterm infants, with minimal effects in very preterm infants from PMA of 30 weeks onwards. The QS state has a more marked effect than the prone position in very preterm infants. This evidence should be considered in future recommendations for preterm infant positioning.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 84

TITLE: DO BILIRUBIN/ALBUMIN (B/A) RATIOS CORRELATE WITH UNBOUND BILIRUBIN LEVELS IN PRETERM INFANTS?

AUTHORS: Shinya Abe 1; Kazumichi Fujioka 1; Sadayuki Nagai 1; Ruka Nakasone 1; Shutaro Suga 1; Mariko Ashina 1; Sachiyu Fukushima 1; Shohei Ohyama 1; Toshihiko Ikuta 1; Kousuke Nishida 1; Hajime Nakamura 1; Kazumoto Iijima 1

AFFILIATIONS: 1 Department of Pediatrics, Kobe University Graduate School of Medicine, Kobe, Japan

CONTENT:

Unbound bilirubin (UB), which is bilirubin not bound to albumin, can pass the blood-brain barrier and has been considered as a sensitive marker for bilirubin encephalopathy. However, UB levels is not used clinically to assess an infant’s risk for developing bilirubin neurotoxicity in areas outside of Japan. Assessment is usually done using the ratio of total bilirubin/albumin (B/A) levels, which has been shown to theoretically correlate with UB. We have previously reported a strong correlation between the B/A ratio and UB concentrations in serum of newborns ≥35 wks’ gestation (Sato Y, et al., $y = 1.35x - 0.089$, $R^2= 0.88$, $p < 0.0001$) ; however, in preterm infants, the binding capacity of albumin to bilirubin is weak, and thus the usefulness of B/A ratio is unclear. Therefore, in this study, we correlated B/A ratios and UB concentrations in newborns <35 wks’ gestation.

Serum UB concentration was measured using the glucose oxidase–peroxidase method using a UB A1 Analyzer (Arrows Co, Osaka, Japan). Serum bilirubin and albumin concentrations were measured spectrophotometrically. Following our treatment criteria, infants received phototherapy based on threshold levels of TB or UB stratified by post-conceptional age (see Table 1). We excluded the data obtained from the samples received phototherapy. B/A ratios were calculated and correlates with serum UB levels. The subjects were then stratified by gestational age: A (22-27), B (28-29), C (30-31), and D (32-34 wks), and B/A ratios correlated with UB concentrations. Then, the cutoff value of the B/A ratio to serum UB levels that needs treatment of each group were determined by ROC curve analysis.

1221 serum samples were obtained from 381 newborns <35 wks’ gestation [30.8±3.2 (median 32, range 22-34) weeks, birthweight 1,558±589 (median 1604, range 284-2,962) g, Male 205 (53%)], who were admitted to Kobe University Hospital from 2014 to 2018. B/A ratio significantly correlated with serum UB levels in infants <35 wks’ gestation ($y = 1.80 x-0.14$, $R^2 = 0.88$, n=1221). When stratified by gestational age, the correlation remained (Table. 2). The cutoff value of the B/A ratio to serum UB levels that needs treatment of each group is 0.257 (sensitivity 100%, specificity 91%) for UB levels of 0.4 in group A, 0.323 (93%, 93%) for UB levels of 0.5 in group B, 0.359 (92%, 90%) for UB levels of 0.6 in group C, and 0.414 (90%, 85%) for UB levels of 0.7 in group D (Table. 3).

Even in preterm infants <35 wks’ gestation, the B/A ratio showed a strong positive correlation with serum UB concentrations. Therefore, we conclude that B/A ratios can be used as an index of UB values with a high sensitivity and specificity, even in preterm infants <28 wks’ gestation.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=444fe2a3c215fdfe41c72af170c31bd-MjAoS0wNSM1Y2UyNjY2YmM2YZil

IMAGE / TAB CAPTION:

COI: None declared
ID: 93

TITLE: DEFERRED CONSENT FOR THE ENROLMENT OF NEONATES IN DELIVERY ROOM STUDIES: THE PROVIDERS’ PERSPECTIVE

AUTHORS: M.C. den Boer 1,2; M. Houtlosser 2; E.E. Foglia 3; E. Lopriore 1; M.C. de Vries 2; D.P. Engberts 2; A.B. te Pas 1

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CONTENT:

Several studies reported usage of a deferred consent approach for delivery room (DR) studies. Using a deferred consent approach can speed up patient accrual and reduce selection bias. However, as jurisdiction and guidance for deferred consent varies, actual experience with deferred consent for DR studies is limited and in-depth understanding of providers’ views on deferred consent for DR studies is lacking. We conducted interviews with providers of Neonatal Intensive Care Units (NICUs) that participate in the same studies, but differ in their consent approaches. With this study, we aim to gain insight in providers’ perceptions of deferred consent for DR studies in actual scenarios.

We conducted semi-structured interviews with 46 NICU staff members of the Leiden University Medical Center (the Netherlands) and the Hospital of the University of Pennsylvania (United States of America). At the time interviews were conducted, both NICUs conducted the same DR studies, but differed in their consent approaches. Interviews were audio recorded, transcribed and analysed using the qualitative data analysis software Atlas.ti 7.0.

Although providers reported to regard the prospective consent approach as the most preferable consent approach, they acknowledged that a deferred consent approach is needed for high quality DR management. However, providers reported concerns about parental autonomy, approaching parents for consent, and ethical review of study protocols that include a deferred consent approach. Providers furthermore differed in perceived appropriateness of a deferred consent approach for the studies that were being conducted at their NICUs. Providers with first-hand experience with deferred consent reported positive experiences that they attributed to appropriate communication and timing of approaching parents for consent.

Insight in providers’ perceptions of deferred consent for DR studies in actual scenarios suggests that a deferred consent approach is considered acceptable, but that actual usage of the approach for DR studies can be improved upon.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared.
ID: 97

TITLE: TIDAL BREATHING PARAMETERS IN INFANTS WITH TRANSIENT TACHYPNEA OF THE NEWBORN: IS STRUCTURED LIGHT PLETHYSMOGRAPHY FEASIBLE IN NICU?

AUTHORS: Evrim Alyamaç Dizdar 1; Davut Bozkaya 2; Fatma Nur Sari 3; Esra Beşer 4; Cüneyt Tayman 5; Şerife Suna Oğuz 6

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CONTENT:

Measurement of lung function helps in diagnosis, monitoring and treatment of respiratory diseases but conventional techniques such as spirometry are not possible in newborn babies. Structured Light Plethysmography (SLP) is a novel, non-contact, bed side respiratory assesment technique. It provides non-invasive tidal breathing measurement in patients difficult to cooperate such as newborns. Transient tachypnea of the newborn (TTN) is a self-limited disease commonly seen in late preterm infants born at gestational age between 34 and 37 weeks. Term and postterm babies are also at risk for TTN. The onset of TTN usually occurs within two hours after delivery. Tachypnea, nasal flaring, mild intercostal and subcostal retractions and expiratory grunting are the most prominent features.

In this study we aimed to measure tidal breathing parameters by SLP in infants with transient tachypnea of newborns (TTN) and compare with controls.

In this observational study, infants ≥34 gestational weeks with the diagnosis of TTN requiring NIV support and controls were recruited. The diagnosis of TTN was confirmed by clinical and laboratory data. Infants were excluded if they had major congenital anomalies, meconium aspiration, sepsis, perinatal asphyxia and RDS. Five minutes of tidal breathing was recorded using SLP (Thora-3Di, PneumaCare Ltd) in each infant. Various tidal breathing parameters including timing indices (RR, tI, tE, tTot, tI/tE and tI/tTot) flow-based parameters (tPTEF/tE, tPTIF/tI, IE50) and regional parameters (HTA, TAA, rCT) were obtained from SLP data.

Totally 87 infants underwent SLP measurements in the study. Evaluable recordings from 53 infants with TTN and 28 controls were analyzed after exclusions. Characteristics of the study infants were shown in Table 1. Among the timing indices RR was significantly higher in infants with TTN when compared with controls while tI, tE and tTot were significantly lower (p=0.017, p=0.024, p=0.013 and p=0.017 respectively). Median IE50 levels in infants with TTN were significantly lower than controls (1.08 vs 1.29, p=0.015). Regional contribution of thorax, right and left hemithorax to total thoracoabdominal displacement in percentage were significantly higher in infants with TTN compared to controls (p=0.006, p=0.003 and p=0.013, respectively)

SLP is feasible to obtain measures of tidal breathing parameters even in newborns and it can give information about the respiratory parameters of infants with TTN.

IMAGE / TAB:
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IMAGE / TAB CAPTION:

COI: None declared
ID: 114

TITLE: DOES PREGNANCY DURATION OR HOLDER PASTEURISATION INFLUENCE MACRONUTRIENTS OR BIOACTIVE PROTEIN CONTENT IN HUMAN MILK?

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2 - Children’s Hospital, Affiliate of Vilnius University Hospital Santaros Klinikos

CONTENT:

Donor human milk is the second best food for sick newborns when their mothers’ milk is unavailable. Holder pasteurisation (milk heating for 30 minutes at 62.5 ºC) is the most commonly used method in donor milk banks for microbiological safety of the donated human milk. Holder pasteurisation not only destroys microorganisms, but it can also change human milk’s nutritional and biological properties. The aim of our study was to evaluate the influence of Holder pasteurisation on macronutrients, energy, or bioactive protein content in human milk. Comparison of macronutrients and bioactive protein concentration in preterm and term milk was the secondary aim of our study.

The study was conducted at the Neonatal Centre of Vilnius University Children’s Hospital in the period of October 2017 – July 2018. Human milk samples from 42 women (22 preterm and 20 term infants’ mothers) between 14 – 16 days after childbirth were collected. Macronutrients and bioactive proteins (lactoferrin, lysozyme) concentrations from each sample were evaluated twice – in fresh milk and after milk being kept frozen at -40 ºC for up to 10 months, then thawed and pasteurised. The Miris human milk analyser (mid-infrared spectrophotometry method) for macronutrients and energy evaluation in human milk samples was used, and an immune-enzymatic ELISA assay – for estimation of lysozyme and lactoferrin concentrations in human milk. Statistical data analysis was performed using the R program.

Forty-two paired human milk samples were analysed for macronutrients (protein, fat, and carbohydrate), energy, and bioactive protein (lysozyme and lactoferrin) content. Human milk freezing and pasteurisation did not influence macronutrients and energy content in human milk (p > 0.05). Concentrations of lactoferrin and lysozyme were significantly lower in thawed pasteurised milk compared with fresh milk (p < 0.05). The average loss of lysozyme and lactoferrin was 35% and > 99%, respectively after pasteurisation (figure 1). The samples from preterm and term infants’ mothers did not differ significantly according to the infants’ gender, birth-giving method, mothers’ age, or ethnicity. There were no statistically significant differences in any macronutrient, energy content, or lysozyme and lactoferrin concentrations in preterm and term fresh human milk samples (p > 0.05).

No significant differences in macronutrients, energy, lysozyme or lactoferrin content in preterm and term milk were detected. Freezing and Holder pasteurisation caused a significant loss of bioactive proteins but did not change the macronutrients content in human milk. It is important to look for new methods of milk processing in order to minimise loss of bioactive components of human milk.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=b272226b67fc5123262448a6daa5d2d4-MjAxOS0wNSM1Y2UyNjJy2YmQxYWE0

IMAGE / TAB CAPTION: Figure 1. Holder pasteurisation influence on bioactive protein content in human milk

COI: None declared
ABSTRACT BOOK
POSTER PRESENTATIONS

ID: 117
TITLE: IMPACT OF BODY POSITIONING ON LUNG DEPOSITION OF NEBULIZED PORACTANT ALFA DELIVERED BY A CUSTOMIZED EFLOW NEOs INVESTIGATIONAL VIBRATING-MEMBRANE NEBULIZER SYSTEM
AUTHORS: Anders Nord 1; Rikard Linner 1; Fabrizio Salomone 2; Federico Bianco 2; Francesca Ricci 2; Xabi Murgia 3; Martin Schlun 4; Doris Cunha-Goncalves 1; Valeria Perez-de-Sa 1
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CONTENT:
Nebulization of poractant alfa with a customized eFlow Neos investigational vibrating-membrane nebulizer system achieves relatively high lung deposition under experimental preclinical neonatal conditions. We investigated whether body positioning during poractant alfa nebulization would influence the intrapulmonary deposition and distribution of surfactant in spontaneously-breathing healthy piglets.

Twenty-four full-term one-day-old piglets (1.3-2.2 kg) were sedated, supported with nasal continuous positive airway pressure (nCPAP), and assigned to one of four experimental groups: 1) lateral decubitus with right side up, 2) lateral decubitus with left side up, 3) prone position, and 4) supine position (n=6 per group). While on nCPAP, all animals received technetium-99m-labeled surfactant, poractant alfa 200 mg/kg, via continuous nebulization. Surfactant deposition was measured from scintigraphic images obtained in the gamma-camera.

All groups compared, the mean total lung surfactant deposition was significantly higher in the prone position group (32.4 ± 7.7%, p=0.03). In the prone and supine position groups, surfactant deposition was higher in the right lung. When surfactant nebulization was performed with the animals in the lateral decubitus position, most of the surfactant was found in the dependent lung, regardless of which side the piglet laid on. (Table 1)

The mean lung deposition was relatively high irrespective of the animal position during nebulization. We also observed a significantly greater surfactant deposition in the lungs of piglets lying in the prone position. The observation of a higher deposition in the dependent lung while on lateral decubitus suggests that deposition was also influenced by gravity.

COI: The study was funded by a grant from Chiesi Farmaceutici SpA
Fabrizio Salomone, Federico Bianco and Francesca Ricci are employees of Chiesi Farmaceutici
Martin Schlun is employed by Pari Pharma
Xabi Murgia is a consultant for Chiesi
Valeria Perez de Sa, Anders Nord, Doris Cunha Goncalves, Rikard Linner, "None declared"

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=8d54826223c63dba3e088a3afa0cb90a-MjJaxOS0wNSM1Y2UyNjY2YmQzMjA3

IMAGE / TAB CAPTION: Table 1 - Lung deposition of nebulized surfactant
ID: 120

TITLE: DOES DEXTROSE GEL IMPROVE BREASTFEEDING IN NEONATES AT RISK OF HYPOGLYCAEMIA?

AUTHORS: Georgina Farmer 1; Hannah Steedman 2; Madhuvanthi Dhamodharan; 3 Aakarshan Mehta ; 4 Alok Sharma 5

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CONTENT:

The British Association of Perinatal Medicine introduced national guidance regarding management of neonatal hypoglycaemia (NH) in 2017. In addition to proposing higher thresholds for treating NH they also endorsed use of Dextrose gel (DG) as a treatment option. The guidance recommends the use of DG when blood glucose level is 1.0-1.9mmol/L but in keeping with the Waikato 'Sugar Babies' trial' we retained a treatment threshold of 2.6mmol/L. The intention was to keep the baby breastfeeding offering up to 3 doses of DG with clinical review prior to administration of the 3rd dose. A key question was whether we would see benefits such as better breast-feeding rates, a decline in the use of formula and less hypoglycaemia.

A retrospective study (2018) of a cohort of 50 neonates (CH1) at risk of hypoglycaemia was performed after implementation of DG treatment for neonates at risk of NH. The data was compared with a cohort of 48 babies (CH2) for the same data set (Table 1). The 2nd cohort was chosen before any QI initiatives, education or new guidance was implemented. Data was collected regarding demographics, reason for monitoring, timing of blood sugars, dextrose gel administration, doses used and incidence of hypoglycaemia and symptoms if any. The use of preventative strategies like skin to skin care and early breastfeeding were analysed. The type of feeding and whether the baby received or transitioned onto formula was also analysed. Statistical analysis was performed using Fishers Exact test (Table 1).

The top 4 reasons for monitoring babies in both groups were similar but there were a higher number of babies who were IUGR and preterm in CH1. The most common reason for monitoring in CH2 was maternal diabetes followed by hypothermia. The rates of exclusive breast feeding (54% vs 33%; p=0.04 ), early skin to skin care (84 % vs 72%) and feeding within the hour (70 vs 50%) were higher in CH1 vs CH2. The incidence of hypothermia was less in CH1 compared to CH2 (11% vs 22%). There were 3 babies admitted in cohort 2 and none in cohort 1. 9 babies in CH1 received DG and all of them received a single dose after which they were discharged. This helped maintain breastfeeding in 6/9 (66%) babies who would have previously gone onto formula. Fewer babies were symptomatic in CH1 compared to CH2 (6% vs 17%), but the incidence of hypoglycaemia in both groups was the same.

After starting DG we have seen rise in the breastfeeding amongst babies at risk of NH. Early breastfeeding and skin to skin care may have contributed to this by promoting bonding. However, 66% of neonates were able to continue breastfeeding while on DG. They avoided formula. DG appears to be a beneficial intervention for sustaining breastfeeding. The study limitations are that it is retrospective and there is demographic variation in the cohorts.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=2773fd58023290b343c9678c053a8ff3-MjAxOS0wNSM1Y2UyNjY2YmQ0YmFh

IMAGE / TAB CAPTION: Table 1 Comparison of Cohort 1 (CH1) with Cohort 2 (CH2)

COI: None Declared
ID: 129

TITLE: ULTRASOUND MEASUREMENTS OF INTRACRANIAL STRUCTURES IN GROWTH-RESTRICTED NEONATES WITH EVIDENCE OF FETAL REDISTRIBUTION

AUTHORS: Pramod Pharande 1, Mohan Krishnamurthy 1, Gillian Whiteley 2, Atul Malhotra 1,3,4

AFFILIATIONS: 1: Monash Newborn, Monash Children’s Hospital, Melbourne, Australia
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CONTENT:

Fetal growth restriction (FGR) is an important cause of perinatal mortality and morbidity, and long-term neuro disabilities. Fetal circulatory redistribution is a common cause of delivery of the “at risk” FGR neonate. The impact of this “brain sparing” on corpus callosum, cerebellum and lateral ventricle measurements has not been well studied.

Aim: To compare corpus callosum, cerebellar, and ventricular measurements of FGR neonates with fetal redistribution (abnormal antenatal umbilical/middle cerebral artery Dopplers) with those of gestation-matched appropriately grown for age (AGA) neonates.

Prospective observational study conducted at a tertiary neonatal unit in Melbourne, Australia. Cranial ultrasound was done between D 1-3 of life in FGR (with fetal redistribution necessitating delivery) neonates born at a gestational age between 24 – 42 weeks, and gestation-matched AGA neonates. Measurements of different brain structures (Lateral ventricles (width and depth), corpus callosum (length, fastigium length, antero-posterior diameter of the genu, width of genu, body and splenium), and cerebellum (vermis height and antero-posterior diameter, transverse cerebellar diameter) and extra-axial space) were done in both groups of neonates and the measurements were subjected to statistical analysis.

Cranial ultrasounds on 20 FGR [mean (SD) gestation: 31.4 (3.1) weeks, mean (SD) weight 1205 (463) grams] and 20 AGA neonates [31.1 (3.0) weeks; 1667 (490) grams] were done. Corpus callosum length (mean ± SEM) was significantly decreased in FGR neonates [35.4 ± 0.91 vs. 37.9 ± 0.76 mm, p=0.01] as compared to AGA neonates, but corpus callosum fastigium length (mean ± SEM) was similar [40.37 ± 0.99 vs. 41.6 ± 0.93 mm, p=0.6]. Similarly, FGR neonates showed decreased transverse cerebellar diameter (mean ± SEM) [35.06 ± 1.09 vs. 37.49 ± 1.33 mm, p=0.03] as compared to AGA neonates, but cerebellar vermis height and antero-posterior diameter were comparable. Bilateral lateral ventricle volume, corpus callosum genu, body and splenium thickness and extra-axial space measurements were comparable between the groups.

Corpus callosum and cerebellar measurements seem to be most affected in FGR neonates with fetal redistribution. This may have implications for their future neurodevelopmental outcomes.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 132

TITLE: Bovine colostrum to prepare or repair the intestine for formula feeding in preterm neonates

AUTHORS: Yanqi Li1, Xiaoyu Pan1, Duc Ninh Nguyen1, Shuqiang Ren1, Per Torp Sangild1,2,3

AFFILIATIONS: 1 Comparative Pediatrics and Nutrition, University of Copenhagen, Copenhagen, Denmark; 2 Department of Pediatrics and Adolescent Medicine, Rigshospitalet, Copenhagen, Denmark; 3 Hans Christian Andersen Children’s Hospital, Odense University Hospital and University of Southern Denmark

CONTENT:

Mother’s own milk (MM) improves gut health and protect against necrotizing enterocolitis (NEC) in preterm infants. Due to absence or insufficient supply of mother’s milk, many infants often receive formula before or after MM feeding during the first weeks. It is unknown how such ‘diet shifts’ may affect intestinal health. Bovine colostrum (COL) has been shown to improve gut health and protect against NEC in preterm pigs, relative to infant formula (FOR). Using preterm pigs as a model for preterm infants, and bovine colost r (COL) to reflect MM, we tested the hypothesis that COL feeding before or after formula (FOR) feeding protects against FOR-induced intestinal impairment.

Seventy-four preterm pigs received increasing volumes of COL or FOR until d 5. At this age, pigs were euthanized or fed either COL or FOR for another 4 d, resulting in six groups: COL or FOR until d 5 (C5, F5, both n=11), COL or FOR until d 9 (CC, FF n=12-13), COL followed by FOR (CF, n=14) and FOR followed by COL (FC, n=13). Blood and tissues were collected on d 5 and d 9 for measurement of clinical variables together with structural, functional and gene expression parameters in the intestine.

FOR reduced the weight gain and physical activity and increased the NEC incidence (64 vs. 27%) on d 5, relative to COL (F5 vs C5, P<0.05). Intestinal structure and function, measured as villus height and crypt depth, brush border enzymes, hexose absorption, and intestinal integrity, were reduced in F5 vs. C5 pigs, together with evidence of a proinflammatory response, as indicated by increased proinflammatory innate immune gene expression (LBP, MYD88, IL8, C3). On d 9, NEC incidences became similarly reduced among groups (15-21%), but the CC, FC, and CF pigs showed improved intestinal structure and function, relative to FF pigs (P<0.05). Gene expressions related to tissue hypoxia (HIF1A) and apoptosis (CASP3) were similar on d 5, while HIF1A expression was increased in CF and FF, relative to CC and CF pigs and CASP3 expression was increased in CF and FF vs. CC and FC pigs on d 9 (P<0.05).

Natural milk diets, like COL and MM, may protect the immature intestine from NEC by dampening proinflammatory responses to FOR feeding. Diet-dependent NEC sensitivity is highest within the first week after preterm birth and the diet-dependency may decrease with age. Feeding COL could improve intestinal structure and function for a later FOR-induced insult and repair some damages caused by initial FOR feeding.

IMAGE / TAB:

COI: Bovine colostrum was donated by Biofiber Damino, Gesten Denmark that had no influence on study design or results interpretation. The University of Copenhagen has filed a patent on the application regarding the use of BC bovine colostrum for pediatric patients with Per Sangild as the sole inventor. He has declined any share of potential revenue arising from commercial exploitation of a such a patent. All other authors have no conflicts of interest.
ID: 136

**TITLE:** EFFECT OF FENTANYL BOLUSES ON CEREBRAL OXYGENATION AND HEMODYNAMICS IN PRETERM INFANTS

**AUTHORS:** Souvik Mitra1, Ege Babadagli1, Tara Hatfield1, Helen McCord1, Averie dePalma1, Walid El-Naggar1, Georg Schmölzer2, Doug McMillan1

**AFFILIATIONS:** 1Division of Neonatal Perinatal Medicine, Dalhousie University, Halifax; 2Centre for the Studies of Asphyxia and Resuscitation, University of Alberta, Edmonton

**CONTENT:**

Fentanyl, an opioid analgesic, is one of the most commonly used off-label medications for pain control and sedation in preterm infants. However, there is a growing concern with the link between fentanyl use and poor neurodevelopmental outcomes in preterm infants. Animal studies have shown that fentanyl infusion significantly reduces cerebral oxygenation in newborn piglets. Yet the effect of this medication on cerebral perfusion in preterm neonates remains unexplored. The objective of our study was to evaluate the effect of a bolus dose of fentanyl on the regional cerebral oxygen saturation (RcSO2), cerebral fractional tissue oxygen extraction (cFTOE) and left ventricular output (LVO) as compared with pre-administration baseline in preterm infants.

A prospective observational study was conducted from October 2017-October 2018. Infants born <37 weeks of gestation receiving a bolus dose of fentanyl (1-2microgram/kg/dose) were eligible. Infants with major congenital anomalies, medically unstable infants and those who received fentanyl bolus in the past 48 hours were excluded. Cerebral oximetry monitoring using near-infrared spectroscopy (INVOS 5100c) was started 15 minutes prior to and continued for 6 hours post fentanyl administration. Cardiac output (LVO) was measured using a non-invasive doppler ultrasound (USCOM) at 5 mins prior and at 5, 15, 30 mins and 6 h post fentanyl bolus. The primary outcome was difference between RcSO2 measured 5 mins prior to and at the above-mentioned time points after administration of fentanyl.

29 infants were enrolled during the study period [Median gestational age 28 weeks; Interquartile range (IQR) 25-30 weeks; median birth weight 1020 g (IQR 830-1275 g); median age 4 days (IQR 2.5-7.5 days)]. 28 infants received fentanyl for peripherally inserted central catheter insertion and one received fentanyl for endotracheal intubation. Mean (± standard deviation) baseline RcSO2 was 72.8% (±11.4), cFTOE was 21.9 (±11.2) and LVO was 335 (193) ml/kg/min prior to fentanyl infusion. One-way ANOVA showed no statistically significant difference between baseline and any of the post-fentanyl cerebral oxygenation or hemodynamic measures ( Figures 1-3).

Administration of fentanyl bolus for procedural pain and sedation in preterm infants does not affect cerebral oxygenation, cerebral tissue oxygen extraction and cardiac output in preterm infants.

**IMAGE / TAB:**
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=06b763982048d887bc6c4b7410ea34e0-MjAxOS0wNSM1Y2UyNjY2YmRhZjQ5

**IMAGE / TAB CAPTION:** Figure 1. Boxplot of regional cerebral oxygenation (RcSO2) values at 5 time points pre- & post fentanyl
Figure 2. Boxplot of cerebral tissue oxygen extraction (cFTOE) values at 5 time points pre- & post fentanyl
Figure 3. Boxplot of left ventricular output (LVO) values at 5 time points pre- & post fentanyl

**COI:** None declared
Fetal growth restriction (FGR) is a serious pregnancy complication associated with increased risk of perinatal morbidity and adverse neurodevelopment. Conventional brain imaging in the neonatal period is relatively insensitive for detection of subtle changes in brain microstructure in FGR infants. We examined whether advanced MRI analysis techniques can detect early neonatal brain injury caused by chronic hypoxia-induced fetal growth restriction in preterm lambs.

Background on lamb model: Surgery was undertaken in twin bearing pregnant ewes at 88 days gestation (term, 147 d) to induce FGR in one fetus. At 127 days gestation (~32 weeks human brain development), FGR and control (appropriate for gestational age, AGA) lambs were delivered by caesarean section, intubated, sedated and commenced on ventilation. (Reference: Malhotra A, et al. Neuropathology as a consequence of neonatal ventilation in premature growth restricted lambs. Am J Physiol Regul Integr Comp Physiol 2018 Dec; 315(6): R1183-1194)

Brain imaging was conducted within the first two hours of life using a 3T MRI (Siemens Skyra, Erlangen, Germany). T1 and T2 structural imaging, magnetic resonance spectroscopy (MRS), and diffusion MRI (dMRI) data were acquired. Advanced analysis techniques, including fixel-based analysis of 3-tissue constrained spherical deconvolution (CSD) of the dMRI data, were applied to compare brain scans from FGR and AGA lambs. Diffusion tensor imaging (DTI) modelling of dMRI included the following brain regions of interest (ROI): subcortical white matter, periventricular white matter, hippocampus, corpus callosum and thalamus. Lambs were euthanized immediately after the scans and brain histology was performed the regions of interest to confirm FGR related injury.

Six pairs of FGR and AGA lamb (body weight, mean(SD): 2.2(0.5) vs. 3.4(0.3) kg) brain scans were studied. Brain histology confirmed subtle white matter injury in FGR lambs. There were no differences observed between the groups in conventional T1, T2 or MRS brain data. Axial, mean and radial diffusivity and fractional anisotropy indices obtained from DTI modelling of the dMRI data also did not show any differences in any ROI. Fixel-based analysis of 3-tissue CSD revealed a decrease in fibre cross-section (FC, p<0.05) but not in fibre density or combined fibre density and cross-section (FD or FDC) in FGR vs. AGA lamb brains. The specific tracts that showed a decrease in FC were in the region of the periventricular white matter and hippocampus, and were associated with histological evidence of white matter loss, inflammatory cell infiltration and microbleeds in FGR lamb brains.

The neuropathology associated with FGR in neonatal preterm lambs is subtle and requires advanced MRI and tract-based analysis techniques for detection on imaging. Fixel-based analysis of 3-tissue CSD offers new avenues to measure tract-specific differences in brain microstructure, not seen on conventional imaging or voxel-based analysis. These findings may inform analysis of similar brain pathology in neonatal infants.
COI: None declared
ID: 138
TITLE: PERIPHERALLY INSERTED CENTRAL VENOUS CATHETER VERSUS PERIPHERAL VENOUS CATHETER. GROWTH AND NEURODEVELOPMENT OF VERY LOW BIRTH WEIGHT NEWBORN. A RANDOMISED TRIAL
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AFFILIATIONS: 1 Department of Neonatology, Medical Academy, Lithuanian University of Health Sciences, Lithuania; Hospital of Lithuanian University of Health Sciences, Lithuania
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CONTENT:

In very low birth weight (VLBW) newborns, parenteral nutrition (PN) is delivered via a peripheral venous catheter (PVC), a central venous catheter (CVC), or a peripherally inserted central venous catheter (PICC). Up to 45% of PICCs are accompanied by complications, the most common being sepsis. A PVC is an unstable PN delivery technique requiring frequent change. The growth and neurodevelopment of VLBW newborns may be disturbed because of catheters used for early PN delivery and complications thereof. The aim of the conducted study was to evaluate the effect of two PN delivery techniques (PICC and PVC) on anthropometric parameters and neurodevelopment of VLBW newborns.

A prospective randomized clinical trial was conducted at the Department of Neonatology of the Hospital of the Lithuanian University of Health Sciences Kauno klinikos between 1 January 2014 and 31 March 2017. Low birth weight (≥750 - <1500 g) newborns that met the inclusion criteria were randomized into two groups: PICC and PVC. For the entire period of treatment, PN was delivered via a catheter chosen during the randomization. In the trial, we assessed short-term outcomes, i.e., anthropometric parameters (weight, length, and head circumference) from birth until CA 36 weeks or upon discharge, and long-term outcomes, i.e., anthropometric parameters (weight, length, and head circumference) from 3 months to CA 12 months as well as neurodevelopment at CA 12 months according to Bayley II.

In total, 108 newborns (57 in the PICC group and 51 in the PVC group) underwent randomization. Short-term outcomes were assessed in 47 PICC and 38 PVC subjects. Long-term outcomes were assessed in 38 and 33 subjects of PICC and PVC groups, respectively. There were no differences observed in anthropometric parameters between the subjects of two groups in the short and long term. Delayed mental performance (MDI <85) was observed in 26.3% and 21.2% (p=0.781), and delayed psychomotor performance (PDI <85) was observed in 39.5% and 54.5% (p=0.239) of PICC and PVC subjects, respectively. Significantly delayed mental performance and psychomotor performance were observed only in the group of PICC subjects (10.5% and 13.2%, respectively); meanwhile, no such delay was determined in the group of PVC subjects; however, this difference was not statistically significant (p=0.118 and p=0.057).

In the short and long term, no differences were observed in anthropometric parameters of newborns when PN was delivered using PICC and PVC. At 12 months of corrected gestational age (CGA), there was no difference in the rate of mental and motor neurodevelopment in both groups.
COI: "None declared"
ID: 144

TITLE: STRICT EVALUATION OF CLINICAL SIGNS IS MORE ACCURATE THAN A MULTIVARIATE RISK ASSESSMENT TO REDUCE THE RATE OF ANTIBIOTIC USE IN NEWBORNS AT RISK OF NEONATAL EARLY-ONSET SEPSIS

AUTHORS: Renato S Procianoy 1, Bianca C Benincasa 1, Rita C Silveira 1

AFFILIATIONS: Department of Pediatrics, Newborn Section, Hospital de Clinicas de Porto Alegre and Universidade Federal do Rio Grande do Sul

CONTENT:

The abusive use of antibiotics in newborns is frequent. There is an increasing evidence that strict evaluation of clinical signs is effective in detecting newborns at risk of early-onset sepsis that require antibiotic therapy. The objective of this study is to compare the use of EOSCalc with a strict evaluation of clinical signs for antibiotic use in term and late preterm infants.

Newborns with gestational age (GA) ≥ 34 weeks who received antibiotics in the first 72 hours from June 2014 to December 2016 were studied. Exclusion criteria: newborns with congenital infections, major malformations and hypoxic-ischemic encephalopathy in a protocol of therapeutic hypothermia. In the first 24 hours of life EOSCalc was applied, and clinical signs of sepsis were observed. Clinical signs observed were: presence of maternal risk factor for infection plus two neonatal clinical signs of different systems or presence of three neonatal clinical signs of different systems (thermal instability, hemodynamic changes, respiratory, gastrointestinal, hematological and neurological symptoms as well as subjective evaluation).

8321 individuals were born, 505 treated by medical indication; 121 fulfilled exclusion criteria; resulting a total of 384 treated empirically with antibiotics (mean GA 38.9 ± 1.8 weeks; mean birth weight 3266 ± 588 grams). In only 219 (57.1%) would be indicated empiric antibiotic by EOSCalc and in 61 (15.9%) by clinical signs. 10 had positive blood cultures (1.2 per thousand live births). All patients with positive blood culture were detected by EOSCalc or the use of clinical signs with absence of false negative in both evaluations. In both approaches the negative predictive value (0.65-1) and the sensitivity (0.97-1) were equal to 1, the specificity of the strict attention of clinical signs was 0.86 (0.82-0.89) and the specificity of EOSCalc was 0.44 (0.39-0.49). Positive predictive value of strict evaluation of clinical signs was 0.16 (0.08-0.28) and of EOSCalc was 0.04 (0.02-0.08).

Risk assessment based on strict evaluation of clinical signs in the first 24 hours is a more accurate strategy than EOSCalc in the antimicrobial management of neonatal early-onset of term and late preterm newborns.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared.
ID: 152

**TITLE:** ACTIVE PERINATAL CARE OF PRETERM INFANTS IN THE GERMAN NEONATAL NETWORK

**AUTHORS:** Alexander Humberg, MD1, Christoph Härtel, MD1, Tanja K. Rausch1,2, Guido Stichtenoth, MD, PhD1, Philipp Jung, MD1, Christian Wieg, MD3, Angela Kribs, MD4, Axel von der Wense, MD5, Ursula Weller, MD6, Thomas Hoehn, MD7, Dirk Olbertz, MD8, Ursula Felderhoff

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CONTENT:

Active perinatal care was reported to improve survival rates of extremely immature infants in nationwide cohort studies and research networks as well as in single centre reports. Between-hospital variation with regard to active care of extremely premature infants is huge. Furthermore, causes and timing of death in premature infants are associated with gestational age. In our network, centres receive yearly written reports comparing their own outcome and treatment data with data from all other centres and a subgroup of centres with extremely low mortality rates. We analysed whether gestational age specific changes in survival occur over time and whether these are influenced by centre specific performance in the past.

We analysed data of VLBWI born between 22 0/7 – 28 6/7 weeks of gestation from 43 tertiary centres participating in the GNN between 1st of January 2011 and 31st of December 2016. Infants not receiving active perinatal care were excluded. Active care was defined as any postnatal intervention (e.g. continuous positive airway pressure, mechanical ventilation). Participating NICUs were categorized according to their death rate in 2011-2013. We used total death rate without adjusting for gestational age or other differences between NICUs. Estimation of overall mortality was calculated. We compared baseline and mortality data for the years 2011-2013 vs. 2014-2016.

Total survival increased from 85.8 % in 2011-2013 to 87.4 % in 2014-2016. This increase was due to reduced mortality of NICUs with low survival rates in 2011-2013. Survival increased in these centres from 53% to 64% in the 22-24 weeks strata and from 73% to 84% in the 25-26 weeks strata.

Range of centre specific proportion on all infants who received active care was wide for infants at 22 weeks. Some centres did not execute active care in this age group, but one centre performed active care in 43.3% of all infants in our database at 22 weeks. Infants receiving active care in NICUs with high survival rates in 2011-2013 had a lower gestational age and lower birth weight compared to both other groups (NICUs with survival > P75: 26.27 ± 1.72 weeks and 831 ± 255 g vs. NICUs with survival P25-75: 26.47± 1.62 weeks [p<0.001] and 851 ± 256 g [p=0.005]; and vs. NICUs with survival <P25: 26.57± 1.67 weeks and 873 ± 255 g [pP75]).

Active perinatal care of very immature infants appears to improve outcomes at the border of viability and survival rates at higher gestational ages. However, long-term neurological outcome data are needed before recommendations for parental counselling should be reconsidered.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: Travel stipend from Chiesi
ID: 155

TITLE: The efficiency of early and late administration of various doses of recombinant human erythropoietin in extremely and very low birth weight infants

AUTHORS: Sharafutdinova D.R.1,2; Balashova E.N.1; Ionov O.V.1,2; Kirtbaya A.R.1,2; Zubkov V.V.1,2; Degtyarev D.N.1,2

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CONTENT:

Anemia of prematurity is a common disorder of premature infants. The prevalence of anemia of prematurity is inversely proportional to the gestational age and body weight at birth. The pathogenetic importance of impaired erythropoietin (EPO) production in anemia of prematurity provides the rationale for therapy with erythropoiesis stimulating agents (ESAs) including recombinant EPO. The aim of the study was to assess the effectiveness and safety of different applying schemes of human recombinant erythropoietin in extremely and very low birth weight infants (ELBW and VLBW).

A randomized, placebo-controlled study of 133 VLBW and ELBW infants was conducted. Gestational age (GA) of newborns ranged from 26 to 33 weeks, more than half of them – 30 weeks or less (56%). All newborns were divided into 5 groups according to anemia prevention and treatment schemes: group 1 (n=26) – were administered ESAs 200 IU/kg 3 times per week from 3 day after birth; group 2 (n=21) – were administered ESAs 400 IU/kg 3 times per week from 3 day after birth; group 3 (n=37) – were administered ESAs 200 IU/kg 3 times per week from 8 day after birth; group 4 (n=18) – were administered ESAs 400 IU/kg 3 times per week from 8 day after birth; group 5 (n=31) – did not receive treatment with ESAs (control group). Subgroups of newborns ≤ 30 gestational weeks were identified in each group.

There were no statistically significant differences in the age of the 1st transfusion, the frequency and total volume of transfusions, the duration of respiratory therapy, the duration of hospitalization, including treatment in NICU, body weight and postnatal age at discharge, the frequency of retinopathy of prematurity stage ≥ 3, periventricular leukomalacia, bronchopulmonary dysplasia, intraventricular hemorrhages, necrotizing enterocolitis. The concentration of peripheral blood hemoglobin of premature infants at discharge was significantly different: lower level in the control group (94 g/l) compared with the groups of early ESAs administration (109 g/l and 107 g/l in groups 1 and 2, respectively; P0-1=0.048 and P0-2=0.047) due to newborn GA ≤30 weeks.

The administration of early or late EPO in VLBW and ELBW infants did not significantly reduce the use of one or more RBC transfusions, the number of transfusions per infant, so the routine use of EPO is not recommended. Among newborn with GA ≤30 weeks the early administration of EPO leads to increase the level of hemoglobin at discharge. The effectiveness of erythropoietin therapy remain controversial, therefore further researches are necessary.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 157

TITLE: PHYSIOLOGICAL-BASED CORD CLAMPING IN PRETERM INFANTS - NON-INFERIORITY TRIAL OF EFFECTIVENESS OF STABILISATION.

AUTHORS: R. Knol 1; E. Brouwer 2; T. van den Akker 3; P. DeKoninck 4,5; N. van Geloven 6; E. Lopriore 2; G.R. Polglase 5; I.K.M. Reiss 1; S.B. Hooper 5; A.B. te Pas 2

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CONTENT:

Preterm infants often fail to aerate their immature lungs at birth and need respiratory support for cardiopulmonary stabilisation. Delaying cord clamping until the lung is aerated and the infant is breathing may be beneficial, therefore optimizing hemodynamic transition and placental transfusion. The feasibility of this approach of Physiological-Based Cord Clamping (PBCC) has been shown before. The aim of the present trial was to test whether stabilising preterm infants performing PBCC was at least as effective as the standard approach of time-based Delayed Cord Clamping (DCC).

A randomised controlled non-inferiority trial was performed in two centres, including preterm infants born at less than 32 weeks of gestation. Infants were allocated to either PBCC or standard DCC. In the PBCC group, infants were stabilised on a purpose-built resuscitation table (the Concord) with an intact umbilical cord. The cord was clamped when the infant was considered respiratory stable, defined as establishment of regular spontaneous breathing, heart rate ≥ 100 bpm and SpO2 > 90% while using FiO2 < 0.40. In the DCC group, infants were clamped after 60 seconds before being transferred to the standard resuscitation table for stabilisation. The primary outcome was the time to reach respiratory stability as previously defined, with pre-defined non-inferiority limit at -1:15 minutes.

Thirty-seven infants (mean GA 29+0 weeks) were randomised. Mean (SD) cord clamping time was 1:02 (0:30) min for the DCC group and 5:49 (2:37) min for the PBCC group. Intention-to-treat analysis for the primary outcome showed a shorter time to reach respiratory stability in the PBCC group (PBCC mean 5:54 (2:27) min; DCC mean 7:07 (2:54) min; mean difference 1:13 min, 95% CI [-0:37 – 3:03]), amply reaching the pre-defined non-inferiority limit. No significant differences between the groups were found for maternal blood loss, postpartum haemorrhage, infant temperature at NICU admission, maximum bilirubin levels or short-term neonatal outcomes.

Stabilisation of preterm infants performing Physiological-Based Cord Clamping using a purpose-built resuscitation table is at least as effective as standard DCC. A large randomised clinical trial is started to show possible short- and long-term benefits.

IMAGE / TAB:
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IMAGE / TAB CAPTION: Illustration (by Sophie Cramer) of the Physiological Based Cord Clamping approach using the Concord. Stabilisation of the infant is performed while the cord is intact and the cord is clamped after the infant is respiratory stable.

COI: None declared.
ID: 166

**TITLE:** ELECTROCARDIOGRAPHIC SCREENING IN THE FIRST WEEK OF LIFE FOR DIAGNOSING HIGH-RISK CARDIOVASCULAR DISEASE

**AUTHORS:** Holger Michel1, Alexander Simma2, Antonia Potapow2, Stephan Döring1, Susanne Brandstetter1, Michael Melter1, Birgit Seelbach-Göbel3, Christian Apfelbacher4, Michael Kabesch1, Stephan Gerling1 and the KUNO kids Study Group

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**CONTENT:**

Conduction abnormalities or pathological de- or repolarisation in the ECG can lead to the diagnosis of high-risk cardiac disease. With a prevalence of 1:2000 - 2500 the congenital long QT-syndrome (LQTS) is far more common than previously thought. LQTS can cause life threatening arrhythmias in infants, children and adults. It has been well documented that a prolonged QT-interval itself is associated with an increased risk of sudden infant death syndrome and an ECG screening in newborns has been proposed. Timing, QT-thresholds and methodological issues have been subject of an ongoing debate. In this study we evaluated an ECG screening in the first week of life.

We evaluated 2251 ECGs from participants of the KUNO Kids birth cohort study, recorded between the first and the eighth day of life. A medical history regarding hereditary cardiac disease, maternal medication and pregnancy was documented. All ECGs were evaluated by pediatric cardiologists and further cardiologic examinations were carried out in case of ECG abnormalities. QT-time was manually measured and corrected for time using Bazett’s formula (QTc). If QTc was borderline or prolonged in lead II, a mean value of lead II, V5 and V6 was calculated. Newborns with a mean QTc over 450 ms received a control ECG before discharge and/or after 3-4 weeks. Participants showing a QTc time over 500 ms were admitted and monitored until improvement of the QTc time or therapy was started.

High risk cardiac disease was found in 4 of the 2251 participants. Overall the mean QTc was 414 ms (SD 24,5 ms). In 99 (4.4%) of the participants the initial QTc was prolonged (>450 ms) and in 80 ECGs it was not measurable, leading to 8,3% of the participants receiving a second and 1,2% a third ECG. In these, the mean QTc declined from 482 ms to 426 ms. After 4 weeks only two participants showed a QTc > 450 ms. In these two, genetic analysis revealed a KCNQ1 gene mutation causing LQTS type 1. Family screening detected three more previously undiagnosed individuals. Furthermore one ECG showed a preexcitation, parents were instructed in respect to possible tachycardia. In one participant abnormal depolarization triggered echocardiography revealing a presymptomatic hypoplastic left heart syndrome. 56 participants received a second ECG recording for other reasons than QT prolongation.

In our study cohort, ECG screening in the first week of life could detect newborns with long QT-syndrome and other high-risk cardiac conditions. Early ECG screening leads to a considerable amount of control recordings but life-threatening conditions could be diagnosed and therapy could be started before newborns were discharged. More studies concerning influencing factors, methodological and timing issues are needed.

**IMAGE / TAB:**

**IMAGE / TAB CAPTION:**
COI: None declared
ID: 169  
TITLE: STILLBIRTH OUTCOME BY MATERNAL NATIONALITY IN GREECE DURING THE YEARS OF ECONOMIC CRISIS: TRENDS AND RISK FACTORS  
AUTHORS: Tania Siahanidou 1; Maria Karalexi 2; Maria Kantzanou 2; Nick Dessypris 2; Christos Christodoulakis 2; Peter Daoutakos 2; Kyveli Aggelou 2; Dimitrios Loutradis 3; George Chrousos 1, Eleni Petridou 2, 4 
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CONTENT:  
The perinatal mortality rate is a key population health indicator reflecting economic development, social equity and health care services within a population. Stillbirths constitute more than 70% of perinatal deaths in developed countries, including Greece. The recent economic crisis has been linked with declines in population health with the most vulnerable groups being disproportionally affected. However, evidence on the impact of the crisis on stillbirth rates is scarce and dubious. The aim of this study was to assess time trends of stillbirth rates in Greece during the pre-crisis (2004-2008) and crisis period (2009-2015) and explore stillbirth risk factors.  
In this nationwide population study conducted in Greece, primary data on all births (N=1,276,816), out of which 5,023 stillbirths, during the period 2004-2015, were provided by the Hellenic Statistical Authority. Information was recorded for index child’s sex, birth order, birthweight and size at birth (small, appropriate or large for gestational age), prematurity, multiplicity, as well as for parental age, maternal nationality, place of residence, maternal marital status and maternal education. Stillbirth rates were calculated and time trends were assessed through Poisson and joinpoint regressions. Multiple adjusted logistic regressions and population attributable fractions (PAF) for stillbirths by maternal nationality were also undertaken.  
The average stillbirth rate was 3.9 reaching a significantly higher 5.0/1,000 births/year rate among non-Greeks. Non-significant trends were noted for Greek (-0.5%, 95% confidence intervals (CI) -1.4%, +0.4%) and non-Greek mothers (+1.4%, 95% CI -0.5%, +3.3%); joinpoint regression showed non-significant time breaks. Male sex, multiple pregnancies, first and fourth birth, low maternal education, residency in rural areas, unmarried status, small or large for gestational age size at birth, as well as increased maternal age (≥35 years), were recognized as significant determinants of stillbirth outcome. After adjusting for possible confounders, the stillbirth risk increased significantly during the crisis versus the pre-crisis period [odds ratios (OR) for Greeks 1.70 (95% CI 1.57, 1.84), population attributable fraction (PAF) 24.0%; OR for non-Greeks 1.94 (95% CI 1.65, 2.28), PAF 27.7%].  
During the 12-year study period, non-statistical, albeit of different direction, stillbirth trends among Greek and non-Greek mothers were observed. However, after adjusting for sociodemographic determinants, the period of the economic crisis (2009-2015) conferred a significantly higher stillbirth risk, especially among non-Greek mothers.  

IMAGE / TAB:  

IMAGE / TAB CAPTION:  

COI: None declared
ID: 171

TITLE: A MATCHED COHORT STUDY OF SURGICAL AND NON-SURGICAL TREATMENT FOR PATENT DUCTUS ARTERIOSUS IN EXTREMELY PRETERM INFANTS

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CONTENT:

Patent ductus arteriosus (PDA) continues to be a challenging problem in the care of preterm infants. PDA in extremely preterm newborn infants (<28 weeks gestational age, GA) might lead to detrimental cardiac and pulmonary complications. Due to contraindications and low efficacy of treatment with cyclooxygenase inhibitors and acetaminophen, surgical ligation is often required to close a hemodynamically significant PDA in this group. The aim of this study was to investigate the differences in peri- and postnatal factors, and outcomes, between matched surgically and non-surgically treated infants born at 22-27 weeks GA.

Between January 1st 2010 and December 31st 2016, 463 infants were born between 22-27 weeks GA at the tertiary NICU in Uppsala, Sweden. Forty-four infants were retrospectively identified as being surgically treated for their PDA (Ligated group) and matched with non-surgically treated infants (Control group; n=44) at the same gestational age (+/- 1 GA week) and time of birth (+/- 1 month). Birth weight, gender, prolonged premature rupture of membranes, administration of prenatal steroids, mode of delivery, Apgar-scores, days and type of ventilatory assistance, erythrocyte transfusions, inotropic treatment, postnatal steroids, echocardiographic variables, details of pharmacological PDA treatment, morbidity such as NEC, BPD, IVH/PVL, ROP, sepsis and mortality were compared between the groups.

There were no differences in GA or birth weight between the Ligated and the Control groups (mean ± SD; 24+4 ± 1+3 vs 24+3 ± 1+3 weeks; 683 ± 167 vs 704 ± 166 g; NS). No other major differences in perinatal characteristics were found between the groups. Larger ductal diameter prior to and lack of diameter decrease after pharmacological treatment were seen in the Ligated group (p=0.022 and p=0.048, respectively). Transfusions, postnatal steroids and longer duration of invasive respiratory support were more common in the Ligated group (p<0.01). Mortality was the same in both groups (n=5 vs n=5; NS). A higher incidence of severe BPD in the Ligated group was the only difference in long-term outcomes between the groups (p=0.025).

Early large ductal diameter and lack of decrease in ductal diameter during pharmacological treatment indicate future need for surgical ligation. Infants surgically treated for PDA required more invasive respiratory support and postnatal steroid treatment, and had a more severe BPD than infants without surgery.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 174  
TITLE: MANAGEMENT OF PATENT DUCTUS ARTERIOSUS IN VERY PRETERM NEWBORNS: DO WE HAVE A PREFERENCE?  
AUTHORS: Dmytro Dobryanskyy 1; Solomia Yaremchuk 1; Anna Menshykova 1,2; Lesia Sekretar 1; Zoryana Salabay 2  
AFFILIATIONS: 1 Paediatric Dept., Lviv National Medical University, Lviv, Ukraine; 2 Neonatal Intensive Care Unit, Lviv Regional Clinical Hospital, Lviv, Ukraine

CONTENT:

Patent ductus arteriosus (PDA) is a common problem in preterm infants, which can cause complications and worsen the results of treatment. However, there is currently no unambiguous approach to the management of PDA. Both, ibuprofen and indomethacin, which are used in preterm infants to promote ductal closure, have undesirable side-effects and many contraindications. That is why, there is a need for alternative treatment, that will be not inferior in comparison with ibuprofen or indomethacin but result in fewer adverse effects.

The aim of this study was to compare the effectiveness of the pharmacological closure of the PDA with ibuprofen and paracetamol in very preterm newborns. Also, the effectiveness and feasibility of expectant management without pharmacological treatment has been evaluated.

Eighty very preterm infants (gestation age < 32 weeks and birth weight < 1500 g) with PDA diagnosed with echocardiography were enrolled into retrospective study. Thirty of them received oral or rectal ibuprofen at a dose of 20/10/10 mg/kg/day (ibuprofen group), 21 newborns were treated with IV paracetamol 15 mg/kg/dose every 6 hours (paracetamol group), and 29 neonates did not receive any medication for pharmacological closure of PDA (expectant management group). The first dose of both agents was introduced at a median [IQR] age of 6 days (6 [1-21] days for ibuprofen and 6 [3-14] days for paracetamol; p>0.05) after confirmation of haemodynamic significance of the duct. The study groups were not different in terms of birth weight or gestational age (1161.67±321.55 grams and 28.33±2.28 weeks in the ibuprofen group and 1177.14±343.15 grams and 28.24±2.022 weeks in the paracetamol group vs. 1068.97±291.22 grams and 27.62±1.88 weeks in the expectant management group; p>0.05).

The median ductus size was 3 [1.5-4.5] mm in the ibuprofen group, 2.5 [1.5-4] mm in the paracetamol group and 2.5 [1.5-4] mm in the expectant management group (p>0.05). Ibuprofen was effective in 27 (90%) and paracetamol – in 15 (71%) babies (p>0.05). Spontaneous PDA closure was observed in 21 (72%) untreated infants. The babies’ age at the time of PDA closure was not statistically different. Two infants (7%) in the ibuprofen group and three infants (14%) in the paracetamol group required surgical intervention (p>0.05). There were no statistically significant differences in the incidences of bronchopulmonary dysplasia (BPD), BPD/death, intraventricular haemorrhage, necrotizing enterocolitis, and mortality rates between the groups. No complications associated with pharmacological treatment were observed.

Paracetamol can be an effective and safe alternative to ibuprofen for pharmacological closure of the haemodynamically significant PDA. At the same time, PDA closure can occur without pharmacological and/or surgical interventions in a large proportion of very preterm infants.

COI: "None declared"
ID: 175

TITLE: Short-term outcomes in neonates born to women with absent or reverse end diastolic flow (AREDF) in a neonatal network of a developing country

AUTHORS: Binoy shah 1; Ashish mehta; Praveen kumar 3; Srinivas Murki 4; Deepak Chawala 5; Nandkishor kabra 6; Ashok Deorari 7; naveen jain 8; suman rao 9; Tandur Baswaraj 10; Sreeram Subramniam 11;

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CONTENT:

A number of observational studies have reported neonatal outcomes in intrauterine growth restriction with abnormal antenatal Doppler flow patterns but there are few such studies from the developing world.

Twenty centres participating in the network prospectively collected data of all neonates fulfilling pre-defined criteria which included need of admission to neonatal intensive care unit (NICU). Mutually agreed upon pre-defined uniform definitions were used across all sites for collecting data. Antenatal, intrapartum and postnatal variables influencing outcomes across centres were analysed. Continuous variables were analysed by using Descriptive statistics. Odds ratio was derived by using binary logistic regression. P value was derived by using independent t test while P value for median was derived from Mann Whitney test.

From 1st January 2017 to 31st October 2018, 3287 infants born at ≤32 weeks of gestational age were enrolled. In the subgroup of neonates born at ≤28 weeks (n=783) 49 (6.2%) had AREDF and 298 (38%) had normal diastolic flow. In those born at 29-32 weeks (n= 2504) 249 (10%) had AREDF while 714 (28.5%) had normal diastolic flow. In the remaining infants Doppler details were either not available or Doppler was not done. Baseline characteristics of both the groups are shown in Table 1.

Incidences of NEC (≥ stage 2) and death were higher in infants with AERDF (Table 2). Median time of reaching full feeds was lesser in subgroup with normal Doppler as compared to AERDF group (9 Vs 15 days in < 28 weeks , 6 Vs 9 days in 29-32 weeks), it was stastically significant (P value <0.05) (Mann Whitney test).

Neonates born to women with absent/reverse end diastolic flow neonates are at increased risk of death or NEC (≥ stage 2).

IMAGE / TAB:
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IMAGE / TAB CAPTION:

COI: None Declared
ABSTRACT BOOK
POSTER PRESENTATIONS

ID: 177
TITLE: FEEDING DURING RED CELL TRANSFUSION: A PILOT RANDOMISED CONTROLLED TRIAL
AUTHORS: Tim Schindler 1,2; Kee Thai Yeo 3; Srinivas Bolisetty 1,2; Joanna Michalowski 1; Alvin Tan 4; Kei Lui 1,2
AFFILIATIONS: 1 Royal Hospital for Women, Sydney, New South Wales, Australia
2 University of New South Wales, Sydney, New South Wales, Australia
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4 Flinders Medical Centre, Adelaide, South Australia, Australia

CONTENT:

Necrotising Enterocolitis (NEC) is a devastating neonatal disease associated with high risks of death and disability. The pathogenesis of NEC is incompletely understood but a temporal association between red cell transfusion and NEC has been recognised. There are also certain feeding practices that have an impact on the chances of a preterm infant developing NEC. As a result, there have been concerns about the effects of feeding during transfusion. We aimed to assess the effect of enteral feeding on splanchnic oxygenation in preterm infants receiving red cell transfusions and hypothesised that enteral feeding would have no effect on splanchnic oxygenation.

This was a pilot randomised controlled trial of three different enteral feeding regimes during a single red cell transfusion. Preterm infants <35 weeks gestation were randomised to either: (1) Withholding enteral feeds for 12 hours from the start of the transfusion or; (2) Continuing enteral feeds or; (3) Restriction of enteral feed volume to 120 ml/kg/day for 12 hours. The primary outcome was a comparison of mean splanchnic-cerebral oxygenation ratio (SCOR) and mean splanchnic fractional oxygen extraction (FOE) before (1 hour prior), during (1 hour into transfusion) and after (end of transfusion; 12 and 24 hours post) transfusion. A sample size of at least 16 transfusion episodes in each group was required to detect a 10% change in mean oxygenation with 80% power at 0.05 level.

There were 60 transfusion episodes (20 transfusion episodes in each group) included in the analysis. 41 infants with a median gestational age at birth of 27 weeks (range 23-32 weeks) were enrolled. The median postnatal age was 43 days (range 19-94 days) and the median pre-transfusion haematocrit was 0.27 (range 0.22-0.32). All three groups were similar at baseline. There were no differences in mean SCOR and mean splanchnic FOE at any of the pre-specified time points (see figure). There were also no differences in clinical outcomes. There were no episodes of NEC in any infant involved in the study. Across all groups the mean SCOR increased from the start to the end of each transfusion (0.97 [CI95% 0.96-0.98] vs 1.00 [CI95% 0.99-1.01]; p=0.04) and the mean FOE decreased from the start to the end of each transfusion (0.22 [CI95% 0.21-0.23] vs 0.17 [CI95% 0.16-0.18]; p<0.001).

Inherently limited by a low background incidence of NEC, this pilot study did not demonstrate any physiological differences in splanchnic oxygenation when enteral feeds were either withheld, continued or restricted during a transfusion. However, the successful conduct of this study suggests that a large, adequately powered trial is achievable to answer this important clinical question.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=1dbf757f19c758a22ace0f368ea33497-MjAxOS0wNSM1Y2UyNyY2YmU5YTvk

IMAGE / TAB CAPTION: Figure. Mean splanchnic-cerebral oxygenation ratio (SCOR) and mean splanchnic fractional oxygen extraction (FOE) before (1 hour prior), during (1 hour into transfusion) and after (end of transfusion; 12 and 24 hours post) transfusion.
TITLE: A RANDOMIZED CONTROLLED TRIAL OF POSITIVE END-EXPIRATORY PRESSURE IN BAG-MASK VENTILATION DURING RESUSCITATION OF TERM NEWBORNS

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CONTENT:

In 2010 the ILCOR committee recommended to use positive end-expiratory pressure (PEEP) during newborn resuscitation. However, in 2015 the recommendation was modified for term infants due to lack of evidence. Available equipment have major limitations: T-piece resuscitators depend on compressed air, and PEEP-valves for self-inflating bags (SiBs) have so far not been able to deliver reliable PEEP. A SiB that can deliver PEEP is wanted, and studies of PEEP-effect on term newborns are needed. The aim of this randomized controlled trial was to compare ventilation by SiB with or without a new, integrated PEEP-valve during resuscitation of term and near-term newborns.

All live-born infants (n=6225) who received positive pressure ventilation at birth (n=473) at Haydom Lutheran Hospital in Tanzania between September 2016 and June 2018 were eligible for inclusion after maternal consent. Helping Babies Breathe-trained midwives performed resuscitation using SiBs with or without PEEP-valve (Laerdal Upright Resuscitator, 320ml, Cat.no 846060/846050). Randomization to use PEEP or not was done for periods of seven days. Heart rate (HR) data was collected by dry-electrode ECG and ventilation data by sensors for pressure, flow and side-stream expired carbon dioxide (ECO2) sampled between the bag and the mask. Research assistants observed all resuscitations. Primary outcome was change in HR per ventilation sequence defined as >5 seconds continuous ventilation.

Among 473 ventilated newborns, 99 were excluded due to missing data or lack of consent. Of 374 included newborns, 191 were ventilated without and 183 with PEEP. For the primary outcome, change in HR per ventilation sequence, we found no significant difference between the two groups (mean increase 9 bpm/minute with vs. 15 without PEEP, P=0.31). The SiB with PEEP-valve delivered a median (IQR) PEEP of 4.6 (2.0, 5.6) mbar. Normal clinical outcome (survived and not admitted to neonatal ward at 24 hours) were similar with or without PEEP (64 and 66%, P=0.84). The PEEP-group received lower tidal volumes (P=0.003) and had borderline significant higher mask leak (P=0.07) and lower ECO2 (P=0.07). Adjusting for mean tidal volumes per ventilation sequence in the main analysis changed the results only marginally, but we found improved HR increase with higher volumes (P=0.02) in both groups.

We did not find significant differences in HR response or clinical outcome at 24 hours between newborns ventilated with or without PEEP-valve, despite ensuring adequate PEEP. Lower tidal volumes in the PEEP-group may have counteracted eventual positive effects of PEEP.
IMAGE / TAB:
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IMAGE / TAB CAPTION: Table 1: Baseline characteristics and outcome for newborns who received bag-mask ventilation without or with PEEP-valve during newborn resuscitation

COI: Joar Eilevstjønn and Øystein Gomo are employees of Laerdal Medical. Jørgen Linde is married to an employee of Laerdal Global Health. Jørgen Linde and Monica Thallinger have received unrestricted grants from the Laerdal Foundation.
ID: 197

TITLE: Impact of pro-inflammatory cytokines on premature rupture of membrane

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CONTENT:

Inflammation at the maternal-fetal interface has been known to involve in the pathogenesis of premature rupture of membrane (PROM) and many inflammatory mediators have been proposed to be related. Toll like receptors (TLR) plays a key role in the innate immune system while MCP-1 is one of the main chemokines that regulate the migration of monocytes/macrophages. In this study, we aimed to determine impacts of these proteins on PROM.

We consecutively recruit 98 PROM patients and 40 intact membrane patients from September 2017 to January 2018. The PROM patients were subdivided by 52 term PROM patients (tPROM group) and 46 preterm PROM patients (pPROM group). And pPROM group was also subdivided into chorioamnionitis positive group (pPROM1) and chorioamnionitis negative group (pPROM2) by histologic evaluation. After delivery placentas were subjected to H&E staining and immunochemical analysis for Toll like Receptor-2, 4 (TLR-2, 4). Cord blood samples were obtained to perform ELISA for monocyte chemoattractant protein-1 (MCP-1). Factors affecting PROM along with placental TLR-2, 4 and cord blood MCP-1 were analyzed.

Among many precipitating factors, postpartum hemorrhage, puerperal infection, fetal distress and histological chorioamnionitis were found to be associated with PROM. The placental TLR-2, 4 expressions in pPROM group and tPROM group were higher than those of normal control group (P<0.05). The placental TLR-2 expression and cord blood MCP-1 in pPROM1 group is significantly higher than those of pPROM2 group (P<0.05). Moreover there has been a positive correlation between placental TLR-2 expression and cord blood MCP-1 in pPROM1 group.

The placental TLR-2, 4 expressions as well as cord blood MCP-1 are increased in PROM patients. However, more studies are required to determine the role of TLRs in pregnancy immunology and to establish its relationship with PROM.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: none
ID: 212

TITLE: INPATIENT BURDEN OF INFECTIONS WITH RESPIRATORY SYNCYTIAL VIRUS (RSV) AND UNSPECIFIED BRONCHIOLITIS (UB) IN CHILDREN DURING THE FIRST 2 YEARS OF LIFE

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CONTENT:

RSV testing is not routinely undertaken in many hospitals; hence, epidemiological studies often combine confirmed RSV infection and unspecified bronchiolitis (UB) when assessing the burden of RSV hospitalisation (RSVH). The aim of this study was to compare the inpatient burden of confirmed RSVH with that of UB hospitalisation (UBH) in children during the first two years of life.

All children born in Scotland between 2000-2011, as collated by the National Health Services (NHS) Information Services Division (ISD), were followed until 2 years of age and admissions for confirmed RSV infection (ICD-10 codes: J12.1, J20.5 & J21.0) and UB (ICD-10 codes: J20.9, J21.9, J12.8, J12.9, J18.0, J18.9 & J22) identified. Age at first admission, high dependency unit/intensive care unit (HDU/ICU) requirement and duration, and overall hospital length of stay (LOS) were assessed and compared.

Of 623,373 children, 28,743 (4.6%) were hospitalised for bronchiolitis (RSV & UB), the overall admission rate being 56.5/1,000 (16.4% with >1 hospitalisation). Confirmed RSVH occurred in 13,362 children (2.2%) at a rate of 27.2/1,000 (19.1% with >1 RSVH). Age at first admission was significantly younger for those with a confirmed RSVH compared with those with a UBH (median 137 [interquartile range (IQR) 62-264] days vs. 231 [IQR 117-395] days, respectively; p<0.0001). A significantly higher proportion of children with RSV infection than UB required HDU/ICU admission (4.3% vs. 1.5%, respectively; p<0.0001). Children with RSV infection also stayed in the HDU/ICU significantly longer (median 5 [IQR 2-8] days vs. UB: 4 [IQR 1-9] days; p=0.01). Overall hospital LOS was significantly longer for those with RSV infection than UB (median 2 [IQR 1-4] days vs. 1 [IQR 0-2] days; p<0.0001).

Epidemiology studies assessing the burden of RSVH should include only children with confirmed RSV infection (using a reliable test), as the inclusion of UB may underestimate the severity of disease.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: Acknowledgements
Matthew Freddi (Strategen Ltd) for editorial services. Funding for his editorial services was provided by AbbVie.

Disclosures
Financial support for this study was provided by AbbVie. AbbVie participated in analysis and interpretation of data, drafting, reviewing, and approving the publication. All authors contributed to the development of the publication and maintained control over the final content.

JC, RT and XCE have received research funding and/or compensation as advisor/lecturer from AbbVie.

BRG and JF, working for Strategen, have previously received payment from AbbVie for work on various projects.

EG is an employee of AbbVie and may hold stock in AbbVie.
CM, working for ISD Scotland, has received payment from AbbVie for work on this project.
ABSTRACT

TITLE: ADVANTAGES IN RESPIRATORY OUTCOMES IN VERY-LOW-BIRTH-WEIGHT FEMALE INFANTS (24 TO 30 WEEKS) SEEM TO BE CONSISTENT THROUGHOUT GESTATIONAL AGE.

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CONTENT:

Several studies have shown differences in outcomes according to sex in Very-Low-Birth-Weight (VLBW) infants favoring females, but some of them suggest that differences disappear with increasing gestational age (GA). The aim of our study was to determine whether there are sex differences in respiratory morbidity, in mortality, and in survival without bronchopulmonary dysplasia in VLBW infants under 30 weeks GA, adjusting for perinatal risk factors, and whether these differences, if present, are consistent throughout different GA.

Retrospective analysis of prospectively collected data of VLBW infants, born at 240 to 306 weeks gestational age (GA) between January 2013 and December 2016 in the collaborative centers of the Spanish Neonatology Society (SEN1500) and in the South American Collaborative Neonatal (NEOCOSUR) Networks. The following patients were excluded: 173 infants (1.6%) who died in the delivery room, 467 (4.2%) with major congenital anomalies (74 of them dying in delivery room), and six infants with ambiguous genitalia or whose sex was not properly. Differences in proportions between sexes were compared by the Chi-square test, and survival without BPD throughout GA by the Cox proportional hazards regression model adjusting for confounding factors. Results are expressed as HR with 95% CI.

During the study period, 11,140 VLBW inborn infants were recorded in the study centers, 6,385 (57.3%) in the SEN1500 network and 4,755 (42, 7%) in Neocosur. After exclusions, 10,568 patients were analyzed. Mean (SD) GA was 27.7 (1.8) weeks; birth weight 1023.1 (257.4) grams; male sex: 53.2%; multiples: 28.1%. Females received more antenatal steroids (at least one dose): 89.8% vs. 88% (p=0.003), and magnesium sulfate: 55.6% vs. 51.3% (p<0.001). Females were born more frequently by C-section: 70.8% vs. 68.7% (p=0.016). After birth, males were intubated more frequently during resuscitation: 46.8% vs. 43.2% (p=0.001), and they received more postnatal steroids for BPD: 11.1% vs. 9.2 (p=0.02). The following Figure shows the incidence of respiratory distress syndrome (RDS), total time of invasive mechanical ventilation, survival and survival without BPD, specific by GA.

After adjusting for confounding factors, female infants exhibited a lower risk of RDS throughout all GA although it was statistically significant from 28 weeks GA on. Among those who needed intubation, the total time of invasive mechanical
ventilation was shorter in females in almost all GA. They also had a consistent higher likelihood of survival and survival without BPD.

IMAGE / TAB: https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=70f3f58269d98ea49b98c2b829fd30a7-MjAxOS0wNSM1Y2UyNjY2YzAxNDImlm

IMAGE / TAB CAPTION:

COI: No conflicts of interest.
ID: 219

TITLE: ASSESSMENT OF NEWBORN BREATH SOUNDS USING DIGITAL STETHOSCOPE TECHNOLOGY

AUTHORS: Ashwin Ramanathan 1; Faezeh Marzbanrad 2; Kenneth Tan 1,3; Fatema-Tuz Zohra 2; Robert Roseby 1,4; Ajay Kevat 1; Atul Malhotra 1,3

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CONTENT:

Digital stethoscopes (DS) offer a convenient, cost-effective and easy to use device, designed to enhance the auscultation capabilities of the modern-day clinician. DS have been used to record and study normal and abnormal breath sounds in the paediatric population, including in conjunction with machine learning to accurately produce automated diagnoses for respiratory pathologies (1). Currently there are no studies documenting the use of this technology to assess breath sounds at birth. We aimed to determine whether DS is a feasible method to capture breath sounds in the transitioning newborn and determine whether there is an identifiable change in sound characteristics with time.


A commercially available DS (Clinicloud Pty Ltd, AUS) and sound acquisition software were used to record breath sounds of term infants (37-40 weeks) born via normal vaginal delivery (NVD) and elective caesarean section (CS) at 1 minute and 2 hours of life. Two 1-minute recordings were taken at each time point from the anterior and posterior chest. Recordings had crying segments removed, a bandpass filter 100-1000 Hz was applied to isolate respiratory sound, and analysis was conducted using MATLAB R2018a (MathWorks Inc, MA, USA). Features such as mean frequency (MF), frequency percentiles (p25, p75), and power within frequency bands: low 100-200 Hz (LBF), medium 200-400 Hz (MBF), high 400-800 Hz (HBF) were used to describe the frequency spread and concentration of the breath sound profile.

A total of 61 newborns were studied. Mean (SD) gestation and weight of 32 NVD infants was 38 (0.9) weeks and 3165.6 (447.1) grams, and 29 elective CS infants was 38 (0.9) weeks and 3222.1 (297.1) grams. 83.6% of 1 minute and 100% of 2-hour recordings were analysable. We found a clear shift in frequency profile to lower range over the first 2 hours with decrease in MF and an increase in the proportion of power in the low frequency band 100-200 Hz. Mean change in NVD cohort: MF 40.50 Hz (p<0.001), p25 46.82 Hz (p<0.001), and LBF 0.16 (p<0.001). Mean change in CS cohort: MF 17.46 Hz (p=0.06), p25 24.66 Hz (p=0.03), and LBF 0.07 (p=0.06). Additionally, in a small number of newborns who developed respiratory distress (RD), we found significant differences in frequency profiles compared to those without RD. Mean difference RD vs no RD: MF 64.05 Hz (p=0.002), LBF 0.15 (p=0.02).

It is feasible to use digital stethoscope technology to assess breath sounds in the newborn during the transition period. We were able to depict a change in breath sound characteristics over the first 2 hours of life in newborns delivered via elective CS and NVD as well as suggesting a recognisable difference in infants with respiratory distress. This may be associated with lung fluid clearance over time and be of clinical importance.

IMAGE / TAB: https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=d03230d158ad2489e351e19295642f3-MjAxOS0wNSM1Y2UyNyYuYzAxYzI2

IMAGE / TAB CAPTION: Average power spectrum comparison for NVD and Elective CS cohorts at 1 minute and 2 hours of life.
COI: None Declared. No author holds any interest in the commercially available stethoscope manufacturer. Dr Atul Malhotra is supported by a Royal Australasian College of Physicians Research Fellowship
ID: 224

TITLE: CEREBRAL AND PERIPHERAL TISSUE OXYGEN SATURATION AND CARDIAC FUNCTION IN NEONATES

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CONTENT:

The cerebral and peripheral tissue oxygen saturation is influenced by oxygen delivery that depends on arterial oxygen saturation and tissue perfusion. Cardiac function affects perfusion and might therefore affect the tissue oxygen saturation. Aim of the present study was to analyse possible associations of cardiac function and regional cerebral and peripheral muscle tissue oxygen saturation (crSO2 and prSO2) on the first day after birth.

Secondary outcome parameters of an observational study conducted in neonates were analysed. Neonates with crSO2 and prSO2 measurements on the first day after birth and in whom echocardiography was performed were included. For near-infrared spectroscopy measurements the sensors were placed on the left forehead and right forearm. Arterial oxygen saturation (SpO2) and heart rate (HR) was measured at the right wrist. Cerebral and peripheral muscle fractional oxygen extraction (cFTOE and pFTOE) were calculated out of crSO2, prSO2 and SpO2. Parameters of cardiac function (left ventricular ejection fraction (EF), the tricuspid annular plane systolic excursion (TAPSE) and superior vena cava (SVC) flow) were correlated to crSO2, prSO2, cFTOE and pFTOE at time of echocardiography.

61 neonates (GA: 34.0±2.8 weeks, BW: 2150±775 grams) were included, of which 14 were born on term and 47 were born preterm. CrSO2 and prSO2 were 76±11% and 87±9%, cFTOE and pFTOE were 0.20±0.11 and 0.09±0.25, respectively. EF was 65±%, TAPSE was 7±2mm and SVCflow was 62±45 ml/kg/min. CrSO2 did not correlate significantly with EF (p=0.173, p=0.223), TAPSE (p=-0.032, p=0.822) and SVCflow (p=-0.083, p=0.657). PrSO2 did not correlate significantly with EF (p=0.251, p=0.089), TAPSE (p=0.787) and SVCflow (p=0.318, p=0.087). CFTOE did not correlate significantly with EF (p=0.099, p=0.509), TAPSE (p=0.039, p=0.792) and SVCflow (p=0.106, p=0.572). PFTOE did not correlate significantly with EF (p=0.221, p=0.144), TAPSE (p=0.213, p=0.155) and SVCflow (p=0.291, p=0.125).

In the present study we found no correlation between the cerebral and peripheral tissue oxygen saturation and cardiac function (EF, TAPSE and SVCflow) in newborn infants on the first day after birth.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 225

TITLE: A preterm neonate-focused, non-invasive nebulized surfactant delivery strategy provides stable lung function improvement in multiple experimental respiratory distress models in line with its lung deposition performance.

AUTHORS: Dani C1, Bianco F2, Perez-de-Sa V3, Rey-Santano C4, Cunha-Goncalves D3, Mielgo V4, Schlun M5, Bucholski A5, Hetzer US, Nord A3, Linner R3, Bonelli S2, Lombardini M2, Pasini E2, Nutini M2, Murgia X6, Villetti G2, Civelli M2, Ricci F2, Minocchieri S7, Sal

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CONTENT:

Non-invasive delivery of nebulized surfactant has been a neonatology long-pursued goal. A phase 2 dose ranging clinical trial (NCT03235986, Figure 1) is ongoing for investigating safety, tolerability, and efficacy of nebulized poractant alfa in premature infants ≥ 28 weeks by a customized eFlow Neos vibrating-membrane nebulizer system in preterm neonates with respiratory distress syndrome (RDS). Prior to human investigation, we characterized in vitro and in vivo this preterm neonate-tailored surfactant aerosolization treatment.

We investigated the aerosol output rate and particle size in vitro by laser-diffraction and Next Generation Impactor (NGI). Lung deposition was studied in vitro by breath-simulation experiments in a preterm upper-airway 3D model (PrIN-T-model) and in vivo by gamma scintigraphy in neonatal piglets managed with nasal continuous positive airway pressure (nCPAP) receiving technetium-labeled surfactant (200 mg/kg). Gas exchange, pulmonary mechanics, and reintubation rate were monitored in surfactant-depleted newborn piglet and adult rabbit RDS models managed with prongs-delivered nCPAP for either 3 or 72 hrs and treated with surfactant nebulization (dose investigated: 100, 200, 400, and 600 mg/kg). Animals treated with a surfactant-bolus (200 mg/kg) or nCPAP-only served as controls (n=9/group).

In vitro investigation identified reproducible aerosol characteristics (volume median diameter of 3.0 μm and respirable fraction of 93.7%) for achieving an average of 17.9% surfactant lung delivery in clinical-like conditions on PrIN-T-model.

Mean lung-deposition in newborn piglets validated these findings (15.9% of the nominal dose) in the in vivo setting. Nebulized surfactant treatments in both RDS models were well-tolerated and, according to the data in Table 1, associated both in acute (for dosages in the interval 200-600 mg/kg), at 3hrs, and at long term (for 400 mg/kg), at 72 hrs post-treatment, with significantly-improved arterial oxygen, lung function, and reintubation rate, comparable to bolus instillation recovery.

On the basis of the preclinical results three doses (200, 400 and 600 mg/kg) have been selected for the clinical investigation. The first part of the trial has been successfully concluded showing the safety of the procedure, the second part of the trial aimed at assessing efficacy is ongoing.

IMAGE / TAB:
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**IMAGE / TAB CAPTION:** Figure 1. Phase 2 clinical trial design.

Table 1. Arterial partial pressure of oxygen versus fraction of inspired oxygen (PaO2/FIO2, mmHg), and dynamic compliance (ml/cmH2O/kg) values ± SEM at confirmation of respiratory distress before treatment and at the end of experiment (3 or 72 hrs according to each study design). Statistical analysis: 2-ways ANOVA with Tukey’s test. *p<0.05 comparing end of experiment value with respiratory distress value. #p<0.05 comparing surfactant treated groups vs. nCPAP group. Reintubation protocol has not been implemented for the 3 hours design. Consequently, values in the reintubation rate column for the 3 hrs studies are reported as not applicable (n.a.).

**COI:** SM, BA, HU are employees of Pari Pharma GmbH. ML, EP, MN, GV, FR, BF, RF, CC, BS, LM, PE, NM, PM, VG, CM, and SF are employees of Chiesi Farmaceutici S.p.A..
MX, MS, and CD served as scientific consultants for this study.
ID: 228

TITLE: Changing Dutch approach towards periviability: evaluating a perinatal guideline implementation

AUTHORS: Pauline van Beek 1; Lisa Broeders 2; Floris Groenendaal 3; Monique Rijken 4; Wes Onland 5; Guid Oei 6; Hendrik ter Horst 7; Frank Schuerman 8; Koen Dijkman 1; Arno van Heijst 9; Frank van den Dungen 5; Ruben Witlox 4; René Kornelisse 10; Marc van der Hoeve

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CONTENT:

In 2010, the Dutch guideline for active treatment of extremely preterm infants was adjusted: the gestational age (GA) threshold for active treatment for spontaneous birth was lowered from 250/7 to 240/7 weeks’ gestation. Our knowledge of the impact of this change on survival is limited. Availability of up-to-date longitudinal, GA-stratified Dutch data on survival is important, as this may influence antenatal counselling, resuscitation policies and evaluation of the guideline. Therefore, the aim of this study was to assess GA-adjusted survival in Dutch extremely preterm infants in the past decade.

In a national cohort study, data from the Dutch Perinatal Registry were used. The study population included 4,990 infants born between 230/7 and 266/7 weeks of gestation in the period between January 1, 2011 and December 31, 2017. As a reference group, 2,162 infants born at the same GA in the period between 1 January 2007 and 31 December 2009 were used. Because of implementation of the guideline in 2010, this year was excluded from the analysis as it was considered as a year of transition.

After guideline implementation, there were significantly more live born infants between 240/7 and 246/7 weeks’ gestation after 2010 (69% vs 63%, as a percentage of total born infants, p = 0.04). Also, there was a significant increase in neonatal intensive care unit (NICU) admission rate (% of live born infants) for 24 weeks’ infants (69% vs 27%, p<0.001). Survival in 24 weeks’ live born infants increased significantly from 13% to 34% (p<0.01), while survival in admitted infants remained comparable (46% before vs 50% after). Figure 1 shows GA-stratified in-hospital survival rates in the years following the implementation of the guideline. Survival in admitted infants in the period 2011-2017 was 50% at 24 weeks’ gestation, 71% at 25 weeks’ gestation and 81% at 26 weeks’ gestation. No trend in survival rate was seen between 2011 and 2017.

Implementation of the 2010 guideline resulted in more live births, more NICU admissions, and increased survival. There were small fluctuations in survival between 2011 and 2017, but no trend in survival rate was seen. Survival rates were comparable to the results of the EXPRESS, EPICure 2 and EPIPAGE-2 studies. Further evaluation of the effect of extremely preterm birth on neonatal complications and long-term outcome is in progress.
IMAGE / TAB CAPTION: Figure 1. In-hospital survival rate (A. % of live born infants, B. % of admitted infants) for subgroups of gestational age in the years following implementation of the guideline, with the years 2007-2009 as a reference period, 2010 as the year of guideline implementation and the years 2011-2017 as the study period.

COI: None declared
ID: 232
TITLE: COMPARISON OF SURVIVAL AND NEONATAL COMPLICATIONS, IN EXTREMELY PREMATURE NEONATES 22+0 -27 +0 WEEKS OF GESTATION, OVER THREE CONSECUTIVE TIME PERIODS.
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CONTENT:

Background: Life support of extremely premature infants increases the chance of survival without increasing the rate of neonatal morbidity. The incidence of short term major neonatal complications remained stable. A significant number of extremely premature neonates presented neurosensory disabilities at 18-30 months corrected age. The aim of the study is to compare survival and neonatal complications in extremely premature neonates from 22+0 to 27+0 weeks of gestational age during three time periods, 2001-2005, 2008-2012 and 2013-2017.

Methods: All neonates with gestational age 22+0-27+0 w. GA., born at our hospital during the above periods were included. Total No=288 babies. In electronic file we recorded: Survival or death , Gestational age, birth weight , clinical characteristics, neonatal complications such as(intraventricular hemorrhage, intraventricular hemorrhage >III grade, periventricular leukomalacia, bronchopulmonary dysplasia, retinopathy of prematurity, laser photocoagulation, necrotizing enterocolitis), and data from the follow up clinic, as far as neurosensory outcome is concern, (blindness, hearing loss, diplegia, hemiplegia, quadriplegia) at 18 months corrected age. Statistical analysis: t-test, X2test, Fisher exact test, Logistic regression analysis.

Results: Survival rate was stable (47 % vs 45.5 vs 40.9). Survivors were significantly more mature (25.4+- 1.03 vs 24.2+-1.3 ), p = < 0.001 and heavier(813.7+ -131 vs 693.06+- 278 ) p = < 0,001 , in comparison with non survivors. Gestational age was (24.8+- 1.34 ) consecutively smaller but not statistically significant between the three time periods. Birth weight (743.3+-231gr ) was significantly smaller in the third time period (p= 0,002) Table 1. Neonatal complications in all three time periods are stable as shown. In follow up an increasing rate (93,10 %, (p= 0,003 ) of babies in the third period were followed. Neurosensory disability in the third period was blindness 0%, hearing loss 3.7%, diplegia 7.4% and total neurological disability 11.1% (p=0,035 ).

Conclusion: In our population survival rate was stable and the birth weight (743.3+-231gr) of survivors was significantly smaller in the third time period (p= 0,002). Neonatal complications were not significantly reduced but the rate of NEC was very low in all time periods. Neurological disability in the 3d period was improved.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=123be746c7b79982c4e7fdd2ef3a27-MjAxOS0wNSM1Y2UyNjY2YzA2YWF1

IMAGE / TAB CAPTION: Short-term complications and neurosensory complications in all three time periods

COI: NONE DECLARED
ID: 234

TITLE: WHY PROSTAGLANDIN INHIBITION IS NOT ALWAYS SUCCESSFUL IN PATENT DUCTUS ARTERIOSUS TREATMENT – A PATHOBIOLICAL VIEW ON PROSTAGLANDIN E2 SIGNALLING IN THE DUCTUS ARTERIOSUS

AUTHORS: Tim Hundscheid 1, Pelle Hoek 2, Martijn van den Broek 2, Willem de Boode 1

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CONTENT:

The ductus arteriosus (DA) is the most intriguing vessel in postnatal haemodynamic transition. In utero patency is maintained mainly due to prostaglandin subtype E2 (PGE2), produced both by the placenta and the DA itself. PGE2 stimulates the PGE2 receptor 4 (EP4) thereby producing cyclic adenosine monophosphate (cAMP) inducing vasodilation. After birth, the production by the placenta seizes and circulating PGE2 is catabolised in the lungs, facilitating DA closure. However, after preterm birth a patent DA (PDA) is commonly seen and might be treated with PGE2 inhibition either with paracetamol or cyclooxygenase (COX) inhibition. Although often successful, failure occurs in a substantial group.

We reviewed the (patho)biological role of PGE2, in utero and after birth, both in term and preterm neonates in an attempt to better understand the reason for therapeutic failure. We reviewed the literature regarding PGE2 and its role in DA patency in utero and postnatal closure. We mainly relied on animal models, in which some contradictory results have been found and it should be noted that due to inter-species differences this cannot always be directly translated to the human infant.

After birth, the vasodilatory effect of PGE2 is reduced as PGE2 concentrations drops and thereby the production of cAMP is reduced. Recently, researchers gained interest in the role of PGE2 in programming the DA for, both functional and anatomical, postnatal closure. This was triggered by the observation that both COX and EP4 knockout mice models unexpectedly presented with PDA. PGE2 concentrations rises as gestation advances, thereby enhancing 1) gene expression of phosphodiesterase, facilitating the breakdown of cAMP; 2) ion channel expression, necessary for oxygen induced Ca2+ influx facilitating vasoconstriction; and 3) intimal cushion formation, necessary for anatomical closure. Apart from this functional immaturity, the preterm DA is not yet dependent on vaso vasorum for oxygenation of the muscle media, compromising anatomical closure after partial vasoconstriction of the lumen.

In advanced gestation, PGE2 not only prevents antenatal DA closure, but is also very important in programming the DA for postnatal functional and anatomical closure by enhanced gene expression. In prematurity this programming is disrupted, presenting as a PDA. Pharmacological inhibition of PGE2, although successful in most patients, does not enhance DA maturity and might even inhibit final DA closure by reduced PGE2 induced gene expression.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 235

TITLE: ACCELEROMETRY ASSESSED PHYSICAL ACTIVITY AS A RESILIENCE FACTOR FOR MENTAL HEALTH AND WELLBEING IN PRETERM BORN EARLY ADOLESCENTS

AUTHORS: Asteria Brylka 1; Dieter Wolke 1; Sebastian Ludyga 2; Anna Gkiouleka 1; Markus Gerber 2; Serge Brand 2,3,4; Natalie Urfre-Maurer 5; Alexander Grob 5; Peter Weber 6; & Sakari Lemola 1

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CONTENT:

Preterm birth increases the risk of later mental health problems. The objective of the current study is to examine whether physical activity is a promotive factor that protects equally preterm and full-term adolescents from negative outcomes or whether it is a resilience factor that benefits especially those born preterm. In particular, we investigate the relationship between objectively assessed physical activity (measured with accelerometry) and self- and parent-reported emotional and behavioral problems and well-being.

Physical activity was measured with accelerometry for 7 consecutive days. Emotional and behavioral problems (emotional problems; hyperactivity/inattention; conduct problems; peer problems) were assessed with the Strengths and Difficulties Questionnaire, and wellbeing (physical wellbeing; psychological wellbeing; moods and emotions; self-perception; social support; school environment; social acceptance/peer bullying) was assessed with the Kidscreen-52 Questionnaire answered by the adolescents and both their parents. Hierarchical regression analyses were used to predict emotional and behavioral problems and wellbeing with physical activity, preterm status, and their interaction (physical activity × preterm status) controlling for sex, age, ethnic background, and parental education.

A sample of 109 adolescents between 11 and 15 years of age from the Basel Study of Preterm Children (BSPC) was studied including 44 children born at 32 weeks of gestation or earlier and 65 term-born controls (age M=12.3 years, SD=1.1). Physical activity was significantly associated with higher levels of child- and parent-reported overall wellbeing, pleasant moods and emotions, and more social acceptance/less bullying by peers among preterm adolescents. Furthermore, we found that higher levels of physical activity were associated with less parent-reported overall mental health problems, lower levels of hyperactivity and inattention, and higher levels psychological well-being and more positive self-perception among preterm adolescents. No significant relationship between physical activity and emotional and behavioral problems and wellbeing emerged for term-born adolescents.

The study shows that physical activity associates with positive mental health and wellbeing in preterm born adolescents suggesting that it may act as a resilience factor particularly for this group. A mediating mechanism could be related to improved self-image and better peer acceptance. Intervention research is needed to elucidate causality and to inform about the relevant mediating mechanisms.

COI: None declared
ID: 236

TITLE: THE CURRENT TREND TOWARDS CONSERVATIVE TREATMENT FOR PATENT DUCTUS ARTERIOSUS IN PREMATURITY – HOW EVIDENCE BASED IS IT?

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CONTENT:

A patent ductus arteriosus (PDA) is common in preterm and very low birth weight infants (VLBWI). PDA is associated with mortality and neonatal morbidity, such as bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC) and intraventricular haemorrhage (IVH). Although both pharmacological and surgical treatment show a significant effect on ductus arteriosus closure rate, overall clinical outcome is not improved. Together with growing evidence of high rates of spontaneous closure in untreated patients, this has led to an increase in a conservative approach towards a PDA in which preterm infants are withheld from possible adverse effects of pharmacological treatment.

We performed a systematic literature review from 2000 till 2018 in PubMed, EMBASE and CENTRAL with the following search terms preterm infant, VLBWI, PDA, conservative treatment and placebo. We included both randomised controlled trials (RCTs) and cohort studies if they compared a conservative approach with at least one intervention group. Since many studies have high open label treatment rates we only included studies with an open label treatment rate <25%. Outcome measurements of a conservative approach for a PDA in preterm (gestational age <32 weeks) and/or VLBWI compared to both pharmacological and/or surgical treatment were extracted, analysed in Review Manager Software for meta-analysis with random effects model and presented as risk ratios (RR) with 95% confidence interval (95%-CI).

Our search revealed 401 unique articles, of which 15 could be included. Three articles were RCTs. From the included cohort studies 11/12 were retrospective. There was a heterogeneity in diagnostic approach and criteria for (haemodynamic significant) PDA. Conservative treatment ranged from watchful waiting to fluid restriction, diuretics and/or ventilator adjustments.

Conservative treatment was associated with a significant increased RR for mortality, but a significant reduced RR for BPD, IVH and ROP (Table). Since most studies were retrospective there is a high risk of treatment/selection bias, since patients were treated conservatively due to contraindications for either pharmacological and/or surgical treatment or due to a benign phenotype. This might explain the current finding of an increased risk of mortality on the one hand and a decreased risk of morbidity on the other hand.

The current trend towards a conservative approach is based on scarce, mainly retrospective and very heterogeneous cohort studies. In an attempt to answer the question whether we should treat a PDA in preterm infants or not we cannot rely on this retrospective data. Currently recruiting RCTs like the BeNeDuctus trial will form a less heterogeneous group and will give more insight whether the current conservative treatment trend remains valid.

IMAGE / TAB:
https://www.eiseverywhere.com/eeselectv3/v3/events/351149/submission/files/download?fileID=5bd761f9371d81c3b9be2fbac032daa1-MjAxDsOWNMM1Y2UyNyY2YzA4MzI=

IMAGE / TAB CAPTION: Conservative treatment versus any (pharmacological and/or surgical) treatment BPD, bronchopulmonary dysplasia; IVH, intraventricular haemorrhage; NEC, necrotizing enterocolitis; ROP, retinopathy of prematurity; 95%-CI, 95% confidence interval
COI: None declared
TITLE: THE EFFECT OF A FACE MASK FOR RESPIRATORY SUPPORT ON BREATHING IN PRETERM INFANTS AT BIRTH

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CONTENT:

Applying a face mask for respiratory support could induce a trigeminocardiac reflex leading to apnoea and bradycardia. We explored the effect of applying a face mask on breathing and heart rate in preterm infants at birth.

Resuscitation videos of infants ≤ 32 weeks gestation recorded from 2010 until 2018 at the Leiden University Medical Centre and the General University Hospital in Prague were reviewed. Infants received respiratory support via face mask. Breathing and heart rate before and after application of the face mask and in the first 5 minutes were noted.

Recordings of 429 infants were included (median (IQR) gestational age of 28+6 (27+1-30+4) weeks). In 368/429 (86%) infants breathing was observed initially of which 197/368 (54%) infants stopped breathing after application of the face mask. Apnoea occurred after 5 (3-17) seconds after application of the face mask with a duration of 28 (22-34) seconds in the first minute. In a logistic regression model, the occurrence of apnoea after face mask application was inversely associated with gestational age (OR=1.424 (1.281-1.583), p<0.001). In infants who stopped breathing, a significantly lower heart rate (84 (66-125) vs 134 (100-152) bpm, p<0.001) and oxygen saturation (49% (33-59) vs 66% (50-82), p<0.001) was observed in the first minute after face mask application when compared to infants who maintained breathing.

Applying a face mask for respiratory support affects breathing in a large proportion of preterm infants and this effect is gestational age dependent.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 250

TITLE: PLATELET COUNT WITHIN THE FIRST WEEK OF NICU ADMISSION MAY PREDICT IVH SEVERITY IN VERY PRETERM INFANTS

AUTHORS: Fatma Nur Sari 1; Mehmet Buyuktiryak 2i; Evrim Alyamac Dizdar 3; Cuneyt Tayman 4; Serife Suna Oguz 5

AFFILIATIONS: University of Health Sciences, Ankara Dr Zekai Tahir Burak Women's Health, Health Application and Research Center, Ankara, Turkey

CONTENT:

Despite recent advances in neonatal care, the absolute numbers of infants with intraventricular hemorrhage (IVH) still remain significant which is due to the increased survival rate of very preterm infants. In this study we aim to determine whether there is an association between platelet indices and severity of IVH in very preterms.

Preterm infants born before 32 weeks of gestation and hospitalized in the NICU were retrospectively evaluated. Platelet counts, mean platelet volume, platelet distribution width and platelet mass of the infants on the first day of life (DOL) and on DOL 2-7 were recorded. IVH was evaluated by cranial ultrasonography according to standard NICU protocol. The infants further categorized according to findings of cranial ultrasonography as; no IVH, mild IVH or severe IVH.

Totally, 1051 infants were evaluated. Mean gestational age and birthweight of the whole cohort were 27.9±1.6 weeks and 1058±247 g, respectively. Of the infants, 93 (9%) were diagnosed with severe IVH. Severe IVH group had a lower gestational age (p<0.001) and birthweight (p<0.001) compared to no or mild IVH groups. Male gender and mechanical ventilation were more common in severe IVH group. There were significant differences with regard to platelet count and platelet mass between groups on the first DOL and on DOL 2-7. Moreover, trombocytopenia on the first and 2-7 DOL was significantly higher in infants with severe IVH. Logistic regression analysis revealed that gestational age, male gender, mechanical ventilation and thrombocytopenia on 2-7 DOL were independently associated with the severity of IVH.

Consideration of gestational age along with gender and platelet count may be a predictor of severe IVH in very preterms.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 251

TITLE: COGNITIVE TRAJECTORIES OF ADULTS BORN VERY PRETERM AND SMALL FOR GESTATIONAL AGE

AUTHORS: Robert Eves 1; Marina Mendonça 1; Peter Bartmann 2; Dieter Wolke 1,3

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CONTENT:

Very preterm or very low birthweight (<32 weeks gestation/ <1500g; VP/VLBW) infants have been found to be at sustained risk of cognitive deficits into adulthood. Additional risk factors, such as being born small for gestational age (SGA) are debated, partially due to differences in method of classification. VP/VLBW infants are less likely to be classified SGA when using neonatal rather than ultrasound-based references. In addition, social environmental factors such as socioeconomic status (SES) or the parent-infant relationship have largely been overlooked in the VP/VLBW literature. Thus, the aim of this study was to determine longitudinal effects of these early risk factors on cognition.

217 VP/VLBW and 197 term born participants from the prospective Bavarian Longitudinal Study were assessed with developmental and IQ tests from 5 months to 26 years of age. At birth, participants were classified as SGA if they weighed below the 10th percentile for their gestation; determined either by a German neonatal birth database or an ultrasound-based reference. Linear mixed models were used to determine the cognitive trajectories of participants. Analyses were performed using both references for classifying SGA. Effects of VP/VLBW, SGA and social environmental factors were considered as fixed effects. Final models included interactions between VP/VLBW, SGA and time.

Classifying SGA upon the neonatal and ultrasound reference resulted in 61 (28%) and 117(54%) VP/VLBW participants determined to be SGA respectively. In the linear mixed models, VP/VLBW participants performed poorer on cognitive tests than term born participants at all time points. In comparison to participants born at appropriate weight for gestational age, SGA participants classified by neonatal and ultrasound references were determined as having an average deficit of 7.37 and 8.45 IQ points respectively (both p<0.05). No interactions were found, indicating the persistence and main effects of VP/VLBW and SGA over time. High parental SES was associated with an increase of 14 IQ points as compared to low parental SES in both SGA models (p<0.001). A poor parent-infant relationship was associated with an IQ deficit of 10 points in both SGA models (p <0.001).

Different references result in large disparities in the number of VP/VLBW participants classified as SGA. However, this does not appear to change the conclusions that SGA is a sustained risk factor on cognition. Importantly, more modifiable social environmental risk factors were found to have larger effects on cognitive function than SGA, with implications for interventions.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 257  
TITLE: AN EPIC INTERVENTION: PEER TO PEER SUPPORT NETWORK AND POSITIVE FEEDBACK SYSTEM TO IMPROVE JUNIOR DOCTOR MORALE AND WELLBEING WITHIN THE NEONATAL UNIT.

AUTHORS: Magali Dubus 1; Olatokunbo Sanwo 2; Shaveta Mulla 3

AFFILIATIONS: Neonatal Intensive Care Unit, William Harvey Hospital, Ashford, Kent, United Kingdom.

CONTENT:

Burnout is increasingly recognised as a problem among junior doctors; contributing to low morale, physical and mental health issues. Within the United Kingdom there are various regional and national initiatives to support doctors, however local support is variable. Paediatric and neonatal doctors often work in isolation from other specialties, rarely getting the opportunity to share experiences and discuss difficulties with colleagues. We aimed to lead a regular peer-led meeting discussing positive and negative aspects of training, allowing colleagues to come together to solve problems. We also aimed to improve the amount of positive feedback given within the department.

We introduced a monthly peer-led meeting called "Holding Hands" with a set agenda addressing both positive and negative aspects (clinical and non-clinical) of working life, inviting all paediatric and neonatal junior doctors. A dedicated consultant who helped develop the project, provided support and promoted the project also attended one meeting every three months. In conjunction with this we introduced Encouraging Praise in Colleagues (EPIC), a formal positive feedback system, where members of the healthcare team were encouraged to provide feedback on examples of good clinical and personal practice. Data on EPIC were collated via the nomination system. We distributed a modified Copenhagen Psychosocial Questionnaire at the start of the project and after 6 months of Holding Hands meetings.

Likert scales were used to measure a number of outcomes; in comparison to the pre-meeting questionnaire less people felt there was an uneven distribution of work, more people felt supported by colleagues, motivated, involved in work and that they had positive feedback from seniors. 88.9% knew where they could find support for an emotionally challenging situation. EPIC was widely accepted in the department, reflected in the increasing number of nominations which grew to involve the whole multidisciplinary team. This was such a success that it has been adopted by other specialties and will be implemented trust-wide. We also gained qualitative data confirming that this initiative has been helpful to attendees.

In order to deliver high quality and excellent levels of patient care, we have a responsibility to look after our own and our colleagues’ wellbeing. Holding Hands and EPIC have provided a safe, supportive atmosphere for trainees to develop and improve resilience, equipping them with the emotional skills to be able to handle the pressures of clinical work while embedding a culture of positive feedback and community within the team.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 258

TITLE: FACTORS ASSOCIATED WITH PORTAL VEIN THROMBOSIS AFTER UMBILICAL VEIN CATHETERIZATION: IMPLICATION OF THERAPEUTIC HYPOTHERMIA

AUTHORS: Marina Colella 1,2; Anna Zanin 1,3; Paul Picq 4; Marianne Alison 2,5; Sophea Khat 1; Sophie Guilmin-Crepon 4; Olivier Baud 2,6; Valerie Biran 1,2

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CONTENT:

Neonatal portal vein thrombosis (PVT) is generally related to umbilical venous catheterisation (UVC). Nevertheless, sepsis, hemodynamic instability and perinatal asphyxia are recognised risk factors for venous thrombosis but their contribution to neonatal PVT is not clear. Nowadays, therapeutic hypothermia (TH) is the only treatment in case of hypoxic ischemic encephalopathy. Infants undergoing TH have an increased risk for cerebral thrombosis, but the incidence of PVT in this population is currently unknown.

The aim of our study was to analyse the factors associated to neonatal PVT after UVC and to determine if TH can independently increase PVT incidence in newborns.

We performed a monocentric observational prospective analysis of collected data from January 2012 to December 2017 at Robert Debré University Children’s Hospital, Paris, France. All infants with a gestational age (GA) ≥ 36 weeks and a neonatal weight ≥ 1500 g admitted in NICU were considered eligible for this study if a UVC was placed and if they underwent an abdominal radiography and at least one abdominal ultrasound in the first 10 days of life. Clinical data referred to the pregnancy, birth and the clinical evolution within the first 10 days were recorded. Hypothermia protocol was applied according to the established recommendations. Grade and localisation of PVT were also evaluated.

PVT was diagnosed in 57 (27%) of 213 patients included in the study. 87 infants (41%) were cooled for hypoxic ischemic encephalopathy. TH was significantly associated with PVT (P=.01). PVT was nearly 2 times more frequent in cooled infants than in control group (OR 1.94; P=.04). Nearly all PVT (54) were localized in the left portal vein branch; 28 (49%) were of grade 1, 22 (39%) of grade 2 and 7 (12%) of grade 3. There were no significant differences in gender, birth weight, intrauterine growth, preeclampsia, maternal diabetes or antenatal steroid therapy. Apgar score, cord pH, lactates, haemoglobin and platelets did not differ between the groups. Clinical complications as sepsis were similar in the 2 groups. The inappropriate location of UVC was not more frequent in PVT group; in contrast, the duration of UVC was related to an increased risk of PVT (OR 1.36; P=.008).

Left portal venous thrombosis is often observed in nearly term neonates who need an UVC placement. Asphyxiated cooled infants are particularly at risk to develop PVT. We could suggest to limit the duration of UVC and to control the presence and evolution of PVT with routine ultrasound. However, further studies with larger sample sizes are needed to determine the effect of the detection and treatment of PVT, especially in infants undergoing TH.
IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=445d5352d1f87c299a61850dcb4183e0-MjAxOS0wNSM1Y2UyNjY2YzEwZTU4

IMAGE / TAB CAPTION: Figure 1. Portal vein thrombosis (PVT) prevalence in therapeutic hypothermia (TH) group and no TH group (P = .01).

COI: non declared
ID: 260

TITLE: PERINATAL HYPOXIC-ISCHEMIC INJURY OF THE CEREBELLUM: ANTEMORTEM DIFFUSION WEIGHTED IMAGING VERSUS POSTMORTEM HISTOLOGY

AUTHORS: K.V. Annink 1,2; F.E. Hoebeek 2,3; N.E. van der Aa 1,2; T. Alderliesten 1,2; P.G.J. Nikkels 4; C.H.A. Nijboer 2,3; F. Groenendaal 1,2; L.S. de Vries 1,2; M.J.N.L. Benders 1,2; J. Dudink 1,2.

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4 Department of Pathology, University Medical Centre Utrecht, University Utrecht, the Netherlands

CONTENT:

Cerebellar injury is frequently seen in postmortem pathological examination in infants with severe hypoxic-ischemic encephalopathy (HIE), but is, in contrast to supratentorial damage, less visible on diffusion weighted imaging (DWI). The primary aim of this study was to investigate the correlation between the cerebellar apparent diffusion coefficient (ADC)-values on DWI and the extent of histological cerebellar injury in infants with HIE. The secondary aim was compare ADC-values in the cerebellum of infants with HIE to neonates without brain injury.

In this retrospective study, (near-)term infants with HIE with postmortem autopsy and antemortem DWI within 7 days after birth (median 4) were included. ADC-values were measured in the cerebellar vermis, hemispheres and nucleus dentatus (ND) using Horos Imaging software. ADC-values were also measured in a group of neonates with congenital non-cardiac anomalies and normal postoperative MRI (range 3-13; median 7.5) without underlying syndromes. Mean ADC-values were compared using the Mann-Whitney-U test. Histological HLA-DR and CD68 stains of the cerebellar hemispheres, vermis and ND were binarized using ImageJ software. The mean CD68 and HLA-DR positive areas were calculated for these structures. The correlation between ADC-values and the CD68 and/or HLA-DR positive area was calculated.

Thirty-three infants with HIE and 22 infants without brain injury were included. ADC-values in the cerebellar hemispheres were comparable between infants with HIE and the infants without brain injury. ADC-values in the vermis (HIE=786±114 x10-6mm2/s; controls=859±72 x10-6mm2/s; p=0.021) and ND (HIE=1004±152 x10-6mm2/s; controls=1142±79 x10-6mm2/s; p<0.001) were significantly lower in infants with HIE. There were no significant correlations between ADC-values and the CD68 or HLA-DR positive area in the cerebellar vermis, hemispheres or ND.

Infants with HIE with lower ADC-values did not have more microglia activation and macrophage influx. ADC-values in the vermis and ND in patients with severe HIE were significantly lower than in controls. ADC-values in the cerebellar hemispheres were not decreased in infants with HIE. Hematoxylin and eosin stains are currently analysed to study Purkinje cell injury in HIE.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: Floris Groenendaal is expert witness in cases of perinatal asphyxia, the other authors have no conflict of interest to declare.
ID: 266

TITLE: VARIATION IN DIAGNOSTIC CRITERIA FOR HEMODYNAMICALLY SIGNIFICANT PDA IN RANDOMIZED CLINICAL TRIALS: A SYSTEMATIC REVIEW

AUTHORS: Kaitlyn Sheffield 1; Souvik Mitra 2

AFFILIATIONS: 1 Maternal Newborn Program, IWK Health Centre, Halifax, NS, Canada
2 Division of Neonatal Perinatal Medicine, Dalhousie University, Halifax, NS, Canada

CONTENT:

Management of the hemodynamically significant PDA (hs-PDA) has been extensively explored through randomized clinical trials (RCTs). Meta-analyses of such trials often show substantial statistical heterogeneity thus leading to low certainty of evidence. Different diagnostic criteria have been used to diagnose hs-PDA in randomized trials. However, none of the large systematic reviews including Cochrane Neonatal reviews on PDA management have ever explored variability in PDA diagnosis as a potential source of heterogeneity.

Objective: To describe the variability in diagnostic criteria for hs-PDA in randomized clinical trials.

A systematic review of randomized control trials (RCTs) on the management of hs-PDA in preterm infants was conducted. MEDLINE (on OVID platform), EMBASE (on OVID platform), and CENTRAL (Cochrane Central Register of Controlled Trials) were searched up to April 2019. Two reviewers independently screened the search results and applied the inclusion criteria. The included studies were then evaluated for the variation in diagnosis of hs-PDA. Diagnostic criteria were categorized into clinical and echocardiographic. Data was extracted and checked in duplicate.

77 RCTs were included in our review. hs-PDA was predominantly diagnosed by echocardiography only in 43 (55.8%) studies, followed by combined clinical and echocardiographic criteria in 31 (40.3%) studies (Table 1a.). Of the echocardiographic criteria, PDA size and left atrial to aortic root ratio (LA:Ao) were most commonly used. Cut-offs for PDA size ranged from 1.3mm to 1.8mm while cut-offs for LA:Ao ratio ranged from 1.15 to 1.7 (Table 1b.). Only 16 (20.8%) studies used additional measures of PDA shunt volume beyond PDA size and LA:Ao ratio, diastolic disturbance in left pulmonary artery being the most commonly used measure. Only 2 studies graded the PDA as mild, moderate or severe based on echocardiographic criteria.

Wide variation in diagnostic criteria for hs-PDA exists in randomized trials of PDA management. Variation in diagnosis of hs-PDA could be an important contributing factor to heterogeneity obtained in meta-analysis of RCTs on PDA management. Future randomized trials and systematic reviews should use subgroup analyses based on the degree of hemodynamic significance to tease out the effects of this diagnostic variability.

IMAGE / TAB:
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IMAGE / TAB CAPTION: Characteristics of PDA diagnostic criteria in randomized clinical trials

COI: None declared
ID: 268

TITLE: SUSTAINED INFLATION VS INTERMITTENT POSITIVE PRESSURE VENTILATION OR CONTINUOUS POSITIVE AIRWAY PRESSURE DURING NEONATAL RESUSCITATION OF PRETERM INFANTS: AN UPDATED META-ANALYSIS

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CONTENT:

Lung aeration is critical for newborn transition after birth. Respiratory interventions to support lung aeration in preterm infants include intermittent positive pressure ventilation (IPPV) and sustained inflation (SI).

Previous clinical trials of SI demonstrated improved short-term respiratory outcomes in preterm infants, but these results are not consistent. The recently completed Sustained Aeration of Infant Lungs (SAIL) trial compared SI with IPPV to prevent bronchopulmonary dysplasia or death among extremely preterm infants. We undertook this study to update the existing meta-analyses of SI to include the SAIL trial results.

A standard search was conducted for RCTs of preterm infants comparing SI (>5 seconds) versus standard resuscitation with IPPV or continuous positive airway pressure (CPAP). Studies with other co-interventions were excluded.

The primary outcome was death during hospitalization. Gestational age (GA) subgroup analyses were performed for the primary outcome. Secondary outcomes included death in the delivery room (DR), death in the first 2 days, DR CPR, DR intubation, mechanical ventilation in the first 72 hours, surfactant administration in the first 72 hours, air leaks, severe brain injury, BPD, treatment for PDA, and severe ROP.

Data were analyzed with fixed effects meta-analysis, and risk difference was calculated using Bohning approach.

We identified and screened 115 original references, assessed 37 texts for eligibility, and included 9 trials of 1,406 preterm infants. The pooled analysis favored the control group for the primary outcome of death during hospitalization, but this association was not statistically significant, risk difference (RD) 0.04 (95% Confidence Interval [CI] -0.01, 0.08) (Figure).

There was no significant difference in the risk for the primary outcome of death prior to hospital discharge in subgroup analysis based on the following gestational age subgroups: 23-24 weeks; 25-26 weeks; 27-31 weeks; 32-36 weeks.

In pooled analysis, SI was associated with increased risk of the secondary outcome of death in the first 2 days, RD 0.03 (95% CI 0.01, 0.05). There were no significant differences between treatment groups for any of the other secondary outcomes.

Pooled analysis of 1,406 preterm infants in 9 RCTs favors the control group over SI for the outcome of death during hospitalization, but the result does not reach statistical significance. SI is associated with increased risk of death in the first 2 days after birth, and there is no evidence of efficacy for SI to prevent other secondary outcomes. These results do not support the routine use of SI after birth among preterm infants.
IMAGE / TAB: 
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=6119b4d35957a234ca635801b85582-MjAxOS0wNSM1Y2UyNjY2YzE1N2Fm

IMAGE / TAB CAPTION: Forest Plot for Primary Outcome: Death During Hospitalization

COI: Financial Disclosures: M. Keszler : Draeger Medical, Inc (Grant/Research Support, Honorarium) and Mallinckrodt, Inc. (Grant/Research Support); C.Dani: Chiesi Farmaceutici Spa (Consultancy) and Orphan Europe (Consultancy) 
No other conflicts of interest declared.
ID: 272

TITLE: LATE ONSET VITAMIN K DEFICIENCY BLEEDING IN AN EXTREMELY PRETERM INFANT RECEIVING AN EXCLUSIVE HUMAN MILK DIET AND A HUMAN MILK DERIVED FORTIFIER

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CONTENT:

All newborns need phylloquinone (vitamin K1; K1) after birth to prevent vitamin K deficiency bleeding (VKDB). In preterm babies, the main sources are prophylactic K1 given at birth and parenteral and/or enteral nutritional intake. However, preterm babies remain at risk of deficiency if ongoing K1 supplementation during infancy is inadequate. Human milk fortification with either bovine milk based fortifier or human milk derived fortifier (HMF) made from pooled donor milk is a widely utilised strategy to improve the vitamin status and growth of preterm infants. Here, we present a case of late-onset VDKB in an extremely preterm infant who received an exclusive human milk diet and HMF.

A female infant was born at 23+5 weeks gestation via spontaneous vaginal delivery with a birth weight of 555 grams (25th centile). Antenatal sonography and maternal serology were unremarkable. There was no history of maternal medication use.

She required

Preterm babies fed an exclusively human milk-derived diet (including HMF) receive inadequate K1 intake and may be at risk of VKDB without additional K1 supplementation. In this case, the prompt clinical suspicion and treatment may have prevented sentinel bleeding progressing to life-threatening intracranial bleeding. In addition, it highlights the value of PIVKA-II assay for retrospective confirmation of VKDB, even several days post treatment.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 274

TITLE: COMPARISON OF STANDARD VERSUS HIGH DOSE IBUPROFEN FOR THE TREATMENT OF HEMODYNAMICALLY SIGNIFICANT PATENT DUCTUS ARTERIOSUS IN PRETERM INFANTS

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CONTENT:

Hemodynamically significant patent ductus arteriosus (hs-PDA) in premature neonates can lead to persistent ductal shunting which may result in pulmonary hyperperfusion and bronchopulmonary dysplasia (BPD), as well as systemic hypoperfusion, necrotizing enterocolitis (NEC), and renal failure. Standard-dose intravenous (IV) ibuprofen has been used as first-line therapy for the treatment of hs-PDA. Recent evidence suggests that the use of high-dose IV or oral ibuprofen is associated with a greater likelihood of PDA closure, without increasing adverse outcomes. The objective of this study was to examine the effectiveness and safety of high-dose ibuprofen (oral or IV) for hs-PDA closure.

This is a single-center, retrospective, observational study of preterm infants who received ibuprofen for hs-PDA treatment. The study is divided into two separate time epochs (June 2015-May 2017; June 2017-February 2019) reflecting changes to the centre-wide ibuprofen dosing protocol from standard (Dose 1: 10 mg/kg, Dose 2,3: 5 mg/kg) to high-dose ibuprofen (Dose 1: 15-20 mg/kg, Dose 2,3: 7.5-10 mg/kg). The primary outcome is need for PDA ligation. Secondary outcomes are need for repeat pharmacotherapy, oliguria, BPD, and NEC. Inverse probability weighted marginal structural equations were constructed to explore the association of ibuprofen dosage with clinical outcomes. Categorical data were analyzed by X2 tests. Continuous data were analyzed by unpaired t-test or Mann-Whitney U tests.

Fifty-five neonates were included (Nstandard-dose=36; Nhigh-dose=19) in the analysis. The groups were similar at baseline with a mean birthweight (BW) of 902 (±262) g, gestational age (GA) of 26.4 (±2.3) weeks, and time to ibuprofen initiation of 7.9 (±5.4) days. Following the introduction of high-dose ibuprofen, there was a 22.8% absolute reduction in PDA ligation rate in epoch 2 (p=0.06). There were no differences in the need for repeat pharmacotherapy (p=0.78), oliguria (p=0.51), or NEC (p=0.79) between groups. The inverse probability weighted marginal structural equations adjusting for GA, BW, time to first ibuprofen dose, antenatal steroids, and prophylactic indomethacin use showed that high-dose ibuprofen was independently associated with a significant reduction in PDA ligation rates (OR: 0.05, 95% CI: 0.01-0.42; p=0.005).

Introduction of high-dose ibuprofen was associated with a 20-fold reduction in PDA ligation rates. There were no increases in adverse outcomes, such as oliguria or NEC, in neonates being treated with high-dose ibuprofen for hs-PDA when compared to neonates being treated with standard-dose ibuprofen.

IMAGE / TAB:
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IMAGE / TAB CAPTION: Table 1. Baseline characteristic and study outcome data.

COI: None declared
ID: 275

TITLE: EFFECTS OF HOLDER PASTEURIZATION ON LEVELS OF METABOLIC HORMONES IN HUMAN MILK

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CONTENT:

During human development, environmental conditions can be communicated by signaling molecules delivered across the placenta or within breast milk. While the fetus or newborn matures, hormones exert both metabolic and trophic effects on target organs. Preterm infants are deprived of the transplacental hormone transfer that typically occurs during the final months of pregnancy, but they have two potential sources of human milk, their own mothers and milk bank donors. When donor milk replaces maternal milk, Holder pasteurization (HoP) is required, but that process may further impact the concentration of metabolic hormones in the breast milk.

Breast milk samples were donated by 26 mothers who gave birth to preterm infants hospitalized in the University of Iowa Children’s Hospital. At the Mother’s Milk Bank of Iowa, 31 donor mothers breastfeeding their term infants were recruited. Leptin, cortisol, insulin, luteinizing hormone, thyroid-stimulating hormone, and follicle-stimulating hormone were measured in the preterm milk and donor milk samples by custom magnetic bead array. Then, the donor samples were processed by HoP, heating at 62.5 °C for 30 min, and the microarray was repeated. Samples were run in duplicate, and the data were analyzed by two-way ANOVA. The study was powered to detect moderate effect sizes (Cohen’s d = 0.6).

Compared to donor milk, leptin levels were significantly higher in milk provided by mothers of preterm infants (586 ± 121 [m ± SEM] vs. 198 ± 28 pg/ml, P<0.01), and leptin concentration was significantly decreased by HoP in both cohorts (HoP preterm: 52 ± 15 pg/ml and HoP donor: 34 ± 9). Cortisol concentration was not affected by HoP, but HoP donor milk contained significantly higher cortisol level compared to the preterm milk samples (4063 ± 707 vs. 1471 ± 433 pg/ml, P<0.01). Insulin concentration was not influenced by cohort or HoP. Pituitary glycoprotein hormones were present in similar amounts in human milk produced for preterm infants and term infants, but HoP increased the concentration of TSH by 17% (P<0.05), decreased the LH level by 29% (P<0.05), and did not influence FSH concentration.

In a hormone-specific fashion, the content of breast milk is impacted by maternal factors and HoP. Compared to non-pasteurized maternal milk, provision of HoP donor milk to preterm infants decreases leptin and LH intake and increases cortisol and TSH exposure. Further research is necessary to define the breast milk feeding practices that best mirror intrauterine hormone exposure and optimize the development of highly vulnerable preterm infants.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
Neonatal hypoglycaemia is common and associated with neurodevelopmental impairment. Guidelines recommend screening infants with risk factors for neonatal hypoglycaemia, including small for gestational age (SGA) and large for gestational age (LGA). Without calculated birth weight centiles, usually required to identify SGA and LGA infants, clinicians may not identify infants at-risk of neonatal hypoglycaemia. We aimed to determine if the introduction of routine calculation of birth weight customised centiles in all infants improved adherence to a neonatal hypoglycaemia guideline and if adherence to the guideline was associated with the identification of neonatal hypoglycaemia in at-risk infants.

Retrospective audits of adherence to the neonatal hypoglycaemia guideline in a tertiary maternity hospital in Auckland, New Zealand in a randomly selected cohort of newborn infants at risk of neonatal hypoglycaemia before (2011) and after (2015) the introduction of routine use of calculated birth weight centiles for all infants. Inclusion criteria were newborns at-risk of hypoglycaemia: infants of diabetic mothers (IDM), late preterm, SGA and LGA infants. The primary outcome was adherence to the guideline, defined as (i) blood glucose concentration screening in the first 48h after birth, (ii) the initial measurement taken 1-2h after birth, and (iii) at least three consecutive blood glucose concentrations ≥2.6mmol/L, over 12h, prior to cessation of screening.

The records of 400 infants (200 each in 2011 and 2015) were included. The proportion of infants with any blood glucose concentration screening was greater in 2015 (106/200 (53%) v 167/200 (84%), p<0.001). Adherence improved from 2011 to 2015 (59/200 (30%) v 95/200 (48%), p<0.001), with the largest improvement in LGA infants (7/50 (14%) v 25/50 (50%), P=<0.001). Guideline adherence was more likely for IDM than infants with other risk factors (IDM, 63/100 (63%), Preterm 33/100 (33%), SGA 26/100 (26%), LGA 32/100 (32%), p<0.001). Adherence to the guideline was higher in infants born by caesarean section than in infants born by vaginal delivery (caesarean 79/161 (49%) v vaginal 75/239 (32%), p<0.001). Screened infants whose care was adherent to the guideline had a higher incidence of hypoglycaemia detection (adherent, 64/154 (42%) versus non-adherent, 34/246 (14%), p<0.001).

Routine use of calculated birth weight centiles was associated with improved adherence to the neonatal hypoglycaemia guideline and increased detection of neonatal hypoglycaemia in at-risk infants. Thus, identifying practices that improve guideline adherence may improve the detection of hypoglycaemia in asymptomatic at-risk infants.

ID: 277
TITLE: ADHERENCE TO NEONATAL HYPOGLYCAEMIA SCREENING GUIDELINES: A RETROSPECTIVE COHORT STUDY
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CONTENT:

The records of 400 infants (200 each in 2011 and 2015) were included. The proportion of infants with any blood glucose concentration screening was greater in 2015 (106/200 (53%) v 167/200 (84%), p<0.001). Adherence improved from 2011 to 2015 (59/200 (30%) v 95/200 (48%), p<0.001), with the largest improvement in LGA infants (7/50 (14%) v 25/50 (50%), P=<0.001). Guideline adherence was more likely for IDM than infants with other risk factors (IDM, 63/100 (63%), Preterm 33/100 (33%), SGA 26/100 (26%), LGA 32/100 (32%), p<0.001). Adherence to the guideline was higher in infants born by caesarean section than in infants born by vaginal delivery (caesarean 79/161 (49%) v vaginal 75/239 (32%), p<0.001). Screened infants whose care was adherent to the guideline had a higher incidence of hypoglycaemia detection (adherent, 64/154 (42%) versus non-adherent, 34/246 (14%), p<0.001).

Routine use of calculated birth weight centiles was associated with improved adherence to the neonatal hypoglycaemia guideline and increased detection of neonatal hypoglycaemia in at-risk infants. Thus, identifying practices that improve guideline adherence may improve the detection of hypoglycaemia in asymptomatic at-risk infants.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 280
TITLE: VISUAL PERCEPTION, FINE MOTOR, AND VISUAL MOTOR SKILLS IN VERY PRETERM AND TERM BORN CHILDREN BEFORE SCHOOL ENTRY
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CONTENT:

Survival rates of very preterm [VP] infants have increased over past decades. While prevalence of severe disabilities has decreased, VP children are still at risk of developmental delay in visual perception, fine motor, and visual-motor skills (Geldof, et al., 2016; Hitzert, et al., 2014; Thomas, et al., 2017). We hypothesized that VP children born after 2010 would show lower average performance and higher rates of developmental delay in visual perception, fine motor, and visual-motor skills than term born controls.

A sample of n = 60 very preterm children (<32 weeks gestation; mean [M] age 5.9 years, standard deviation [SD] = 0.3; 50% females) and n = 60 matched term-born control children (M age 5.9 years, SD = 0.3; 50% females) were examined with the Movement Assessment Battery for Children – 2 (M-ABC-2) and the Developmental Test of Visual Perception (DTVP-2). Multiple and logistic regressions were run to test differences between groups in performance and rates of clinically diagnosed developmental delay in visual motor skills, fine motor skills, and visual perception. Socioeconomic status (SES) and sex were added as covariates.

Very preterm children were less skilled in visual motor tasks ($\beta = -0.461$; p < .001), fine motor tasks ($\beta = -0.435$; p < .001), and visual perception Tasks ($\beta = -0.249$; p = .006) than term born controls. The risk for clinically diagnosed developmental delay (> - 1 SD) was higher among VP children in visual motor skills (OR = 13.4; 95% confidence interval [4.1 – 43.9]), fine motor skills (OR = 6.2 [2.4-16.0]) and visual perception (OR = 3.4 [1.1-10.6]) than in term born controls. The effects persist after adjusting for family SES and child sex.

These results confirm that infants born VP today are at significantly increased risk for subtle and clinically relevant developmental delays in visual perception, visual motor and fine motor skills. Even minor problems may have a negative influence on daily functioning and school readiness. Thus, VP children should be followed up at least until preschool age to identify potential problems early on. Studies are needed to evaluate interventions.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 282

TITLE: EARLY CHANGES IN BLOOD PRESSURE PREDICT THE NEED FOR SURGICAL INTERVENTION OF A PATENT DUCTUS ARTERIOSUS IN VERY LOW BIRTH WEIGHT INFANTS

AUTHORS: Robert Boldt 1, Markus Leskinen 2, Pauliina Mäkelä 3, Lotta Immeli 4, Päivi Luukkainen 5, Sture Andersson 6

AFFILIATIONS: Children’s Hospital, University of Helsinki, and Helsinki University Hospital, Helsinki, Finland

CONTENT:

Very low birthweight infants are at an increased risk of developing a patent ductus arteriosus (PDA). Early recognition of infants likely to develop a hemodynamically significant PDA would allow immediate preventive measures, such as reduced fluid intake. Here we aim to find the infants with an increased risk for a PDA by using a data-driven method to analyse blood pressure changes during the first 24 hours after birth.

Our study material consisted of very low birthweight infants (birthweight < 1500 g) treated at the NICU at the Helsinki University Hospital between years 2004-2013. For this study, we included the 885 subjects for whom we had reliable continuous arterial blood pressure measurement from 4 to 24 hours after birth. Figure 1A displays average systolic (blue), mean (red) and diastolic (yellow) arterial blood pressure from 4 to 24 hours after birth for all 885 subjects. We used k-means clustering to divide the infants into two groups with distinct temporal blood pressure changes (Figure 1B). We used these groups to predict the probability of needing either a primary surgical PDA intervention or surgical intervention after unsuccessful pharmacological treatment.

During the first 24 hours of life, the majority of infants (Group 1, 514 subjects, Figure 1C) displayed an upward trend in systolic (blue), mean (red) and diastolic (yellow) blood pressure. On the contrary, in a minority of infants (Group 2, 371 subjects, Figure 1D), the systolic (blue), mean (red) and diastolic (yellow) blood pressure trends waned throughout the first 24 hours after birth. Compared to infants with rising blood pressure (Group 1), infants with waning blood pressure (Group 2) were twice as likely to need either a primary surgical PDA intervention or surgical intervention after unsuccessful pharmacological treatment (Figure 1E, p < 0.01).

In very low birthweight infants, waning blood pressure during the first 24 hours after birth predict the need for surgical intervention of a patent ductus arteriosus.

IMAGE / TAB:
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IMAGE / TAB CAPTION:

COI: None declared
ID: 290

TITLE: THE ROLE OF SKIN FOLD MEASUREMENTS, AIR DISPLACEMENT PLETHYSMOGRAPHY AND DUAL-ENERGY X-RAY ABSORPTIOMETRY IN THE ASSESSMENT OF ADIPOSITY IN PRETERM INFANTS AT TERM EQUIVALENT AGE

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CONTENT:

In adolescence and adulthood, preterm birth is associated with a higher percentage of body fat, higher blood pressure and increased risk of dysglycemia. Nevertheless, differences between premature and term infants in fat distribution are already seen in infancy and early childhood. As body fat percentage and fat mass index have been shown to positively correlate with the occurrence of metabolic syndrome components, monitoring body composition in early life could help to implement timely preventive measures.

The purpose of the present study was to assess the agreement between adiposity measured by air displacement plethysmography (ADP) and Dual-energy x-ray absorptiometry (DXA) in preterm infants at term equivalent age. In addition, the potential predictive value of the sum of skinfolds (∑SFT) in an anthropometric model was assessed.

Sixty-five preterm infants, mean (SD) gestational age 29 (1.6) weeks, were assessed for growth and body composition at term equivalent age. ∑SFT were successfully completed in 63 infants, ADP was in 58 and DXA in 32 infants. The level of agreement and potential bias were examined using the Bland-Altman analysis and multiple regression analysis was used to investigate prediction models for adiposity.

DXA showed 4.5% higher fat mass percentages than ADP (limits of agreement: -4.2% and 13.0%). Seventy-five percent of the variance in fat mass percentage, measured with DXA, could be explained by waist circumference and the ∑SFT (P < 0.001). Only the ∑SFT was a significant predictor of fat mass percentage, measured with ADP (R² = 0.311, p <0.001). Fat mass estimation based on the formula by Schmelzle and Fusch, which was originally modeled to predict fat mass measured with DXA, could not be validated in our population.

Despite the need for a reliable, low-cost, point of care instrument, this study has not been able to show that ∑SFT would qualify as such. ADP seems to be more practical to assess adiposity in preterm infants in early life. Nevertheless, it remains to be elucidated whether or not a properly executed DXA is more accurate than ADP.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: There is no conflict of interest.
ID: 291

**TITLE:** INSULIN-LIKE GROWTH FACTOR 1 IN BRONCHOPULMONARY DYSPLASIA, LATE-ONSET SEPSIS AND NECROTIZING ENTEROCOLITIS

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**CONTENT:**

Insulin-like growth factor 1 (IGF-1) is known to influence the development of the premature gut and lungs. In addition, IGF-1 has an anti-oxidative and protective effect on inflammation. The study explores the relation between IGF-1 and the occurrence of bronchopulmonary dysplasia (BPD), late-onset sepsis (LOS) and necrotizing enterocolitis (NEC) in preterm infants.

88 preterm infants born between 24 to 32 weeks of gestation were enrolled in the NUTRIE Study (nutrition in relation to the endocrine regulation of preterm growth). Serum IGF-1 measured at birth and at 2, 4 and 6 weeks postnatal age was compared in infants with and without BPD, LOS and NEC. Mixed models were used to explore the interaction between IGF-1 and the occurrence of LOS and BPD. The models were adjusted for gestational age. Due to the limited patients with NEC (n=8) this could not statistically be explored.

During the first weeks of life preterm infants with BPD (n=30) showed lower IGF-1-levels compared to those without BPD (-1.47; CI -2.18 — - 0.75; p < 0.001). Furthermore, IGF-1 levels were significantly lower around the onset of LOS (n=31) (-1.20 nmol/l; CI -2.34 — -0.06; p 0.039). After correction for gestational age these findings only remained significant for BPD.

IGF-1 has a pertinent role in the occurrence of comorbidity in preterm infants as low postnatal levels of IGF-1 are associated with the occurrence of BPD and LOS. A larger study population is needed to explore the interaction between IGF-1 and the development of NEC.

**IMAGE / TAB:**

**IMAGE / TAB CAPTION:**

**COI:** None declared
ID: 292

**TITLE:** MATERNAL CENTRAL ADIPOSITY AND INFANT BIRTH WEIGHT

**AUTHORS:** Emelie Lindberger 1; Inger Sundström Poromaa 2; Fredrik Ahlsson 3

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**CONTENT:**

Background: Obesity and overweight during pregnancy are associated with several adverse pregnancy outcomes for the mother and the infant. It is well known that central adiposity is a stronger predictor of obesity related health issues that peripheral adiposity in non-pregnant individuals. Currently, body mass index (BMI) is used for risk stratification of pregnant women, but BMI does not differentiate central from peripheral adiposity. It is suggested that central adiposity increases the risk of adverse pregnancy outcomes, and that central adiposity could be a better risk marker than BMI only. This study aimed to evaluate the relation between maternal central adiposity and infant birth weight.

Methods: Subcutaneous (SCF) and visceral fat (VF) depths were measured in healthy women subjected to routine antenatal ultrasound in gestational week 16-19 at Uppsala University hospital from January 2015 to December 2017. Maternal age (years), parity (first born or all other), smoking, BMI, in vitro fertilization (IVF), maternal country of origin (EU or non-EU), obstetric diagnoses, gestational age, and infant birth weight were obtained from the standardized antenatal, and obstetric medical records. We excluded women with gestational diabetes mellitus, pre-eclampsia and gestational hypertension. Only singleton and term infants were included. Visceral fat and SCF was modelled separately due to covariance. Adjustments were made for BMI, maternal age, parity and smoking.

Results: 2334 healthy women were included in the study. The women were between 16 and 44 years of age, 41.1 % were primiparous, and 39.1 % were either pre-obese or obese. Parity, IVF and maternal origin were all significantly associated with birth weight. Parous women and women born in EU gave birth to heavier children. Mothers who had gone through IVF gave birth to lighter children. Birth weight did not differ between non-smoking and smoking mothers. In a linear regression model adjusted for BMI, maternal age, parity and smoking, every 5-mm increase in VF predicted an increase in birth weight by 8.6 grams. Subcutaneous fat depth was not a predictor of birth weight.

Conclusion: High maternal VF depth at gestational week 16-19 is associated with an increase in infant birth weight. Thus, VF measuring could easily and inexpensively be added into the routine antenatal ultrasound in order to predict infant birth weight, and to help determine which obese and overweight women who should get extended surveillance during their pregnancy.

**IMAGE / TAB:**
https://www.eiseverywhere.com/eeselectv3/v3/events/351149/submission/files/download?fileId=25be4bb3878b12c60143d0f9a270c65d-MjAxOS0wNSM1Y2UyNjY2YzIwMDk3

**IMAGE / TAB CAPTION:** Table 1. Association between maternal SCF and VF depths and birth weight. Linear regression model.

**COI:** None declared.
ID: 297
TITLE: SETTING A STANDARD FOR GROWTH OF LIMB CIRCUMFERENCES IN VERY PRETERM INFANTS
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CONTENT:
Recent work has demonstrated that early weight loss and discharge below the birth centile (or z-score) is not inevitable in preterm infants. However, the composition of improved weight gain remains uncertain. Clinicians need convenient tools to robustly assess body composition (and especially lean growth). Limb circumference measurement is a candidate, but its implementation is hindered by a lack of longitudinal data and standards. This study prospectively and longitudinally collected limb circumference data from a cohort of growing preterm infants, compared these measurements to routine anthropometry and has begun to form standards and growth charts which can be used to track infant growth.

Infants born prior to 30 weeks post-menstrual age were recruited from a single neonatal unit. Mid-upper arm circumference (MUAC) and mid-thigh circumference (MTC) were measured with routine anthropometry at recruitment and weekly until discharge. Circumference measurements underwent correlation analysis to assess their change over time. Slopes of change over time for circumferences were compared to slopes for standard anthropometric measurements to assess whether limb circumference measurements reflect distinct patterns of growth. Growth charts were constructed from the measurement data, using the LMS method, so that the feasibility of such charts could be assessed. Data for the whole cohort were compared with published data from the first 93 infants to validate the earlier findings.

212 infants were recruited (mean gestational age at birth: 27 weeks; mean birthweight: 930g). All parameters were strongly correlated with time, weight increasing by 162g per week, length by 7.4mm, left MUAC by 2.9mm, right MUAC by 3.0mm, left MTC by 5.2mm and right MTC by 5.1mm (all p<0.002). Comparison of regression slopes demonstrated that those for right and left MUAC could not reliably be distinguished from each other, and nor could those for right and left MTC. MUAC and MTC slopes were significantly different from those for weight, length and head circumference (and slopes for MUACs were different from those for MTCs). Growth charts were created using the LMS method (e.g. Fig 1). When compared with data for only the first 93 recruited infants, demographics had not significantly changed but rates of gain in weight, MUACs and MTCs had increased.

Patterns of growth of MUAC and MTC are distinct from each other and from those for weight, length and head circumference. Further work should focus on whether they offer insight into changes in body composition, and change in relation to patterns of nutrient intake. Growth charts were formed from MUAC and MTC data, though whether these patterns of growth are optimal requires further investigations in a larger cohort with long term follow up.
IMAGE / TAB: https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=ed934150f8a6f186ee967f22df2bbeae-MjAxOS0wNSM1Y2UyNjY2YzlyOWRk

IMAGE / TAB CAPTION: Posited growth chart for assessing the growth of right MUAC of preterm infants (LMS method, n=212) (lines at 0.4th, 2nd, 10th, 25th, 50th, 75th, 90th, 98th and 99.6th centiles)

COI: None declared
TITLE: EFFECT OF ORAL CARE ON THE INCIDENCE OF EARLY-ONSET VENTILATOR-ASSOCIATED PNEUMONIA IN PRETERM INFANTS

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CONTENT:

Ventilator-associated pneumonia (VAP) is a potentially serious complication related to mechanical ventilation in critically ill patients. Oral hygiene care using chlorhexidine has been reported to be effective in reducing the incidence of VAP in adult patients. However, few studies have investigated the efficacy of an oral care protocol in reducing VAP in preterm infants. This study aimed to investigate the efficacy of an oral care protocol in reducing the number of oral bacteria and incidence of early-onset (within 4 days of intubation) VAP in preterm infants.

We conducted a prospective study on preterm infants born between January 2015 and March 2019. The study protocol was approved by an IRB at our hospital. The number of oral bacteria was measured for approximately 1 min on-site using the Bacterial Counter (PHC Holdings Corporation, Japan). Oral hygiene care was performed by swabbing the oral cavity in six locations using a sponge brush moistened with sterile water. The number of oral bacteria was measured before and after oral care in preterm infants supported by endotracheal intubation (ETI), continuous positive airway pressure (CPAP), or high-flow nasal cannula (HFNC). The incidence of early-onset VAP in infants undergoing oral care prior to re-intubation was compared with that of infants before the initiation of our oral care protocol.

Mean (SD) gestational age and birthweight for our study population (comparison of oral bacterial number) were 28.0 (2.9) wks and 1148 (483) g, respectively. The mean number of oral bacteria was significantly lower (p < 0.01) after the oral care, respectively: (4.99 × 10^7 vs 3.75 × 10^5, ETI, n = 10; 1.19 × 10^7 vs 7.52 × 10^5, CPAP, n = 28; and 1.74 × 10^7 vs 6.15 × 10^5, HFNC, n = 18). The incidence of early-onset VAP occurred at a rate of 51% (19/37) after re-intubation without performing oral care before the study period and significantly decreased to 20% (6/30; p = 0.008) after initiation of our oral care protocol.

Oral hygiene care using a sponge brush moistened with sterile water appears to be effective in reducing the number of oral bacteria and the incidence of early-onset VAP in preterm infants.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 301
TITLE: SOCIO-CULTURAL DETERMINANTS OF VALUATION OF LIFE WITH DISABILITY: A CROSS-CULTURAL COMPARISON
AUTHORS: Kathryn C. Nesbit 1; Elizabeth Spiegel 2; Ketly Altenor 3; Holly Martin 2; Hoa Thi Nguyen 4; Ly Tran 4; Angela Quifonez Hermosa 5; Julia von Oettingen 6; Emily Treleaven 7; John Colin Partridge 2 for the Utilities Study Group.
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CONTENT:

An estimated 93 million children worldwide live with significant disability. The majority live in under-resourced countries, the burdens of lifelong disability are likely disproportionately worse where disabled persons are perceived as a burden on the family, receive little support services, fall victim to discrimination, or are in other ways stigmatized or marginalized. There are no data on what socio-cultural variables are associated with perceptions of lifelong disability. We assessed societal correlates of adults’ valuation of lifelong disability in 3 developing countries (Vietnam, Peru, Haiti). We hypothesized that there would be culture-specific predictor correlates of utility scores.

We previously reported valuations of disability, quantified as utilities, for 4 disability outcomes (mild, moderate, severe, profound) in Haiti, Peru, and Vietnam using time trade-off methods. For this analysis of the same sample of 150 participants in each country, we gathered socio-cultural data including: age, gender, religion, educational attainment, disability in child/participant/household, mode of transportation to primary care, distance from primary care, family empowerment, instrumental support, emotional support, and wealth quintile. Variables were compared across countries using ANOVA, t-test and Chi-Square test with significance as p<0.05. Predictive models for utilities were examined using multiple linear regression analysis of utilities for each disability outcome by country.

Overall, the sample participants (n=450) were 33.6 (+11.6) yrs old, 38% male, 86% married, 75% parents, 16% disabled, 72% urban dwellers, 18% with < a secondary education, 47% in the lowest 3 wealth quintiles. Significant differences across countries were found in 27 of 31 socio-cultural variables (p<0.05). Significant associations were found between socio-cultural variables and utility scores (Table). Models with a good fit in Vietnam were identified for Moderate, Severe, and Profound disability outcomes; in Peru, models were identified for Mild, Moderate, Severe, and Profound disability outcomes; and in Haiti, they were found for Moderate disability outcomes (F(4,143) = 2.607, p=0.038; F(6,114) = 2.556, p=0.023; F(3,116) = 3.488, p=0.018; F(4,11) = 5.275, p=0.001; F(3,146) = 3.951, p=0.010; F(6,94) = 2.517, p=0.026; F(6,92) = 3.969, p=0.001; and F(4, 37) = 2.863, p=0.037; respectively).

Education, number of children, experience with disability, religion, access to care, wealth quintiles and perceived rejection are associated with valuations of quality of life with disability. Variations in the correlates of utilities within and across countries suggest that sociocultural context differentially shapes local valuations of life with disability. Data on local preferences for disability can be a metric for health policy decisions.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=4bf1fb879a337419a160d526949329aa-MjAxOS0wNSM1Y2UyY2YzI0OTE4

IMAGE / TAB CAPTION: Table. Sociocultural correlates of utilities for 4 disability outcomes significant at p<0.05.
COI: None declared
ID: 311

TITLE: NEONATAL HERPES: 13 YEAR COHORT STUDY OF INCIDENCE, CLINICAL PRESENTATION AND OUTCOMES FROM A SINGLE CENTRE IN THE UK

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CONTENT:

Herpes simplex infection in neonates can have devastating outcomes for otherwise healthy babies. The national published incidence of neonatal herpes in the United Kingdom is low (1.6 per 100,000 live births). We aimed to find the current incidence in our population and compare outcomes from our previous published cohort.

We retrospectively reviewed the case notes of all herpes infected neonates presenting within the first 28 days of life to Nottingham University Hospitals from 2006-2018; identified from laboratory and admission databases.

Thirty two cases of neonatal herpes infection were identified between 2006 and 2018. Five of these cases were transferred from other hospitals for tertiary care and 27 from the local population, giving an incidence of 19.2 cases per 100,000 live births. There were ten (31%) deaths.

Dividing the cohorts in to two periods (2006-2013 and 2014-18); the incidence was similar (17.5 vs 21.3 per 100,000 live births respectively); the age of presentation was similar with a median age of 7 and 8 days, but the incidence of death was lower in the later cohort (7.7% vs 47.3%, figure 1). Presence of central nervous features (p=0.0003), raised ALT above 40 (p=0.0059) and coagulopathy (p=0.0008) were significantly associated with mortality. Presence of skin involvement was associated with survival (p=0.0209). None of the babies with ALT above 750 U/L survived.

We report the incidence of neonatal herpes in our single centre tertiary service to be 19.2 per 100,000 live births between 2006 and 2018. We believe the raised awareness of herpes and early treatment has led to a fall in mortality. We strongly recommend considering herpes infection in previously well babies presenting with suspected sepsis in the neonatal period. ALT should be routinely measured as part of a sepsis screen in such babies.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=5d1e8e7b322cdf3d1d2350157581af92-MjAxOS0wNSM1Y2UyNjY2Yz14ODZi

IMAGE / TAB CAPTION: Figure 1: Outcomes in the two sequential cohorts

COI: None
ID: 312

TITLE: INTRA-TRACHEAL ADMINISTRATION OF BUDESONIDE-SURFACTANT VERSUS SURFACTANT ONLY TO PREVENT BPD IN EXTREMELY PRETERM NEONATES: A RETROSPECTIVE CHART REVIEW

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CONTENT:

Intra-tracheal (IT) administration of budesonide using surfactant as a vehicle has proved to be effective in reducing the risk of bronchopulmonary dysplasia (BPD) and the combined incidence of BPD or death at 36 weeks post-menstrual age (PMA) in very low birth weight (VLBW) infants with severe RDS. However, evidences on the outcomes and adverse effects of this therapy have not been widely explored.

The aims of this retrospective chart review analysis was to compare the effect of IT administration of surfactant/budesonide (SB) with that of surfactant only (S) in VLBW infants with severe RDS on the incidence of BPD, death and duration of mechanical ventilation (MV) before and after the introduction of SB strategy in our NICU.

IT SB strategy was introduced in our NICU in March 2018. Two cohorts of extremely preterm neonates (GA<28 GW, BW<1500 g), admitted at Padua’s NICU (Italy) and born in two consequent epochs (group S: 01/2017-02/2018, group SB: 03/2018-01/2019) were retrospectively compared. 72 neonates with RDS III-IV requiring respiratory support with FiO2≥0.3 within 12 hours of birth were enrolled. The SB group (n=35) received surfactant (200 mg/kg 1st dose; 100 mg/kg following doses) and budesonide (0.25 mg/kg). The S group (n=37) received surfactant only (200 mg/kg 1st dose; 100 mg/kg following doses). Medical team and management protocol of VLBW infants did not change between the two epochs. Data analysis was based on Fisher’s exact test, ANOVA, Kruskal-Wallis test, linear and logistic regression.

24 and 15 neonates from SB and S groups, respectively, were matched for GA, BW, number of SGA infants, and number of treatment doses to avoid possible confounding factors. Perinatal characteristics were similar at baseline in the two groups. The combined therapy of surfactant/budesonide did not affect the incidence of BPD, death, BPD or death at 36 weeks PMA, nor the risk of reintubation, extubation failure and severe IVH compared to surfactant therapy only (significance level 0.05). The incidence of adverse effects (hyperglycemia with 2 values>200 mg/dL in the first 3 days, insulin therapy, leucocytosis with WBC>30000/mmc in the first 5 days, Candida infections in the first 14 days) did not differ between the two groups. A positive effect on hypotension (need for inotropes within the first 5 days) could be seen in the SB group (p=0.031), suggesting a systemic absorption of budesonide.

This retrospective chart review shows that early IT administration of budesonide with surfactant in VLBW neonates with severe RDS does not affect the incidence of BPD, death, and BPD or death at 36 weeks PMA, nor other respiratory outcomes, compared to treatment with surfactant only. Further RCTs studies with larger sample sizes are needed to investigate the benefits and adverse effects of early IT steroids.
ID: 314

TITLE: DETERMINANTS OF LARGE DIFFERENCES BETWEEN SKIN AND SERUM BILIRUBIN AND THEIR POSSIBLE IMPACT ON PHOTOTHERAPY IN LATE PRETERM AND TERM NEONATES

AUTHORS: Emmanuelle Letamendia-Richard MD, Silvia Foligno MD, Giulia Vigo MD, and Daniele De Luca MD,PhD

AFFILIATIONS: Division of Pediatrics and Neonatal Critical Care, “A.Beclere” Medical Center, South Paris University Hospital, APHP South Paris-Saclay University, Paris, France

CONTENT:

Background. AAP recommends predischarge measurement of either transcutaneous (TcB) or total serum bilirubin (TSB) while decisions about treatment should be based on TSB levels.[1] Modern second generation transcutaneous devices are supposed to be more accurate than the older ones,[2] however, large discrepancies between TSB and TcB are rarely observed. It is not clear what are the factors causing these discrepancies and their possible consequences, when TcB is used as pre-discharge screening, in terms of therapeutic decisions. We embarked in a large, prospective cohort study to determine: 1) the factors affecting a large difference TSB-TcB (defined as absolute values >50 µmol/L); 2) if this difference would have had clinical consequences in terms of jaundice treatment, when TcB is used as predischarge screening.

We enrolled term and late preterm neonates who had the TcB measurement (Bilicheck®, Philips inc),as predischarge screening and whose value exceeded the 75th percentile of the European TcB nomogram.[3]In these babies a TSB was obtained within 30’ from the TcB,as per our internal protocol Phototherapy was instigated if TSB fulfilled criteria as per AAP guidelines.[4]Jaundice risk factors (as per AAP guidelines [1]) were also recorded. Patients were divided between those with underestimation or overestimation if the TSB-TcB difference was >50 or >-50 mmol/L,respectively and univariate analyses for all jaundice risk factors were performed.Multivariate logistic regression having as outcome the large TSB-TcB error (as absolute value)was performed,including covariates with an univariate p>0.10.

Results: We enrolled 837 babies, (59% males;GA 40 (1.8) weeks;BW 3458 (537)g;postnatal age 63.5 (29)h). Under- and overestimation were 36 and 110, respectively. Tab.1 shows univariate analyses results. Multivariate analysis (Tab.2) shows the non-Caucasian ethnicity to be the main variable increasing the risk for large TSB-TcB error, while the presence of cephalohematoma seems to reduce it; postnatal age seems to have a milder effect. When TcB largely underestimated TSB, fifteen (1.8%) neonates needed phototherapy, while, when TcB largely overestimated TSB, eight (0.9%) babies did not finally need any treatment.

In a large population of term and late-preterm babies, only non-Caucasian ethnicity seems to increase the occurrence of large discrepancies between TSB and TcB. The vast majority of large errors is represented by overestimation and their impact on therapeutic decisions seems minimal.

References
[2] De Luca, Jackson, Engle. Transcutaneous bilirubinometry, NOVA Publisher 2013

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=742faddededab5b7cc645c7e3c2ad81a2-MjAxCs0wNSM1Y2UyNjY2YzJhMDRj

IMAGE / TAB CAPTION: Univariate and Multivariate analysis
COI: D.De Luca in the past has received travel grants and research technical assistance from PHILIPS inc, outside of the present work
ID: 321

TITLE: IS FLUID BOLUS THERAPY EFFECTIVE IN THE MANAGEMENT OF CIRCULATORY FAILURE IN THE EARLY LIFE PERIOD OF VLBW PRETERM INFANTS?

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CONTENT:

During the early hours of life, very low birth weight (VLBW) preterm infants are at particularly high risk of hemodynamic instability, leading to circulatory failure. The administration of intravenous fluid boluses in this population is a common practice in neonatal units around the world. However, there is little evidence on the efficacy and the safety of fluid bolus therapy and there are no evidence-based recommendations for the type of fluid administered, velocity of infusion or indications for fluid bolus therapy. Aim: To investigate the practice and effects of the administration of fluid boluses in preterm infants <1500g on blood pressure, acid-base equilibrium and short-term outcome.

Six months retrospective single-centre study of the inborn VLBW infants admitted to the NICU of the John Radcliffe Hospital (Oxford) between July and December 2018. Baseline information (birth weight, gestational age, pregnancy and delivery), fluid boluses within the first 72 hours since birth (indication, fluid type, volume, velocity of infusion), clinical data including mode of respiratory support, blood pressure, outcomes at discharge: survival, bronchopulmonary dysplasia (BPD), sepsis, necrotizing enterocolitis (NEC), patent ductus arteriosus (PDA), intraventricular haemorrhage (IVH), periventricular leukomalacia (PVL) were collected. Statistical analysis included comparison of clinical and blood gas parameters and clinical condition before and 1 to 4 hours after the administration of each bolus.

82 infants were born in the study period. 59 were eligible. 15 neonates (25.4%) received fluid boluses in the first 72 hours. They were of lower mean gestational age (25.89 vs 28.97 weeks, p < 0.05) and birth weight (822.29 vs 1076 g, p < 0.05) than those not receiving boluses, but no statistically significant differences in sex, delivery, prenatal steroids were seen. There was a higher rate of IVH, NEC, PDA, inotropes, mortality in the bolus group (p < 0.05); no differences in PVL and BPD. Mean number of boluses per baby was 2.42 (SD = 1.52). Fluids used were 0.9% NaCl (47.4%), packed red blood cells (PRBC, 36.8%), fresh frozen plasma (FFP, 10.5%), 0.45% NaCl (5.3%). Volumes infused were 10 mL/kg in 20 min for NaCl and 15 mL/kg in 4 hours for PRBC. There was an improvement of clinical assessment, mean blood pressure, pH, lactate, bicarbonate level and base deficit (p < 0.05), while no difference in chloride, haemoglobin and heart rate.

Administration of fluid boluses in VLBW infants is a common practice in this tertiary NICU. Infants with a lower birth weight and gestational age are more likely to receive boluses. Administration of boluses shows a short-term improvement in clinical and biochemical parameters. Infants who received a bolus had a higher rate of mortality, IVH, NEC, treated PDA. Further work is required to determine potential benefits or harms of fluid bolus in neonates.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 328

TITLE: THE IMPACT OF HIGHER VS. LOWER CPAP ON CARDIORESPIRATORY TRANSITION IN A LAMB MODEL AFTER PRETERM BIRTH

AUTHORS: Anja Demel 1,2; Karyn Rodgers 1; Kelly J. Crossley 1; Valerie Zahra 1; Erin V. McGillick 1; Alison Moxham 1; Tessa Marthers 3; Arjan B. te Pas 3; Andre Oberthuer 4; Angela Kribs 4; Graham R. Polglase 1,2; Calum T. Roberts 5; Stuart B. Hooper 1,2

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CONTENT:

Most preterm infants require respiratory support after birth to aerate their lungs and initiate pulmonary gas exchange. Non-invasive respiratory support is the most physiological and protective way of providing this support, while minimizing lung injury and improving cardio-pulmonary outcomes. In particular, the combination of spontaneous breathing with Continuous Positive Airway Pressure (CPAP) is the preferred approach, but the optimal way of applying CPAP remains unknown. We hypothesized that a higher CPAP in a spontaneously breathing lamb model, would enhance lung aeration and improve cardio-respiratory stability.

Fetal lambs were randomized in a cross-over experiment to either a high or low CPAP (15 or 5 cmH2O) group. Fetal instrumentation was performed at 130 days gestational age (GA) for cardio-respiratory measurements. Lambs were delivered at 133 days GA via cesarean section and spontaneous breathing was initiated. After immediate cord clamping, all lambs remained for the first 30 minutes after birth at either CPAP level, while spontaneously breathing, before CPAP levels were switched. Non-invasive respiratory support was administered via the Benveniste Valve, a variable jet flow device, through binasal prongs. Circulatory and respiratory aspects were continuously assessed and analyzed every 3 minutes after birth.

Twelve preterm lambs (CPAP 15 vs 5: n=7, mean birth weight 3560±196 (SEM) grams; n=5, mean birth weight 3761±133 (SEM) grams) were assessed. No significant differences were detected in gender, body core temperature and hematocrit levels. Lambs in both CPAP groups reached the targeted minimum of regional cerebral oxygen saturation (65%) (high vs. low CPAP: mean 93.9±5.0% (SEM); 73.6±0.0% (SEM)) at 9 minutes after birth. Lambs receiving higher CPAP required significantly less supplemental oxygen (85.0±3.3% vs. 42.5±1.3%; p< 0.01) up to 27 minutes of life. Partial pressures of carbon dioxide were higher and breathing rates (Fig.1) were lower in lambs receiving lower CPAP. Notably, fewer lambs, allocated to the lower CPAP group, were able to be sustained on CPAP without additional cardiorespiratory support compared to the higher CPAP group (62.5% vs. 100%; p=0.08) at 5 minutes after birth.

A CPAP of 15 cmH2O during non-invasive respiratory support markedly improved gas exchange. The required amount of supplemental oxygen to maintain cerebral oxygenation was lower and the survival rate reached 100% in the higher CPAP group compared to 62.5% in the lower CPAP group. Further research on optimal CPAP administration is required.

IMAGE / TAB:
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**IMAGE / TAB CAPTION:** Figure 1. Respiratory rate changes over time in lower CPAP (black triangles, n=4#) and higher CPAP (red dots, n=7) groups. Data are presented as mean±SEM and significance accepted p=0.05. Asterisk (*) indicates significant differences between groups (*p<0.05, **p<0.01) at individual timepoints below line. #Not assessed due to technical difficulties in n=1.

**COI:** Anja Demel: Supported by the German Research Foundation (DFG-grant: DE 1909/ 2-1)
ID: 334

TITLE: MORTALITY PREDICTION IN VERY LOW BIRTH WEIGHT NEONATES DURING HOSPITAL ADMISSION

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CONTENT:

New mortality predictive models in Spanish premature infants have been recently developed by our group. During hospital admission, causes of mortality vary depending when death occurs. Mortality predictive models exist for specific times during hospitalization (delivery room, 7th day, 28th day and 36 week’s postmenstrual age -Ambalavanam N, 2012). The aim of this study was to develop and validate a dynamic survival prediction model during hospitalization, integrating length-of-stay as a key variable, for preterm infants registered in the Spanish SEN1500 database.

Inclusion: Infants born alive with BW <1500g or GA <30 weeks without congenital defects or chromosomal disorders registered in SEN1500 database. Periods: Development (DP) (2009-12) and Validation (VP) (2013-15). Predictive mortality model: during hospital admission. Statistical analysis: dependent variable: hospital mortality. Independent variables: significant maternal, perinatal and neonatal data were used in multivariable regression models. Cut-off points for “death” and “no death” (Kappa index), Negative and Positive Predictive Values (NPV, PPV), accuracy and area under the curve (AUC) were calculated. This model is a composition of two sub-models alternatively applied before or after the 30th day of admission. Length-of-stay was used to evaluate time impact on patient’s outcome.

14953 newborns were included (DP=8734; VP=6219). 1688 of 2015 (84,8%) died during the 1st month of life. AUC for predicted mortality was 0.999 during the 1st month of life (95% CI: 0.998-0.999) (p<0,001) and 0.950 after 30 days of life (95% CI: 0.930-0.961) (p<0,001). The model showed a “very good” concordance (Kappa=0,86). Table 1 shows different prognostic cut-off points for “survival probability”, as well as NPV and PPV. Variables with the greatest impact on predicting mortality during all admission were Gestational age, Birth weight, multiple pregnancy, maternal steroids, Apgar-5 min and severe pneumothorax. During the first month of life variables related to death were necrotizing enterocolitis, severe infection and intraventricular hemorrhage. Cystic periventricular leukomalacia, severe anemia, and bronchopulmonary dysplasia were the outcomes related to death after 30 days of life.

A new mortality predictive model including main variables related to death and incorporating length of stay was developed and validated for preterm infants born in Spain. Application of continuous models of changing probability can improve individual mortality outcome estimation.

IMAGE / TAB:
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IMAGE / TAB CAPTION:

COI: None declared
ID: 345

TITLE: HOSPITALISING PRETERM INFANTS IN SINGLE FAMILY ROOMS VERSUS OPEN BAY UNITS - EFFECT ON PARENTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Jacqueline Limpens 2;
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CONTENT:

Having a preterm baby is a very stressful life event for parents. Due to the setting of the modern neonatal ward, the physical and emotional closeness between the parents and their preterm infants is usually impaired as the infant is admitted to an open bay unit. The effect of the hospital environment on health and specifically psychological outcomes in parents of preterm infants remains under debate. We assessed outcomes of parents of preterm infants hospitalised in single family rooms compared to common open bay units.

For this systematic review and meta-analysis, we searched MEDLINE, EMBASE, PsycINFO, the Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, and Clinicaltrials.gov from inception to the 25th of March 2019 using controlled terms (i.e. MeSH-terms) and text words related to prematurity and NICU design. We included randomised and non-randomised studies. Methodological quality was assessed using The Cochrane Collaboration’s Risk of Bias Tool for randomised controlled trials and the Cochrane Risk of Bias Tool for Non-Randomised Studies of Interventions. Summary estimates for meta-analysis were calculated using random effects models with standardized mean differences (SMD).

We identified 503 records. Ten study populations with parents from 1,568 infants were included. Single family rooms are associated with lower levels of parental stress at discharge (n=454 parents, SMD -0.41, 95%CI -0.61, -0.22, p<0.0001, I² =0%), during follow-up at 3 months (n=381, SMD -0.20, 95%CI -0.41, 0.01, p=0.06, I² =0%), and parental anxiety at discharge (n=162, SMD -0.61, 95%CI -0.93, -0.29, p=0.0002, I² =0%). Higher levels of parental presence, participation, empowerment, degree of family centred care, and satisfaction was found in a majority of studies. No differences were found for scores on parental depression at discharge. No studies examined the effect on post-traumatic stress in parents and parent-infant bonding.

Single family rooms should be considered to hospitalise preterm infants, as beneficial outcomes are present for the parents at discharge of the infant from the hospital and during follow-up after discharge.

IMAGE / TAB:
IMAGE / TAB CAPTION:

COI: PROSPERO registration number: CRD42016050643. NR van Veenendaal is supported by an unrestricted research grant, provided by Nutricia, the Netherlands.
ID: 370
TITLE: GASTRIC RESIDUALS TO PREDICT NECROTIZING ENTERCOLITIS IN PRETERM PIGLETS
AUTHORS: Susanne Soendergaard Kappel 1,2; Per Torp Sangild 1,2; Thomas Thymann 1; Lise Aunsholt 1,2
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CONTENT:

Background: Necrotizing enterocolitis (NEC) is a serious intestinal inflammatory disease associated with enteral feeding in preterm infants. Volume and color of gastric residual (GR) before each bolus feeding are parameters often used to evaluate feeding intolerance, and used as early predictors of NEC. However, the predictive value of GR evaluations is questionable and may lead to unnecessary withholding of feeding, growth restriction and prolonged use of parenteral nutrition. Using NEC-sensitive preterm piglets as a model of preterm infants, we hypothesized that GR mass, acidity and bile acid levels, and plasma gut hormone levels, may predict early onset of NEC.

Methods: In total, 319 piglets were delivered by caesarean section at 90% gestation (from 20 sows) and fed different cow’s milk-based formulas for 5 days before NEC evaluations and GR collection 60 min after a final bolus feeding. The stomach, small intestine (Si) and colon (Co) were evaluated for NEC lesions by macroscopic scoring (1-2: No-NEC, 3-4: mild lesions, 5-6: severe lesions). GR mass, acidity, gastrin and bile acid levels were measured, and plasma glucagon-like peptide 2 (GLP-2), gastric inhibitory polypeptide (GIP) and gastrin.

Results: Across the piglets, 49% were diagnosed with mild or severe NEC lesions in the Si and/or Co. These piglets (ALL-NEC) had a higher GR mass per body weight than No-NEC piglets (p<0.001). The difference was highest for piglets that had Si lesions (relative to only Co lesions). Presence of NEC lesions was associated with lower gastric bile acid concentrations (p<0.05). The positive and negative predictive values for these markers were 55-65%. No differences were observed for acidity, gastrin, GLP-2 or GIP levels.

Conclusion: In preterm piglets, mild to severe NEC lesions was associated with higher mass of GR but not with the other measured biomarkers of gut function. The predictive value of GR mass is low. It is important that unspecific clinical signs of feeding intolerance and NEC, as judged from GR mass and chemical composition, do not lead to unnecessary reduction in enteral feeding volume for preterm infants.

IMAGE / TAB:

IMAGE / TAB CAPTION: Figure 1. Gastric residual (GR, weight of stomach content relative to body weight). a) No-NEC compared to NEC in each of the gastrointestinal regions. b) Gastric bile acid in No-NEC vs. piglets with NEC lesions in the small intestine (Si-NEC, with/without colon lesions) or only in the colon region (Co-NEC). Values are means ± SEMs. * p< 0.05, ** p< 0.01.

COI: None declared
ID: 378

TITLE: LIPOPOLYSACCHARIDE-INDUCED INTRA-AMNIOTIC INFLAMMATION IMPAIRS SYSTEMIC IMMUNE DEVELOPMENT IN PRETERM PIGS

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CONTENT:

Chorioamnionitis (CA), inflammation in the fetal membranes, is the main predisposing factor to preterm birth (<37 weeks of gestation) and may increase the risk of systemic infections after birth. It is, however, unclear if complications after preterm birth result from immaturity alone (e.g. reduced gestational age), or from prenatal factors leading to preterm birth (e.g. CA). To elucidate the possible mechanisms of CA modulating neonatal outcomes, we investigated the impact of CA on fetal and postnatal systemic immune status, using a preterm pig model with separate effects of unstimulated preterm birth and preterm birth following CA.

Pig fetuses at day 103 of gestation received an intra-amniotic injection of lipopolysaccharide or saline (LPS, 1mg/ml or CON, both n = 10) before preterm delivery by caesarean section at day 106 (90% gestation). Pigs were fed formula in incubators until postnatal day 5. The fetal membranes and amniotic fluid were collected at delivery for examination of leukocyte infiltration and pro-inflammatory cytokines. Cord blood and arterial blood on day 5 were used for mRNA extraction followed by whole transcriptome shot-gun sequencing (RNA-seq). Key differentially expressed genes (DEGs) were validated by qPCR.

At birth, LPS fetuses showed elevated levels of amniotic fluid cytokines (IL-8, IL-6, IL-1β) and immune cell infiltration in the fetal membranes (CA). Relative to CON, the cord blood of LPS pigs revealed innate immune activation at birth, with 258 up-regulated genes mainly related to neutrophil-mediated immunity (S100A9, TLR4, LYZ), coagulation cascades (VWF) and complement pathways (C3). Most of these DEGs were not correlated with neutrophil counts, indicating effects of prenatal LPS on neutrophil activation, rather than granulopoiesis. After 5 days of formula feeding, both CON and LPS pigs showed innate immune maturation with ~400 up-regulated innate immune genes, relative to at birth. Importantly, at postnatal day 5, only CON pigs underwent systemic Th1 polarization (increased TNFA/IL6, IFNG/IL4 and decreased fraction of regulatory T cells, relative to CON at birth and LPS on day 5).

Our study showed cellular and molecular evidence for the systemic effects of CA on both fetal and postnatal immune status after preterm birth. The impaired postnatal systemic Th1 polarization following intra-amniotic inflammation may explain the increased susceptibility to neonatal sepsis associated with immune suppression in a population of preterm infants born with CA.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 379

TITLE: Prenatal endotoxin effects on gut immunity and microbiota in preterm pigs

AUTHORS: Xiaoyu Pan 1; Du Zhang 2; Duc Ninh Nguyen 1; Fei Gao 1, 2; Per T. Sangild 1

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CONTENT:

Gut microbiota exposure plays an important role for intestinal immunity development in preterm neonates. Disruption of the gut homeostasis by inappropriate microbial exposure may increase susceptibility to gut diseases, e.g. necrotizing enterocolitis (NEC). Chorioamnionitis, associated with intra-amniotic infections, may expose the immature intestine to bacterial toxins already in utero via fetal swallowing. Using preterm pigs as model for preterm infants, we hypothesized that prenatal exposure to gram-negative endotoxin influences postnatal gut microbiota and immunity development in preterm neonates.

Pig fetuses were given intra-amniotic lipopolysaccharide (LPS, 1 mg per fetus, n=37) 3 d before preterm delivery by cesarean section, and were compared with litter-mate controls (CON, n=32) at birth and after 5 d of formula feeding. Amniotic fluid was collected for analysis of leukocyte counts and cytokines. The distal small intestine was analyzed for endotoxin level, morphology and immune cell counts. Intestinal gene expression and colonic microbiota were analyzed by transcriptomics and metagenomics, respectively.

At birth, LPS-exposed pigs showed higher intestinal endotoxin, neutrophil/macrophage density and lower villi. About 1.0% of intestinal genes were affected and DMBT1 (deleted in malignant brain tumor 1, a regulator of mucosal defense) was a hub gene in the co-expression network. Gene expressions related to innate immune response (TLR2, LBP, CD14, C3, SFTPD), leukocyte transendothelial migration (NCF1, NCF2, NCF4, ITGB2) and antigen processing (MHC II, CD4) were changed and correlated with intestinal neutrophil/macrophage density and amniotic fluid cytokine levels. On day 5, LPS and CON pigs showed similar NEC lesions, endotoxin levels, morphology, immune cell counts and gene expressions, but differences in low-abundant Lactobacillus amylovorus (~0.05% of total bacteria in colon).

LPS exposure affected the expression of intestinal genes in preterm pigs at birth, especially genes related to immune cell infiltration. Five days later, following enteral feeding and bacterial colonization, intra-amniotic LPS had limited effects on intestinal structure and function. A short period of intra-amniotic inflammation prior to preterm birth is unlikely to cause longer-lasting pro-inflammatory responses in the gut of preterm infants.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 384
TITLE: NEUROPROTECTIVE EFFECT OF REMOTE ISCHEMIC POSTCONDITIONING AND THERAPEUTIC HYPOTHERMIA IN A PIGLET MODEL
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CONTENT:
Therapeutic hypothermia (TH) is a safe and efficient treatment of neonates with hypoxic ischemic encephalopathy. However, TH only reduces part of the acquired brain damage and additional treatments are needed to improve outcome. Remote ischemic postconditioning (RIPC) has been shown to be neuroprotective in rats and piglets. It is unknown whether there is any additional neuroprotective effect when combining RIPC with TH.

A total of 33 piglets <12 hours of age were anesthetised. A global hypoxic-ischemic insult was induced by reducing FiO2 during a 45-minute period to achieve aEEG <7uV and a mean blood pressure <70% of baseline for at least 5 minutes. In total, 26 animals were randomized to TH+RIPC or TH while 7 animals were subjected to hypoxia only. RIPC was induced by occluding blood flow to both hind limbs for five minutes followed by five minutes of reperfusion in four cycles. The primary outcome was lactate/n-acetylaspartate ratio measured by magnetic resonance spectroscopy (MRS) in the thalamus, white matter, frontal- and occipital cortex. Secondary outcomes were thalamic oedema, oxygenation, and perfusion measured by magnetic resonance imaging (MRI). MRS/MRI was performed at 6, 12, and 24 hours.

We present preliminary results from the first 24 animals subjected to TH vs. RIPC+TH. Insult severity was comparable in the two groups with respect to duration of aEEG suppression (median; 26.2 vs. 26.8 min.), duration of hypotension (median; 5.5 vs. 5.7 min.), and post-insult metabolic acidosis (median; pH 6.99 vs. 7.05). Three animals died in the TH+RIPC group and four died in the TH group. There was no difference in lactate/n-acetylaspartate-ratio in any of the four brain regions at any time point (Fig. 1A). Further, we found no difference between the two groups in MRI measures of intracellular oedema or oxygenation at any time point (Fig 1B).

These preliminary results showed no additional neuroprotective effect after adding RIPC to TH. Results from the last nine animals and measurements of cerebral perfusion are pending and will be presented at the conference.

IMAGE / TAB:
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IMAGE / TAB CAPTION: Figure 1. Magnetic resonance spectroscopy (A) and imaging data (B) from the first 24 animals at 6, 12, and 24 hours after the hypoxic insult. ADC; apparent diffusion coefficient. BOLD; Blood oxygenation level dependent. NAA; n-acetylaspartate. Data are median with interquartile range.

COI: None declared
ID: 393
TITLE: PHYSIOLOGICALLY BASED CORD CLAMPING AVOIDS TRANSIENT HYPOXIA AND INCREASES PULMONARY BLOOD FLOW IN LAMBS WITH A DIAPHRAGMATIC HernIA
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CONTENT:

Most fetuses with a congenital diaphragmatic hernia survive until term, as their hypoplastic lungs are not required for gas exchange in utero. However, when the umbilical cord is clamped at birth, the infant becomes solely dependent on the lungs for gas exchange and left ventricular preload. Recently, we have shown that aerating the lung before clamping the umbilical cord (physiologically based cord clamping; PBCC) prevents the transient hypoxia and loss in cardiac output associated with immediate cord clamping (ICC) in preterm lambs that require ventilatory support. We aimed to compare the effects of PBCC and ICC on cardiopulmonary physiology during the neonatal transition in lambs with a diaphragmatic hernia.

A diaphragmatic hernia was surgically created at ≈80 days gestational age (GA; term=147d) in all fetal sheep (n=17). At ≈138d GA, all fetuses were instrumented and then delivered via caesarean section. The umbilical cord was clamped either immediately prior to ventilation onset (ICC; n=6) or after achieving a target tidal volume of 4 mL/kg, with a maximum delay of 10 min (PBCC; n=11). Lambs were ventilated for a total of 120 min with real-time monitoring of physiological (pulmonary and carotid artery blood flows and pressures; cerebral oxygenation) and ventilatory (tidal volume and airway pressure) parameters. Data is presented as mean ± SEM. PBCC and ICC were compared across time using two-way repeated measures analysis of variance. Statistical significance was accepted when p<0.05.

Cerebral tissue oxygen saturation (SctO2) sharply decreased in ICC lambs at birth (Figure 1A). In contrast, in PBCC lambs SctO2 remained stable as pulmonary blood flow (PBF), and hence pulmonary gas exchange, was gradually established before the placental circulation was removed by cord clamping (Figure 1B). SctO2 was significantly greater in PBCC lambs at 5 min (55±2 vs. 24±4 %, p<0.001) and 10 min (60±4 vs. 41±7 %, p=0.01) after ventilation onset. PBF was 2-fold greater in PBCC compared to ICC lambs at 15 min following ventilation onset (45 ± 9 vs. 22 ± 3 mL/min/kg; p=0.005), and by the end of the 120 min ventilation period PBF was 3-fold greater (23 ± 4 vs 8 ± 2 mL/min/kg; p=0.048). At 120 min after ventilation onset, pulmonary vascular resistance was 3-fold lower in PBCC lambs (0.6±0.1 vs. 2.2±0.6 mm Hg/(mL/min), p<0.001) compared to ICC lambs.

In lambs with a diaphragmatic hernia, establishing lung aeration prior to umbilical cord clamping avoids transient, severe hypoxia at birth and enables increased PBF for at least the first 120 min after birth, compared to ICC. Our findings suggest that a physiological approach to umbilical cord clamping provides a more stable cardiopulmonary transition and may support better neonatal outcomes for infants with a congenital diaphragmatic hernia.

IMAGE / TAB:
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IMAGE / TAB CAPTION: (A) Cerebral tissue oxygen saturation (SctO2) and (B) pulmonary blood flow (PBF) during the 120 min following ventilation onset in immediate cord clamping (ICC; blue circles, n=6) and physiologically based cord clamping (PBCC; red squares, n=11) groups. Two-way repeated measures ANOVA (group, time) with Holm-Sidak’s multiple comparisons test. * p<0.05 for effect of treatment (ICC vs. PBCC) at each timepoint below line.

COI: None declared
ID: 396

TITLE: CHRONIC LUNG DISEASE OF PREMATURITY SEVERITY SCALE: FACTOR SELECTION AND SCORING

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CONTENT:

Bronchopulmonary dysplasia (BPD; used interchangeably with chronic lung disease of prematurity [CLDP]) is a frequent comorbidity of extremely preterm infants.

We developed the chronic lung disease of prematurity severity scale (CLDPSS) for use in clinical trials with extremely preterm infants (<28 weeks gestational age), for the period between discharge to home from the neonatal intensive care unit (NICU) and 12 months corrected age (CA). Rounds 1 and 2 of a Delphi survey were previously conducted to identify factors in determining CLDP severity for inclusion in the CLDPSS. Here, we report Round 3 findings, including the importance of factors for determining CLDP.

In Round 2, clinicians had rated the importance of respiratory-related factors used to evaluate the severity of CLDP, from 0 (not at all important) to 10 (very important) for the period between discharge home from the NICU and 12 months CA. Clinicians also ranked the relative importance of these factors in determining severity. Thirteen factors were considered (Table). In Round 3 of the online survey utilizing Delphi methodology, clinicians were presented with aggregate results from Round 2 and were allowed to revise their previously provided responses to reach consensus. The relative importance and weighting of factors were explored through a set of 16 single-profile tasks (i.e., hypothetical patient profiles with varying CLDP severity levels).

The Round 3 survey was completed by 88 clinicians experienced in treating prematurity-related lung diseases such as CLDP (pediatric pulmonologists, n=50; pediatricians, n=19; neonatologists, n=19). Participants resided in 11 countries across North America, Europe, Asia, and South America. Findings from Round 3 indicated that the 4 most important factors in determining the severity of CLDP were home mechanical ventilation (mean absolute importance rating = 8.89), supplemental oxygen ≥ 2 L/min (8.49), re-hospitalizations (7.65), and supplemental oxygen < 2 L/min (7.56). The same 4 factors were also ranked most important relative to the others. According to single-profile tasks, supplemental oxygen had the largest influence on the predicted probability that a hypothetical patient profile would be classified as asymptomatic/minimal, mild, moderate or severe lung disease.

The four most important factors for clinicians in assessing CLDP severity during infancy were home mechanical ventilation, supplemental oxygen ≥ 2 L/min, respiratory-related re-hospitalizations, and supplemental oxygen < 2 L/min. Single-profile tasks highlighted the importance of oxygen-related factors. The current phase of CLDPSS development (clinician feedback) is complete. Refinement of the CLDPSS using patient data is planned.

IMAGE / TAB:
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IMAGE / TAB CAPTION: Table. Factors Considered in the Delphi Survey
COI: This study was funded by Shire, a Takeda company. R. Steinhorn, M. Hallman and R. M. Ward, and were paid consultants to Takeda in connection with this study. E.J. Schwartz, M. Vanya and E. Janssen are, or were, employees of ICON and performed contracted research for Takeda in connection with this study. L. Han, A. Mangili and S.P. Sarda are employees of Shire, a Takeda company, and own stock/stock options in Takeda. The authors thank Rosalind Bonomally, MSc, employee of Excel Scientific Solutions, who provided medical writing assistance funded by Shire, a Takeda company.
ID: 398

TITLE: UMBILICAL VENOUS CATHETERISATION: DO WE NEED TO CHANGE OUR CURRENT PRACTICE?

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CONTENT:

Umbilical venous catheters (UVC) are commonly used in neonatal intensive care units (NICU) to provide intravenous fluids, medications and nutrition. The ideal position of UVC tip to minimize complications is just outside the heart at the junction of inferior Vena Cava and right atrium. UVC related complications are mainly due to low or malpositioned catheters as high positioned catheters can be withdrawn to a safe position. The two commonly used formulae to estimate the length of catheter insertion is birth weight based, proposed by Shukla in 1986 and modified by Verheij in 2013. Success rate of achieving optimum position is about 50%, leading to re-positioning or removal with re-insertion, exposing vulnerable infants to unnecessary handling, radiologic exposure and risk of infection.

Retrospective review of preterm infants ≤34 weeks, born in Norfolk and Norwich Hospital and admitted to NICU between 01/01/2017 - 31/12/2017 who required UVC insertion as part of routine care. Insertion length was calculated using birth weight based formula ([3 x birth wt in kg] + 9)/2 + stump length in (cm). UVC tip position was identified on anterior-posterior chest radiographs. Optimum position was defined as tip between the 8th and 10th thoracic vertebrae, ‘too high’ when tip was in the right atrium and ‘too low’ when tip was below T10. Catheter tip that was directed to the portal, splenic & hepatic veins were defined as malpositioned.

Within the study period UVCs were placed in 49 babies. Median gestational age 29+1 weeks and median birth weight was 1028g. Twenty two percent (11) of the babies had their UVC tip in optimal position following insertion. In 20% (10) of babies the UVC tips were "too high", 33% (16) UVC tips were "too low" and in 25% (12) the tips were malpositioned. Of the 20% (10) babies with "too high" position, 9 babies had their UVC withdrawn to optimal position and 1 UVC tip was malpositioned in hepatic vein on withdrawal.

Overall 41% (20) out of 49 babies had their UVC tip in optimal position in our study cohort.

This audit has demonstrated that the success rate of achieving safe UVC position in our cohort was 41%. Usage of low or malpositioned catheter can lead to serious complications of extravasation in the liver with ascites, NEC & cardiac tamponade. We need to re-think whether in future we should look for alternatives like insertion of peripherally inserted central catheters in a stable infant and reserve UVC for emergency access purpose only.

IMAGE / TAB:
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IMAGE / TAB CAPTION: Position of UVC tip in preterm infants after adjustment.

COI: None declared
ID: 399

TITLE: REFERENCE VALUES FOR REGIONAL INTESTINAL OXYGEN SATURATION IN THE FIRST WEEK OF LIFE FOR PRETERM INFANTS

AUTHORS: B.M. Dotinga 1*, M. van der Heide 1*, R.E. Stewart 2, J.B.F. Hulscher 3, S.A. Reijneveld 2, A.F. Bos 1, E.M.W. Kooi 1

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CONTENT:

Near-infrared spectroscopy is a non-invasive, bedside tool to measure regional tissue oxygen saturation (rSO2). Research suggests a potential clinical use of intestinal rSO2 (rintSO2) monitoring for nutritional management and for early identification of infants at risk of gastrointestinal complications, such as necrotizing enterocolitis. However, its value in clinical care is currently limited, due to a lack of reference values derived from studies with a large sample size. Therefore, we aimed to establish group and personalized reference values for rintSO2 in the first week of life for preterm infants.

In infants born at gestational age (GA) <32 weeks and/or birth weight (BW) <1.2 kg, we continuously monitored rintSO2 in the first week of life. We used INVOS 5100c near-infrared spectrometers with infraumbilical placement of neonatal SomaSensors. Infants were excluded in case of chromosomal and congenital abnormalities, necrotizing enterocolitis, sepsis, and death. We calculated mean rintSO2 from 2-hour periods per day. We assessed associations of sex, GA, postnatal age (PNA), patent ductus arteriosus, hemoglobin, nutrition, and z-scores of BW and birth head circumference (according to Niklasson) with longitudinal rintSO2 per infant in multilevel models. Missing values were imputed using predictive mean matching. Analyses were performed with IBM SPSS version 25.0.

We included 220 infants with a mean GA of 29.4 weeks (SD=2.0) and a mean BW of 1.3 kg (SD=0.4). Reference values for rintSO2 are presented in Figure 1. Higher GA was associated with higher rintSO2 (B=1.58 [95%CI 0.74 to 2.43], P<0.001). Higher BW was associated with higher rintSO2 (B=1.28 [95%CI 0.15 to 2.41], P<0.001). Higher PNA was associated with lower rintSO2 (B=-2.31 [95%CI -2.92 to -1.71], P=0.027). Together, these variables form an equation that can be used to calculate personalized reference values: rintSO2= 4.65 + 1.58*GA + 1.28*BWz-score – 2.31*PNA (R21=0.04, R22=0.16), in which PNA represents postnatal age in days, with day 0 being the first day of life. Residual diagnostics were checked and showed approximate normality.

We established reference values for rintSO2 in the first week of life for preterm infants. Higher GA and higher BW were associated with higher rintSO2, whereas higher PNA was associated with lower rintSO2. We generated an equation with GA, BW, and PNA for personalized reference values for rintSO2. Future research is needed to validate the equation presented and to elaborate on different methodological strategies (e.g. non-linear models).

IMAGE / TAB: https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=098aacc168cea359b224545e636de453-MjAxOS0wNSM1Y2UyNjy2YzZRINGY1

IMAGE / TAB CAPTION: Figure 1. Reference values for rintSO2 in the first week of life for preterm infants. Day 0 represents the first day of life. We determined mean rintSO2 (dashed line) with 95% confidence interval (dotted line) using only postnatal age as an explanatory variable in a non-linear model.
COI: None declared
REFERENCE VALUES OF NEAR INFRARED SPECTROSCOPY (NIRS): DIVERSITY BETWEEN DIFFERENT DEVICES.

AUTHORS: S.J. Roerdink 1, J. Hillen 2, W.E. Kappers 3, P.R. Matthijsse 4, K.D. Liem 5

AFFILIATIONS: Department of Neonatology, Amalia Children’s Hospital, Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands.

CONTENT:

Near infrared spectroscopy (NIRS) is a non-invasive method to measure the regional oxygen saturation (rSO2) in tissue continuously. Especially in the neonatology, it is a promising tool to monitor rSO2 in brain tissue and skeletal muscle tissue. Currently, there are multiple kind of NIRS devices on the market. There are indications that the reference values are different between these NIRS devices. The aim of this study is to compare the reference values of rSO2 in muscle tissue and cerebral tissue between INVOS 4100 and NIRO 200NX.

A prospective, observational clinical study with healthy neonates (34-42 weeks) born after an uncomplicated delivery in the Radboud UMC Nijmegen was performed. In the first period the cerebral rSO2 (crSO2) and muscle rSO2 (mrSO2) were determined by the INVOS 4100 Cerebral Oximeter. During the second period the NIRO 200NX monitor was used. The sensors were placed on the forehead and the thigh. Measurements were done in the first 36h post partum for at least 30 min. The mean crSO2 and mrSO2 during the most stable 15 min of the individual neonate in the population of each device were calculated. Then the p2.5 and p97.5 of both rSO2 from each population were calculated which are considered as reference values for the population of each device and were compared using an independent t-test.

A total of 159 neonates were included, 89 neonates in the INVOS group and 70 neonates in the NIRO group. There were no significant differences in baseline characteristics between both groups (table 1). The means ± SD (p2.5 – p97.5) of crSO2 and mrSO2 in the INVOS group were 84% ± 6 (72% - 95%) and 92% ± 5 (76% - 95%), and in the NIRO group were 70% ± 7 (58% - 85%) and 78% ± 6 (67% - 92%). This difference between the reference values in both the cerebral and the muscle tissue oxygenation between the groups was significantly different (p<0.001).

The reference values of regional tissue oxygen saturation in cerebral and muscle tissue of healthy neonates differ significantly between the INVOS 4100 Cerebral Oximeter and the NIRO 200NX near infrared oxygenation monitor. Therefore it is important to determine their own reference values for each NIRS device.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=dbae28523634b7c6a80ae99e58ee32b9-MjAxOS0wNSM1Y2UyNjY2YzUxMTYz

IMAGE / TAB CAPTION: Table 1. Baseline characteristics of the study population

COI: none declared
ID: 407

TITLE: Can whole body vibration, as experienced during neonatal ambulance transportation, cause lung injury?

AUTHORS: Saleh Algarni 1; Dr Lara Shipley 2; Dr Ian Bloor 3; Dr Shalini Ojha 4; Dr Jon Dorling 5; Dr Don Sharkey

AFFILIATIONS: Division of Child Health., School of Medicine, Nottingham University, Nottingham, United Kingdom

CONTENT:

In 2016 there were ~16,000 neonatal inter-hospital transports in the UK (NTG Annual transport Data, 2016). The aim for each transport is to keep the infant stable. However, whole body vibration (WBV) during transport can compromise the infant’s stability (Shenai et al. Pediatrics, 1981). The EPICure 2 study demonstrated an increase in mortality and morbidity following preterm inter-hospital transfer (Marlow et al. BMJ, 2014). The only study examining the impact of WBV on the respiratory system, exposed rat pups to WBV of 27m/s^2, far in-excess of that seen in most neonatal transfers (Shah et al. Perinatal medicine, 2010), which resulted in significant lung injury. We aimed to recreate WBV, at normal levels experienced by neonatal patients during ambulance transfer, to examine the impact on the neonatal rat lung.

Sprague-Dawley rat pups at postnatal day 4 and 7 were randomly divided into two groups: Control (n=26) and WBV exposure (n=28). WBV animals were exposed to moderate (0.9m/s^2, Mod) or high (2m/s^2, High) WBV for 90 minutes. All exposures simulated ranges, in vibration intensity and time, observed during an average UK ambulance transfer (Blaxter et al. Journal of engineering in medicine, 2017). Twenty-four hours after exposure the lung tissues were obtained for QPCR mRNA expression of surfactant proteins A, B, C and D, and inflammatory genes NF-kb, TLR4, MCP1, TGFβ1, IL-1β and TNFα. Lung tissues were also stained for histological analysis using an established lung injury scoring system (Matute-Bello et al. American journal of respiratory cell and molecular biology, 2011).

There were no significant differences between the control and vibration groups in the gene expression of any of the lung surfactant proteins (SPA, SPB, SPC, and SPD) or inflammatory genes NF-kb, TLR4, TGFβ1, MCP1, IL-1β and TNFα (Table 1). The histological analysis of haematoxylin and eosin stained lung slides revealed no presence of lung injury observed following vibration in all groups. Moreover, the recruitment and infiltration of neutrophils, a key marker of acute lung injury, in either alveolar or interstitial space was not observed histologically after vibration. No significant increase in alveolar septal thickness, hyaline membranes, and proteinaceous debris filling the air spaces.

Lungs of neonatal rat pups exposed to real-world WBV, as experienced during neonatal inter-hospital transport, do not have any adverse histological or inflammatory gene changes. These results are contrary to previously published results which used 10 times the amount of WBV with pressure ventilation. Our data suggest real-world WBV does not induce lung injury in this model.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=a1be029b9a7eafdf87ead016a7d832b3d-MjAxOS0wNSM1Y2UyNjY2YzUyM2Ni

IMAGE / TAB CAPTION: Table1: The effect of WBV on QPCR expression of lung mRNA surfactant proteins and inflammatory genes for rat pubs at age of 4 & 7 days.

COI: None declared
ID: 413

TITLE: PHARMACOLOGICAL VERSUS CONSERVATIVE APPROACH FOR HAEMODYNAMICALLY SIGNIFICANT PATENT DUCTUS ARTERIOSUS IN PRETERM NEONATES

AUTHORS: Dimitrios Rallis1, Aikaterini Drougia1, Foteini Balomenou1, Thomas Benekos2, Antonios Vlahos2, Vasileios Giapros1

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CONTENT:

The persistency of haemodynamically significant patent ductus arteriosus (hsPDA) in preterm infants has been associated with intraventricular haemorrhage (IVH), bronchopulmonary dysplasia (BPD) and increased mortality. However, no therapeutic strategy has been found significantly effective in decreasing BPD or mortality, and the evidence regarding the optimal treatment or even no-treatment in hsPDA remains controversial. Our aim was to evaluate the outcomes of premature neonates with hsPDA in comparison to those without, and, in the subgroup of neonates with hsPDA, the effectiveness of pharmacological compared to conservative approach.

The medical records of all neonates ≤28 weeks’ gestation, admitted to the Neonatal Unit of University Hospital of Ioannina during 2006-2017 were reviewed. HsPDA was defined according to echocardiographic indicators of ductal diameter and shunt pattern, degree of pulmonary overflow and magnitude of systemic hypoperfusion. In our institution the treatment of hsPDA had been given upon clinical decision. Neonates that did not survive beyond the third day of age were excluded.

In primary analysis we evaluated the characteristics and outcomes between neonates with hsPDA compared to those without. Moreover, we performed a subgroup analysis of neonates with hsPDA, comparing pharmacological treatment (paracetamol/ibuprofen) during the first 21 days of age and conservative approach (no treatment).

In overall 182 neonates identified; 75 (41%) with hsPDA and 107 (59%) without. Neonates of the two groups were of similar gestational age (26.8 ± 1.5 versus 27 ± 1.2 weeks) and birthweight (938 ± 224 versus 931 ± 198 g). Those with hsPDA received more blood transfusion within the first 28 days, required prolonged mechanical ventilation (32 versus 13 days) and developed in higher proportion IVH (63% versus 45%) and BPD (63% versus 38%). The survival was similar between the two groups (81% versus 82%).

In the subgroup analysis of the 75 neonates with hsPDA, 20 neonates of 26.8 ± 1.7 weeks received pharmacological treatment and 55 neonates of 26.8 ± 1.4 weeks had conservative approach. No significant differences were noted in the IVH rates (55% versus 66%), the duration of mechanical ventilation (30 versus 33 days), the development of BPD (55% versus 66%) or the survival (90% versus 78%).

In preterm neonates hsPDA is associated with prolonged duration of mechanical ventilation and increased rates of IVH and BPD. However, no clear benefit of pharmacological versus conservative approach was demonstrated on those outcomes or the survival. Therefore, the conservative approach might be a feasible option for the management of hsPDA in such neonates.

IMAGE / TAB:
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IMAGE / TAB CAPTION:

COI: None declared
ID: 418
TITLE: FETAL CEREBRAL T2* AFTER MATERNAL HYPEROXYGENATION IN FETUSES WITH AND WITHOUT HEART DEFECTS
AUTHORS: Mette H Lauridsen 1,2; Niels Uldbjerg 2,3; Tine B Henriksen 1,4; Olav B. Petersen 3; David A Peters 5; Steffen Ringgaard 2,6; Vibeke E Hjortdal 2,7

AFFILIATIONS: 1Department of Pediatrics and Adolescent Medicine, Aarhus University Hospital, Aarhus, Denmark, 2Institute for Clinical Medicine, Aarhus University, Aarhus, Denmark, 3 Department of Obstetrics and Gynecology, Aarhus University Hospital, Aarhus, Denmark, 4Perinatal Epidemiology Research Unit, Department of Pediatrics, Aarhus University Hospital, Aarhus, Denmark 5Department of Clinical Engineering, Central Denmark Region, Aarhus, Denmark, 6MR Research Centre, Aarhus University, Aarhus, Denmark, 7Cardiothoracic Research Department T , Aarhus University Hospital, Aarhus, Denmark.

CONTENT:

Children with major congenital heart defects risk impaired cerebral growth, delayed cerebral maturation, and neurodevelopmental disorders. The magnetic resonance imaging modality T2* is low in areas with high concentrations of deoxymeglobin. We have previously shown that the fetal cerebral tissue oxygenation estimated by T2* is lower in fetuses with heart defects compared to fetuses without heart defects and that T2* in the fetal brain decreases with increasing gestational age. In the present study we aimed to evaluate the fetal cerebral T2* after a short trial of maternal hyper-oxygenation.

Recruitment of women expecting fetuses with and without heart defects took place at Aarhus University Hospital between 2014 and 2016. Twice during pregnancy, at mean (range) gestational age (GA) of 32 (30-34) weeks (early) and 37 (35-39) weeks (late), we compared the fetal cerebral T2* after 20 minutes of maternal hyper-oxygenation with 70% oxygen on a facemask in 22 fetuses without heart defects to that of 11 fetuses with major heart defects: transposition of the great arteries (n=3), coarctation of the aorta/hypoplastic aortic arch (n=5), tetralogy of Fallot (n=1), hypoplastic right heart (n=1), common arterial trunk (n=1). T2* was measured using a breath-hold multi-echo gradient-echo sequence with 5-16 echoes ranging from 1.42 to 120 milliseconds (ms) on a 1.5T Philips scanner.

Multilevel mixed-effects linear regression that accounted for repeated measurements within each fetus was used to estimate the relationship between GA and the fetal cerebral T2* value. Among fetuses without heart defects, the mean cerebral T2*-value after maternal hyper-oxygenation was 161 milliseconds (ms) (95% confidence interval (CI) 152 to 171) early and 127 ms (CI 120 to 134) late. These figures were not significantly different among fetuses with major heart defects: transposition of the great arteries (n=3), coarctation of the aorta/hypoplastic aortic arch (n=5), tetralogy of Fallot (n=1), hypoplastic right heart (n=1), common arterial trunk (n=1). T2* was measured using a breath-hold multi-echo gradient-echo sequence with 5-16 echoes ranging from 1.42 to 120 milliseconds (ms) on a 1.5T Philips scanner.

The difference in fetal cerebral T2* between fetuses with and without heart defects, previously reported, are no longer present after a short trial of maternal hyper-oxygenation. This may indicate an effect on the fetal brain of maternal hyperoxygenation. Analyses are ongoing. However, the possible benefits of oxygen therapy may be outweighed by several disadvantages such as free radical and altered fetal blood. Further studies are needed.

IMAGE / TAB:
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IMAGE / TAB CAPTION: Fetal cerebral T2* after maternal hyperoxygenation (ms; y axis) by gestational age (weeks; x axis); Blue dots: fetuses without heart defect. Red dots: fetuses with heart defects. Thick blue and thick red line: regression line
of the fetuses with and without heart defects respectively. Thinner blue line: 95% prediction interval for the fetuses without heart defects. A very thin dashed line connects the results from 2 scans of the same fetus. MRI: Magnetic resonance imaging; ms: milliseconds.

COI: There are no conflicts of interest
ID: 422

TITLE: EARLY CEREBRAL OXYGENATION AND ELECTROCEREBRAL ACTIVITY IN ANEMIC AND NON-ANEMIC TERM INFANTS WITH MODERATE TO SEVERE HYPOXIC-ISCHEMIC ENCEPHALOPATHY

AUTHORS: Willemien S. Kalteren, BSc 1; Leanne de Vetten, MD 1; Hendrik J. ter Horst, MD PhD 1; Arend F. Bos, MD PhD 1; Elisabeth M.W. Kooi, MD PhD 1

AFFILIATIONS: 1 Department of Pediatrics, Division of Neonatology, Beatrix Children’s Hospital, University of Groningen, University Medical Center Groningen, Groningen, the Netherlands

CONTENT:

Perinatal anemia may lead to brain injury by impaired oxygen delivery, causing hypoxic-ischemic encephalopathy (HIE). Previously we found perinatal anemia in HIE to be associated with high mortality rates. Neurodevelopmental outcome (NDO) of survivors, however, appeared to be favorable compared with survivors from other causes for HIE.1 To understand the pathogenesis of these findings, we now aimed to explore the course and interrelation of cerebral oxygenation and electrocerebral activity during the first days after birth, comparing term infants with HIE due to perinatal anemia and term infants with HIE due to other causes.

1 Kalteren WS et al., Neonatology, 2018.

All HIE infants treated with therapeutic hypothermia (2010-2017) were retrospectively included. We measured cerebral tissue oxygen saturation (rcSO2), using near-infrared spectroscopy. We used amplitude-integrated electroencephalography (aEEG) to assess background patterns (BPs), sleep-wake cycling (SWC) and epileptic activity during the first 96 hours after birth. Burst suppression, continuous low voltage and flat trace were considered as abnormal. Additionally, cerebral fractional tissue oxygen extraction (cFTOE) was calculated. Anemic infants (initial Hb<7 mmol/L) were compared with non-anemic infants in both deceased and survived infants. We calculated odds ratios (ORs) to determine whether cFTOE and aEEG were associated with mortality.

One-hundred-eighteen term infants were included of whom 24 were anemic at birth. In total 25 infants (21%) died (88% withdrawal of care). Out of the 24 anemic infants, nine (38%) died versus 16 from 94 (17%) non-anemic infants, p=0.03. Anemic infants had significantly lower rcSO2 and higher cFTOE during the first 48-hours than non-anemic infants (Figure 1). Twenty-one (88%) anemic infants showed abnormal aEEG BPs at some point, compared to 65% of the non-anemic group, p=0.03. SWC was present in six (25%) anemic infants, while 49 non-anemic infants (52%) showed SWC, p=0.03. Seizures were less common in anemic infants (33%) compared to non-anemic infants (52%) showed SWC, p=0.03. Seizures were less common in anemic infants (33%) compared to non-anemic infants (55%), p=0.045. The OR for mortality of an abnormal aEEG BP at 12 hours after birth was 32.6 (4.11-258), p<0.01. In the group of survivors, anemic infants had lower rcSO2 and less seizures than non-anemic infants.

Perinatal anemia in HIE infants is associated with lower cerebral oxygenation and more infants showing abnormal aEEG BPs, but less seizures. Abnormal aEEG BPs, whatever the cause of HIE, resulted in higher mortality risks. The lower rcSO2 in anemic infants was not associated with mortality, nor with seizure activity in survivors. Further studies are required to investigate whether these findings are associated with better NDOs.

IMAGE / TAB:
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IMAGE / TAB CAPTION:

COI: None declared
ID: 423

TITLE: EFFICACY AND SAFETY EVALUATION OF KEDRION HUMAN HEPATITIS B IMMUNOGLOBULIN FOR INTRAMUSCULAR USE IN THE PREVENTION OF HEPATITIS B IN NEONATES BORN TO HEPATITIS B VIRUS CARRIER-MOTHERS: MULTICENTRE, OPEN-LABEL, PHASE IV CLINICAL TRIAL - PRELIMINARY REPORT

AUTHORS: Paolo Biban 1, Andrea Ronchi 2, Patrizia Garzia 3, Silvia Perlini 1, Beatrice Ghirardi 2, Carlo Pietrasanta 2, Angela Bossi 3, Ilaria Bottino 2, Assunta Serena Bongiovanni 4, Chiara Guarnieri 5, Massimo Agosti 3, Fabio Mosca 2, Lorenza Pugni 2

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CONTENT:

HBV infection is an important public health problem worldwide: around 240 million people are chronic carriers of HBV and 780,000 people/year die from the infection. Those born from HBsAg-positive women have a high risk to contract the infection at the time of delivery. Following the introduction of the anti-HBV vaccine in the 1980s, passive-active immunoprophylaxis with anti-HBV immunoglobulin (HBIG) and HBV vaccine proved to be effective in preventing perinatal transmission of HBV infection: the percentage of neonates born to HBsAg-positive mothers dramatically dropped from 30-85% to 0.7-1.1%.

Open label, multicenter, phase IV study. The study is designed to enroll 184 neonates born to HBsAg-positive mothers not treated with HBIG during pregnancy. The study protocol involves the administration of HBV vaccine in the first day of life together with the administration of the first dose of Kedrion HBIG in accordance with SmPC. Subsequently, infants enrolled in the study receive HBV vaccine according to the Italian vaccination schedule. The anti-HBs antibody level is determined in each subject at 1, 3 or 4 months and, when needed, at 13 and 15 months in order to verify that a protective antibody level of ≥10 UI/L persist; if the antibody level is <10 UI/L, an additional dose of Kedrion HBIG is administered. At the beginning and at the end of the study, HBsAg test is also performed.

This is a preliminary analysis of the data from the first 116 enrolled subjects during the period 2012-2017 (GA ≥37 weeks in 87.9%, medium birth weight at the delivery 3140 ± 550 g). All subjects were HBsAg-negative at birth and received a HBV vaccine dose together with Kedrion HBIG in the first day of life.

Ninety subjects out of 116 (77.6%) completed the study (10 drop-out; 3 screening failure; 13 missing data). Fifty-six subjects out of 90 (62.2%) showed seroconversion at the second visit, 26 (28.9%) at the third visit and 8 (8.9%) at the fourth visit.

All subjects were HBsAg-negative at the study termination and nobody needed an additional dose of Kedrion HBIG. During the study, 21 adverse events were collected, none related to Kedrion HBIG administration.

One hundred percent of the enrolled subjects were HBsAg-negative at the end of the study, supporting the efficacy of Kedrion HBIG if administered together with HBV vaccine in the prevention of vertical transmission from HBV mothers to neonates. Moreover, these data confirm that Kedrion HBIG was also well tolerated by all the enrolled subjects.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: Chiara Guarnieri and Serena Bongiovanni are Kedrion SpA employees
For all other authors None declared
ID: 425
TITLE: THE ROLE OF NEUTROPHILS IN NEONATAL HYPOXIC-ISCHEMIC BRAIN INJURY
AUTHORS: Josephine Herz, Kerstin Weißenfels, Christian Köster, Ursula Felderhoff-Müser, Mark Dzietko, Ivo Bendix
AFFILIATIONS: Department of Paediatrics I, University Hospital Essen, Essen, Germany

CONTENT:

Neonatal encephalopathy caused by hypoxia-ischemia (HI) is a major cause of death and disability in newborns. Therapeutic hypothermia is the only recommended therapy. However the therapeutic window of 6 hours is very short. Infiltration of myeloid cells has been linked to worse outcome after neonatal HI, but the specific role of neutrophils as potential therapeutic target is still controversially discussed. The aim of the present study was to characterize the temporal and spatial dynamics of neutrophil infiltration followed by analysis of its functional role in the post-hypoxic disease phase through delayed neutrophil depletion.

Nine day old C57BL/6 mice were exposed to HI through ligation of the right common carotid artery followed by 1 hour hypoxia (10% oxygen). Infiltration and activation of neutrophils was assessed by immunohistochemistry and flow cytometry 1, 3 and 7 days post HI, which was correlated to HI-induced neuronal loss. The functional role of neutrophils was evaluated by intraperitoneal (i.p.) injection of a neutrophil-depleting anti-Ly6G antibody (clone 1A8, 10 µg/g body weight). Depletion efficacy was determined in naïve animals via flow cytometry 6, 12, 24 and 48 hours post injection. According to infiltration and depletion dynamics anti-Ly6G was injected 12 hours after HI followed by analysis of brain injury via histology and immunohistochemistry 36 hours later.

Analysis of cerebral neutrophil infiltration revealed a biphasic infiltration pattern peaking at 1 and 7 days after HI, with most pronounced infiltration in severely injured brain regions (e.g. hippocampus). The amount of activated CD86 positive neutrophils in the brain increased from 7% to 40% between 1 and 7 days after HI, contrasting results from the blood where less than 5% of activated neutrophils were determined up day 7 after HI. Efficacy of neutrophil infiltration by i.p. injection of anti-Ly6G reached its maximum with 90% 12 hours after injection. Aiming to exactly hit the first infiltration peak of neutrophils 24 hours after HI, we initiated neutrophil depletion 12 hours post HI resulting in significantly reduced hippocampal tissue loss and cellular degeneration.

These data suggest a detrimental role of acute cerebral neutrophil infiltration in neonatal HI. Importantly, the therapeutic time window seems larger than the only available therapy HT. Thus, inhibition of neutrophil infiltration by therapeutic pharmacological approaches might present a novel therapeutic option in addition or as alternative to HT.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 441

TITLE: SUCCESS RATE OF NEONATAL INTUBATION WITH TWO DIFFERENT PREMEDICATION STRATEGIES

AUTHORS: Ellen H.M. de Kort 1,2; Irwin K.M. Reiss 2; Sinno H.P. Simons 2; Peter Andriessen 1

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CONTENT:

Awake intubation in neonates is associated with severe adverse physiological events. Premedication can decrease these adverse events, and reduce the number of attempts and the time needed for successful intubation. Since 2001 consensus is reached that premedication should always be used for nonemergency endotracheal intubation in neonates. Almost twenty years later, the most effective and safe premedication strategy is still to be discovered. Aim of this study was to evaluate success rate and technical quality of intubation in two different premedication strategies.

Prospective observational cohort study in a level III neonatal intensive care unit during a 30 month period. Neonates < 32 weeks’ gestation who required endotracheal intubation were eligible for inclusion. Only the first intubation encounter per patient was included. Intubation was performed according to a standardized procedure. At first, the local premedication regimen consisted of a combination of atropine, fentanyl and rocuronium (AFR group). After 17 months, the standard regimen was changed to atropine and propofol (AP group). Patient characteristics, pre-intubation sedation level, quality of intubation, number of attempts for successful intubation, total procedure time, and level of experience of the intubator were prospectively collected for both premedication regimens.

Patient and procedure characteristics of the AFR and AP groups are presented in table 1. In the AFR group 65% of patients was successfully intubated at the first attempt compared to 58% in the AP group (p = 0.32). Time to successful intubation was 15.7 ± 7.4 minutes in the AFR group, compared to 10.8 ± 7.7 minutes in the AP group (p < 0.001). Insufficient pre-intubation sedation level occurred significantly more often in the AP group than the AFR group (12 versus 0%, p = 0.03) and patients in the AP group significantly more often needed extra medication after the first attempt failed compared to the AFR group (48 vs 16%, p = 0.03). Quality of intubation was inadequate in 6% of patients in the AFR group and 8% of patients in the AP group respectively. This difference was not statistically significant (p = 1.0).

Success rates and quality of intubation were comparable between both premedication strategies. The total procedure time was significantly longer in the AFR group, due to our administration protocol taking into account the slower speed of onset of fentanyl. As longer procedure times may lead to adverse events, fast acting agents may be more appropriate. Further research into the efficacy as well as the safety of different strategies is needed.

IMAGE / TAB:
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IMAGE / TAB CAPTION:

COI: None declared
ID: 449

**TITLE:** WHAT IS THE OPTIMAL ARGinine CONTENT FOR NEONATAL PARENTERAL AMINO ACID FORMULATIONS?

**AUTHORS:** Colin Morgan (1,2)
Chandini M Premakumar (2,3)
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**CONTENT:**

Arginine (ARG) is involved in multiple metabolic/immune pathways and required for growth. Current neonatal parenteral nutrition (NPN) amino acid (AA) formulations are associated with arginine deficiency and over-provision of essential AA in NPN dependent preterm infants (1) based on plasma AA data in healthy infants. Higher ARG plasma levels (>80µmol/l) may be required to prevent necrotising enterocolitis (NEC) (2). Recent European NPN guidelines recommend ARG supplementation but do not explain how. Our aims were to use small physiological studies to rebalance NPN AA formulations, identify the optimal ARG content (%) and investigate the relationship between ARG intake/plasma ARG levels.

In a series of ethically approved physiological studies (each n=8), infants <30wks gestation, <1200g and aged <72 hrs were non-randomly allocated control NPN (ARG 6.3%), NPN (ARG 6.3%) with supplementary parenteral ARG equivalent to ARG 12-15% and finally a modified NPN (ARG 14%). Plasma AA profiles (and ammonia levels) were measured on day 3 and 10 of life using ion exchange chromatography. Total daily NPN and enteral intakes (day 1-10) were calculated from the electronic patient record. Changes in total ARG (ΔARG) intake and plasma level between day 3 and 10 were calculated. Infants receiving control NPN (ARG 6.3%) were compared to all infants receiving additional ARG: NPN ARG (12-15%) using t-tests with linear regression used to compare relationship between ARG intake/plasma and levels.

40 infants were recruited to control (n=15) or ARG 12-15% PN (n=25). The mean (SD) gestational age was 26.8 (2.1) & 26.8 (1.8) weeks respectively. The mean (SD) plasma arginine level (µmol/l) for control versus ARG 12-15% PN was 28 (19) versus 47 (23) on day 3 (p<0.01) & 42 (24) versus 62 (39) on day 10 (p=0.08). Plasma essential AA showed a mean reduction of 9% in infants receiving the modified AA formulation. Actual arginine intake varied markedly on day 10 (but not day 3) reflecting the higher enteral feed intake (Figure 1). Actual intake and plasma level were correlated on day 10 (p=0.04) with an increase of 9µmol/l for every 100mg/kg/d increase in arginine intake. ΔARG intake and ΔARG plasma level were also correlated (p=0.01) showing a 13µmol/l increase for every 100mg/kg/d increase in arginine intake between d3 and 10 and 9µmol/l increase attributable to increased postnatal age. Current NPN AA formulations can be successfully rebalanced to correct arginine deficiency and achieve AA plasma profiles closer to healthy pretermers. The data suggest that future NPN AA formulations may require >15% ARG and >600mg/kg/day to achieve ARG plasma levels >80µmol/l in the majority of infants <30 weeks gestation.


**IMAGE / TAB:**
https://www.eiseverywhere.com/eiselectv3/v3/events/351149/submission/files/download?fileID=b0bc79aa9f0d2b77651af509251700ba-MjAxOS0wNSM1Y2UyNjY2YzYxNnM3
**IMAGE / TAB CAPTION:** Figure 1: Scatterplot showing day 10 arginine intake (g/kg/d) versus plasma arginine levels (µmol/l) in preterm infants <30 weeks gestation

**COI:** The modified amino acid formulation is the subject of a patent application
ID: 450

TITLE: ELECTROLYTES AND JAUNDICE IN CORRELATION WITH BODY WEIGHT LOSS IN NEONATES

AUTHORS: George Katsaras 1; Evlampia Tsentemidou 1; Anastasia Batsiou 1; Ilektra Toulia 2; Kalliopi Kappou 3; Evangelos Oikonomou 1

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CONTENT:

A weight loss of 5–10% in term infants and 10–20% in preterm infants is common during the first week of life. Fluid and electrolyte assessment during the first week of life generally focuses on body water, serum sodium, potassium, glucose and calcium concentrations as well as renal function. Even values that are within normal range for gestational/postnatal age may have pathophysiologic consequences that require intervention.

We conducted a retrospective observational study of all neonates born during 2017-2018 in our Maternity Ward and were gone under laboratory tests, especially due to weight loss and/or feeding difficulty. Use of NEWT curves of body weight loss customized for each neonate, postnatal age and nutrition. A multivariable analysis (ANOVA test) took place in order to examine the impact of body weight loss to blood test results of the newborns.

A total of 34 neonates were examined, boys:girls ratio 3:2. Of Greek origin was 85% of the population. The majority of neonates were full terms and 73% of deliveries were cesarean section. Mean birth weight was 3200gr and 68% were under breastfeeding and formula. The remaining neonates were equally divided in only breastfed or formula fed. For each 1% of body weight loss there was an increase of 0.825mg/dL in TBil, 0.572g/dL in Hb, 0.577% in Hct, 1.331mmol/L in Na, 1.363mmol/L in Potassium, 0.351mg/dL in Creatinine and 1.95mg/dL in Urea, but with no statistical significance. A statistically significant correlation was found with the duration of phototherapy, which was increased by 7hrs for every 1% increase in body weight loss (P<0.05). Finally, electrolyte disorders, like hypernatremia and hypocalcemia, were found only in neonates that were above the 90th NEWT curve of body weight loss.

The results of this study are in agreement with the current literature according to the electrolyte or other disorders in the blood test results of the neonates with body weight loss. What is more, the percentage of body weight loss could be a prognostic marker as far as the presence and the severity of jaundice and the duration of its therapy are concerned.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 461

TITLE: Parents as carers on a neonatal unit in a low-income country – different perceptions of parents and staff.

AUTHORs: Lissauer T1,4, Ndiaye S2, Bosowski J2, Tuyisenge L3, Penn-Kekana L2, Moxon S2

AFFILIATIONS: 1 Paediatric Dept, Imperial College London UK
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CONTENT:

Some of the key concepts of increased parental participation embodied in family centred and family integrated care were derived from LMICs. We aimed to identify what care is actually provided by mothers and family in a neonatal unit in a low-income setting, determine the parent’s experiences, and how they and the staff perceive the parent’s role. We also wished to explore the attitude of parents and staff towards extending parents’ role as primary carers, as in family integrated care. The study was conducted in a busy rural hospital in Rwanda, a low-income country in East Africa, which has made considerable progress in reducing neonatal mortality, to 17 per 1000 live births in 2016.

Observation and qualitative analysis of parent and staff interviews were performed by 2 researchers over a 2 week period. 10 mothers and 2 fathers and 15 staff members were interviewed. A semi-structured questionnaire was used. Interviews were audio-recorded and thematic content analysis was performed. The study was conducted in a neonatal unit with 800 admissions/year, 10 incubators, 15 cots and 5 Kangaroo Mother Care (KMC) beds. CPAP and wall oxygen was available, but no milk storage. Water was from tanks; alcohol gel was available. Ethical approval was obtained in the UK and Rwanda.

Mothers provided all non-technical care: breastmilk via nasogastric tube, cup or breast; comforted and cleaned their babies even in incubators. KMC in separate room when infant stable, but babies often left on mother’s bed during the day. Nurses had little time to talk to parents as only 9 nurses in total, 3 on long-term leave; bed to nurse ratio 7:1 to 31:1. Thematic analysis revealed parental satisfaction with care but mothers felt very stressed from need to provide breastmilk directly day and night, fear of baby dying, loneliness from lack of visitors, difficulty in finding food, financial worries and concern about family and home. Nurses preoccupied by shortage of staff limiting care. Discharge - parents desperate to get home, staff concerned about parental ability to provide care and follow-up; thought their educating mothers was key. Neither thought parent’s role could be extended.

Nurses and parents perspectives differed. Nurses thought improving parent’s experience required more nurses, but unavailable. Parents satisfied with care although feared baby’s death, but had severe concerns around practical issues of hospital stay, more likely alleviated by non-clinical assistance e.g. experienced mothers. Post-discharge, nurses wanted to educate mothers, but parent’s had practical concerns, requiring community support.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ABSTRACT BOOK
POSTER PRESENTATIONS

ID: 467
TITLE: A NOVEL ECG ELECTRODE PLACEMENT METHOD FOR IMPROVING HEART RATE MEASURES AT BIRTH
AUTHORS: Caroline Henry 1; Lara Shipley 1; Carole Ward 1; Siavash Mirahmadi 2; John Crowe 2; Barrie Hayes-Gill 2; James Carpenter 3; Don Sharkey 1

AFFILIATIONS: 1 Division of Child Health, Obstetrics & Gynaecology, University of Nottingham, Nottingham, UK
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3 SurePulse Medical Limited, Nottingham, UK

CONTENT:

In the first few golden minutes of newborn resuscitation, accurate heart rate (HR) is a key and a guiding principle for resuscitation algorithms. The 2015 ILCOR guidelines recommend using electrocardiogram (ECG) when available. The challenge is to ensure quick placement of monitoring technology and minimising electrode detachment without delaying the appropriate first resuscitation steps. The normal method of ECG monitoring requires the skin to be dried and electrodes placed individually, taking a median time of 26s (Katheria et al Pediatrics 2012). We aimed to evaluate the application time of pre-set ECG electrodes on the chest by exploiting the wet properties of the newborns’ skin.

Prior to delivery, the ECG electrodes were attached to a small square of plastic wrap normally used for thermoregulation in preterm infants (see figure). Small holes were made in the plastic wrap to allow the electrodes contact with the skin with ECG conduction gel placed onto the electrodes and so avoid adhesive attachment to the skin. Three time points were calculated from video analysis on the resuscitaire: 1) Time to apply pre-set electrodes from when they were picked up ready to be sited until placement; 2) Time taken to detect recognisable QRS complexes after placement; 3) Time after placement until HR value output by the device (GE B450 monitor). Ethical approval was given and the study funded by the Innovate UK.

57 newborns were studied (20 term infants, 30 32-37wks GA and 7 <32wks GA) with 8 born by vaginal birth. 23 needed stabilisation/resuscitation at birth with at least mask positive pressure ventilation. The median ECG application time was 9s (IQR 6-11s). The median time for a recognizable QRS to be displayed after application was 8s (IQR 2-12s) with all babies displaying a QRS signal by 46s. The median time for a visible HR output from the ECG monitor was 24s (IQR 15-47s). Within 1 minute of arrival on the resuscitaire, all babies had a recognisable QRS signal and 79% had an HR value output which increased to 96.5% (55 of 57) by 90s. There were no electrode detachments.

Pre-set chest ECG electrodes allow faster HR detection and output with fewer ECG failure rates than seen in previous studies. From the time of handling the ECG electrodes, our method typically outputs a QRS signal within 17s, far quicker than Katheria’s 26s to apply. This simple technique avoids detachment of single electrodes and potential skin stripping injury from adhesives. We believe this approach is worthy of further evaluation.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=efa7fad15e5bbf6f840290a40d867115-MjAxOS0wNSM1Y2UyNjY2YyMjA4

IMAGE / TAB CAPTION: Figure: Pre-set ECG electrodes on the chest

COI: None declared
ID: 470

**TITLE:** KEY FEATURES OF THE PRENATAL FUNCTIONAL CONNECTOME

**AUTHORS:** Elise Turk a,b,c; Manon J.N.L. Benders a,b; Roel de Heus b; Arie Franx b; Moriah E. Thomason d,e,; Martijn P. van den Heuvel f

**AFFILIATIONS:** a Department of Neonatology, Division of Woman and Baby, University Medical Center Utrecht b UMC Utrecht Brain Center; c Department of Obstetrics, Division of Woman and Baby, University Medical Center Utrecht; d Perinatology Research Branch, NICHD/NIH/DHHS; e Department of Child and Adolescent Psychiatry, New York University, New York, USA; f Dutch Connectome Lab, Department of Complex Traits Genetics, Center for Neurogenomics and Cognitive Research, VU Amsterdam, Amsterdam, The Netherlands

**CONTENT:**

The functional connectome is a complex network of interconnected communicating brain regions. Network development is governed by biological rules to make a trade-off between neural wiring cost and efficiency, resulting in small world topology to balance out efficient global communication and local organization. The last stages of pregnancy are a critical phase in brain development, and emerging evidence supports the notion that functional connectome formation and re-organization already starts as early as the second trimester. We aim to identify which first principles of functional connectome organization are already developed in utero.

A sample of 105 women participated in fetal resting-state fMRI studies during pregnancy (fetal gestational age between 20 and 40 weeks) at Wayne State University, Detroit, MI. Functional connectivity was inferred by measuring fMRI signal covariance across cortical regions. Brain regions were selected using a special made version of the Freesurfer’s Desikan Killiany atlas constructed that was manually fine-tuned on a 32-week preterm neonatal brain template. Group-based and individual graph analysis and permutation testing were used to analyze weighted network characteristics. For a better interpretation of common functional resting-state networks we examined the overlap with the adult resting-state functional connectome.

We identified efficient network features including high clustering (1.20 times higher than in random networks, p < 0.001), short path length (1.14 times higher than random networks, p < 0.001), and small-world index higher than 1 (1.05 times higher than random networks, p < 0.001). Rich club hubs can already be pointed out and have widely distributed communication paths across the cortex. We also identified an overlap of 61.67% (Mantel test p < 0.001) between the fetal and adult network.

Within the fetal brain, we observe efficient functional dynamics, such as small world topology and proto-networks of generally known functional modules, network structures that are known to be key features of the adult connectome. Mapping and understanding the healthy fetal functional connectome may bring opportunities for early detection of functional alterations of the vulnerable developing brain.

**IMAGE / TAB:**

**IMAGE / TAB CAPTION:**

**COI:** None declared
Surgical Closure of the Patent Ductus is a Helpful Treatment Option

Mark Fenner 1; Rachel Anderson 2; Dushyant Batra 3; Bernard Schoonakker 4

1 Nottingham University Hospitals NHS Trust, Nottingham, UK

Ligation of the ductus arteriosus remains a controversial procedure. Evidence suggests that ligation is associated with increased rates of intraventricular haemorrhage (IVH), necrotising enterocolitis (NEC), bronchopulmonary dysplasia (BPD) and death. However, no randomised trials exist and the mechanism of these effects is not clear. Scrutiny of the evidence suggests that these side effects may be related to the haemodynamic effect of the duct rather than the surgical ligation itself. This study aimed to evaluate the chronological sequence of events prior to and after surgical ligation.

Retrospective cohort study of preterm infants undergoing surgical ligation across our tertiary network over a five year period. A search was performed of the national data registry and regional transport registry. 14 infants were identified. Baseline characteristics were collected. The data was interrogated for events prior to and after surgical ligation. Cardiac measurements were obtained from imaging immediately prior to ligation. The primary objective was to assess the need for invasive ventilation prior to and after ligation. Secondary objectives were to assess the rate of major events (IVH, NEC, acute renal failure) prior to and after ligation. Finally assessment was made to determine whether any characteristic suggested a lower likelihood of success from duct ligation.

Gestation at birth ranged from 24 to 30 weeks. Median duration of intubation prior to ligation was 30 days [95% CI 23.7, 42.5] and 9 days after ligation [95% CI 3.9, 25.7]. The Wilcoxon Signed-Rank test was applied to this small non-parametric sample with Z = -2.65, p = 0.009. 2 cases of NEC were encountered prior to ligation with none after. 6 cases of IVH (grade 2+) occurred prior to ligation with no new cases after. A total of 46 episodes of acute renal failure were recorded prior to ligation (median of 3 per infant) with only 4 after ligation three of which occurred in only one infant. Notably the two infants ventilated for more than three weeks after ligation had echocardiographic evidence of PPHN prior to ligation. No other infants had this characteristic. In addition both had an additional significant left to right shunt (VSD, ASD).

Existing evidence attributes serious complications to surgical duct ligation. This study suggests these events are occurring prior to the ligation. For a persistent duct unresponsive to medical therapy then surgical closure increases the likelihood of extubation and does not result in IVH or NEC. Episodes of renal failure significantly reduce. Infants with PPHN or additional left to right shunts may be less likely to benefit with ligation.

COI: None declared

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=d312728fe77959679ec1f4750d401822-MjAxOS0wNSM1Y2UyNjY2YzZiNmM4

IMAGE / TAB CAPTION: Box plot demonstrating ventilation (days) and renal failure (episodes) prior to and after duct ligation

Supported by: COINN Powered by: MCA scientifics
ID: 476

TITLE: PERIPHERAL MUSCLE OXYGENATION MEASURED WITH NEAR-INFRARED SPECTROSCOPY IN PRETERM NEONATES ON THE FIRST DAY AFTER BIRTH

AUTHORS: Christina Wolfsberger 1,2; Nariae Baik-Schneditz, M.D. 1,2; Bernhard Schwaberger, M.D. 1,2; Corinna Binder-Heschl, M.D. 1,2; Nina Höller, M.D. 1,2; Lukas Mileder, M.D. 1,2; Berndt Urlesberger, M.D. 1,2; Gerhard Pichler, M.D. 1,2;

AFFILIATIONS: 1 Division of Neonatology, Department of Paediatrics, Medical University of Graz, Austria; 2 Research Unit for Neonatal Micro- and Macrocirculation, Department of Paediatrics, Medical University of Graz, Austria;

CONTENT:

Near-infrared-spectroscopy (NIRS) measurements combined with venous occlusions enable to assess peripheral muscle oxygenation and perfusion. Changes over time (first minutes after birth and over several days/weeks after birth) have been described in term and preterm neonates. However, behaviour of peripheral muscle oxygenation and perfusion measured with NIRS on the first day after birth is unknown. The aim of the present study was to evaluate peripheral oxygenation and perfusion within the first 24 hours after birth in cardio-circulatory stable preterm neonates.

Secondary outcome parameters of prospective studies were analysed. Preterm neonates were included, in whom peripheral muscle NIRS measurements (NIRO 200, Hamamatsu Photonics) combined with venous occlusion were performed within the first day after birth. Heart-rate and arterial oxygen saturation were measured by pulse oximetry. Neonates had to be without any circulatory support and without signs of infection/inflammation. Measurements of neonates were divided into four “6-hour-periods”. For each period total haemoglobin (HbT), oxygen delivery (DO2), oxygen consumption (VO2), fractional oxygen extraction (FOE), tissue oxygenation index (TOI) and mixed venous oxygenation (SvO2) were calculated. Values of the first “6-hour-period” were compared to values of the following time-periods.

133 preterm neonates (median gestational age: 33.7 weeks (32.6-34.7 weeks); median birth weight: 2070g (1745-2380g)) were included in the present study. Median age of neonates when NIRS measurements were performed was 12 hours. HbT showed a significant increase from the first to the third period (p=0.006). As well, DO2 showed a significant increase from the first to the third period (p=0.009). VO2 did not change significantly. FOE showed a significant decrease from the first to the second (p=0.012) and third (p<0.001) time period. TOI showed a non-significant increase comparing the first time period with the third period (p=0.108). SvO2 showed a significant increase from the first to the second (p=0.012) and third (p=0.001) time period. (Table1)

In preterm neonates HbT, DO2, SvO2 increased, FOE decreased and TOI showed a trend towards increase on the first day after birth, whereas VO2 did not change. The present observed changes show different behaviour when compared to measurements during the first days/weeks after birth. Therefore, the present findings have to be taken into account when preterm neonates are measured especially on the first day after birth.

IMAGE / TAB:
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IMAGE / TAB CAPTION:

COI: None declared.
ID: 478

TITLE: BODY COMPOSITION (FAT MASS AND FAT-FREE MASS) OF PRETERM INFANTS LESS THAN 32 WEEKS AND NEURODEVELOPMENT AT 18 MONTHS

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CONTENT:

Weight measurements alone are insufficient indicators of individual body composition (i.e. fat mass and fat-free mass). Also, there is growing evidence that nutrition and resulting body composition at discharge are related to the neurodevelopment outcome. Air displacement plethysmography (PEA POD) was used to create a database of body composition measurements for preterm and term infants. Aim of the study was to calculate percentiles for body composition measurements and to compare the body composition with the neurodevelopmental outcome at 18 months.

A longitudinal, observational study was conducted for infants (gestational age (GA) 6 cm H2O or high-flow nasal cannula > 6 L/min) were excluded. Body composition indicators including % body fat (%BF), fat mass (FM), fat-free mass (FFM), fat mass/length² (FMI), fat-free mass/length² (FFMI) were graphed against postmenstrual age (PMA). At 18 months, the infants received a Bayley III assessment. For descriptive statistics, the infants were stratified in two gestational age groups: <28 weeks and 28 to 31 weeks. Percentiles were calculated using GAMLSS package in r statistics. Further, the infants were subdivided into three quantiles according to the neurodevelopment.

Of the 147 infants which were enrolled in the original study, 96 infants received a Bayley III assessment at 18 months (Figure 1). In total, 398 body composition measurements were performed. At 35 weeks, the younger preterm infants had higher %BF compared to those born with 28 to 31 weeks. At 50 weeks PMA, %BF leveled out in both groups from 23 to 25% and remained stable at this value until 70 weeks PMA (Figure 2).

Preterm infants with GA <28 weeks had slightly shorter body length and lower neurodevelopmental scores. Infants with higher measurements for fat mass had higher Bayley score. For %BF, and fat mass the average curve for infants with lower language score (<33 percentile) was considerably lower (Figure 3). Also, fat-mass and percent free-mass were significantly correlated with language score (p<0.05).

There seems to be a relationship between body composition and neurodevelopment at 18 months. The strongest relationship was found for language score, for both fat-free and fat mass. Associations with motor and cognitive scores were weaker (p=0.08–0.15). The reported association is an important finding and supports the concept that optimized nutrition during NICU is crucial to achieve a body composition which is related to optimal neurodevelopment.

IMAGE / TAB:
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IMAGE / TAB CAPTION: Association between body composition and neurodevelopment. (Black lines represent body composition of infants with language scores >97, red lines for language scores <87)

COI: None declared
ID: 480

**TITLE:** Executive function training in very preterm children: a randomized controlled trial

**AUTHORS:** Carolien A. van Houdt, 1,2; Aleid G. van Wassenaer-Leemhuis, 1; Jaap Oosterlaan 3,4; Marsh Königs 2; Corine Koopman-Esseboom 5; A.R. Céleste Laarman 6; Anton H. van Kaam 1,6; Corneliëke S.H. Aarnoudse-Moens 1,2,4,7

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**CONTENT:**

Very preterm (VP) children show deficits in attentional, academic, behavioral and emotional functioning compared to term-born peers. Executive function (EF) problems are thought to underlie the deficits in these domains. Therefore, computerized EF training programs may improve these outcomes in VP children. Aim of the current study was to examine effects of a computerized, game-formatted EF training (BrainGame Brian) on attentional, executive, academic, behavioral and emotional functioning and self-perceived competence in VP children.

In our multi-center, double-blind, placebo and waitlist controlled randomized trial, VP children (< 30 weeks of gestation) aged 8 to 12 years with parent rated attention problems were eligible for inclusion. Children were randomized to EF training, placebo training or waitlist. EF and placebo training comprised of 25 sessions played in 6 weeks. Outcome measures were assessed at baseline, at the end of the training program and five months after finishing the training. Outcome measures were parent and teacher rated attentional, executive, academic, behavioral and emotional functioning, neuropsychological tests of attentional, executive and academic functioning and self-perceived competence as rated by children themselves. Data were analyzed on intention-to-treat basis with linear mixed model analyses.

A total of 85 children were included in the trial, of which 29 were randomized to the EF training, 26 to the placebo training and 30 to the waitlist. Twelve infants withdrew from the study before the first follow-up assessment and another four before the second follow-up assessment. Thus, 69 children (81%) completed all assessments. Basic characteristics at the start of the study did not differ between the groups. For children in the EF training group, significant improvements were found across training sessions in the EF training tasks. Despite these improvements, we found no significant differences in improvement over time between the EF training, placebo training and waitlist for any of the outcome measures.

This study does not support the use of computerized EF training programs in VP children to improve attentional, executive, academic, behavioral or emotional functioning or self-perceived competence. Future studies should investigate whether more ecologically valid, real-world like EF training can be effective in very preterm children.
COI: None declared
ID: 483

TITLE: “ASSOCIATION BETWEEN BIOMARKERS AND UNFAVORABLE OUTCOMES IN PRETERM INFANTS WITH VERY-LOW BIRTH WEIGHT WITH HEMODYNAMIC INSTABILITY IN THE FIRST 72 HOURS OF LIFE”


AFFILIATIONS: Department of Pediatrics, Ribeirão Preto School of Medicine, University of São Paulo, Brazil

CONTENT:

Adaptation to extraterine life is a challenge, and it is important to identify unfavorable outcomes predictors in preterm infants in this period of hemodynamic instability. The presence of biomarkers that indicate worse prognoses may be useful in the clinical management of these patients. Therefore, the objective of this study was to evaluate the association of biomarkers (lactate ≥ 5mMol/L and Base Excess (BE) < -8mMol/L) during the first 72 hours of life, with death until 7 days, pulmonary hemorrhage, leukomalacia and perinventricular hemorrhage (PIVH) degrees III and IV in preterm infants with very low birth weight with hemodynamic instability.

Retrospective cohort study. Included preterms < 1500g born in tertiary hospital between January 2015 and December 2018, with vasoactive amines in the first 72hours of life. Excluded: malformations, congenital heart diseases, genetic syndromes and lack of data. The biomarkers were lactate ≥ 5mMol/L and BE < -8mMol/L. Blood sample and pressure measurement was collected before the initiation of vasoactive drugs.

Study groups:
Group 1: Patients with hypotension, but didn’t presented biomarkers
Group 2: Patients with hypotension and presented biomarkers

Relative risks with their 95% confidence intervals were estimated fitting log-binomial regression models. The covariates were gestational age at birth, early sepsis, use of antenatal corticosteroids and peripartum maternal hemorrhage.

For the study, 82 preterm infant were selected. After applying the exclusion criteria, 77 patients completed the study. The mean gestational age and birth weight were 26.68 weeks (SD 2.01) and 811.62 grams (SD 247.15) respectively. There was association between biomarkers and death until 7 days of life and severe PIVH [AdjRR (CI 95%) = 1.81 (1.06; 3.10)] vs 2.48 (1.12; 5.51), respectively. No association was observed between the presence of the biomarkers in the diagnosis of shock with pulmonary hemorrhage and leukomalacia [AdjRR (CI 95%) = 1.60 (0.90; 2.89) vs 1.23 (0.27; 5.60), respectively (Table 1).

There is an association between the presence of biomarkers immediately before the introduction of vasoactive amines and unfavorable outcomes in VLBW infants. Patients with hypotension and lactate ≥ 5mMol/L e BE ≤ -8 mMol/L should have a rigorous clinical evaluation. Also, preterm infants with risk of hemodynamic instability should to be rigorously evaluated to avoid the late diagnosis of shock and the decrease of metabolic situation.

IMAGE / TAB:
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IMAGE / TAB CAPTION:

COI: None declared
ID: 486  
TITLE: Stem cells for the prevention of experimental necrotizing enterocolitis: a systematic review and meta-analysis of preclinical studies  
AUTHORS: Eduardo Villamor-Martínez 1,2, Tamara Hundscheid 1,2, Boris Kramer 1,2,3, Carlijn Hooijmans 4, Eduardo Villamor 1,2  
AFFILIATIONS: 1 School for Oncology and Developmental Biology, Maastricht University, The Netherlands  
2 Department of Pediatrics, Maastricht University Medical Centre, The Netherlands  
3 School for Mental Health and Neuroscience, Maastricht University, The Netherlands  
4 Systematic Review Centre for Laboratory Animal Experimentation (SYRCLE), Department of Health Evidence, Radboud University Medical Center, Nijmegen, The Netherlands  

CONTENT:  
Necrotizing enterocolitis (NEC) is the leading cause of morbidity and mortality from gastrointestinal disease in very and extremely preterm infants. At present, there are no specific therapies for NEC. Stem cell therapy has shown promising protective effects in animal models of intestinal injury, including NEC. Animal models are invaluable tools for enriching our understanding of the pathogenesis and treatment of human diseases but systematic reviews and, where appropriate, meta-analyses are required to summarize the pre-clinical evidence on a given subject. No systematic review has yet evaluated the preclinical evidence of stem cell therapy for NEC prevention/treatment.

PubMed/Medline and EMBASE databases were searched for relevant articles published through October 2018, and electronic alerts were set up to inform us of studies published during the elaboration of the review. Studies were included if they used an animal model of NEC with stem cells or their products as the intervention, according to a previously registered protocol at PROSPERO (ID: 110084). Risk of bias was critically appraised using the SYRCLE Risk of Bias Tool for Animal Studies. To increase reliability, two independent reviewers included studies, collected outcome data and appraised risk of bias. A random-effects model was used to calculate odds ratios (OR) or standardized mean differences, as appropriate. We used the PRISMA guidelines for reporting.

We screened 953 non-duplicate studies, of which 9 (8 rat models and 1 mouse model) met the inclusion criteria. Risk of bias was evaluated as unclear on most items for all studies included. Meta-analysis found that stem cells improved 4-day survival (OR 2.89 95% CI 2.07-4.04) and 7-day survival (OR 3.96 95% CI 2.39-6.55), reduced the incidence of all NEC (OR 0.26 95% CI 0.19-0.35), grade 2 NEC (OR 0.44 95% CI 0.27-0.71), and grade 3-4 NEC (OR 0.28 95% CI 0.19-0.42). Meta-analysis also found that stem cells reduced other indicators of intestinal injury. Subgroup analyses for stem-cell type (mesenchymal, neural or amniotic fluid stem cells) could not find significant differences between subgroups.

Results from this systematic review and meta-analysis of pre-clinical studies suggest that stem cell therapy may be a promising treatment option for infants with NEC. However, unclear risk of bias and incomplete reporting underline that poor reporting standards are common and hamper the pre-clinical evidence for stem cell therapy for NEC. Better reporting and trials in other species are required before implementation of human trials.

IMAGE / TAB:  
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=a1f4c850574fb8358036c404688159d9-MjAxOS0wNSM1Y2UyNyY2Y2cxNWY1  

IMAGE / TAB CAPTION: Figure. Random effects meta-analysis of stem cell therapy and incidence of necrotizing enterocolitis.
AFNSC: Amniotic Fluid Neural Stem Cells; AFNSC: Amniotic Fluid Mesenchymal Stem Cells; BMMSC: Bone Marrow Mesenchymal Stem Cells; CI: confidence interval; ENSC: Embryonic Neural Stem Cell; exp: experiment; hBMMSC: Human Bone Marrow-derived Mesenchymal Stem Cells; IP: Intraperitoneal; IV: Intravenous; NSC: Neural Stem Cells.

COI: None declared
ID: 491
TITLE: RESPIRATORY TREATMENT BURDEN AND MEANINGFUL CHANGE: INTERVIEWS WITH CAREGIVERS OF EXTREMELY PREMATURE INFANTS TO INFORM A PHASE 2B CLINICAL TRIAL ENDPOINT
AUTHORS: Sujata P. Sarda 1, Magdalena Vanya 2, Linda Han 3, Ethan J. Schwartz 4, Keira Sorrells 5, Alexandra Mangili 6.
AFFILIATIONS: 1 Takeda, Lexington, MA, USA; 2 ICON, South San Francisco, CA, USA; 3 Takeda, Cambridge, MA, USA; 4 ICON, Gaithersburg, MD, USA; 5 Preemie Parent Alliance, Madison, MS, USA; 6 Takeda, Zug, Switzerland.

CONTENT:
Extremely premature (EP) infants (born at 23 to <28 weeks gestation age [GA]) who continue to experience respiratory complications post-discharge from the neonatal intensive care unit (NICU) may utilize multiple medical resources, including visits to the emergency room (ER), inpatient hospital admissions, home respiratory technology support (RTS), and respiratory medications. This study explored post-NICU-discharge respiratory burden and perceptions of meaningful change among caregivers of extremely premature infants in the United States (US) and Europe to inform the primary endpoint of a Phase 2b study (NCT03253263).

Adult primary caregivers of EP infants in the US, Northern Ireland, and Germany were recruited through patient advocacy organizations and interviewed by phone. Caregivers were included if their infant (3–14 months corrected age [CA]), post-NICU discharge, experienced ≥1 of these: ER visit/rehospitalization due to respiratory diagnosis, RTS (eg: supplemental oxygen, breathing/heart rate monitor, tracheostomy), respiratory medications (eg: nebulizer, steroids, diuretics). Interviews explored caregiver experiences related to infants with respiratory issues, associated treatment burden, and meaningful change in terms of reducing burden of treatment modalities. Sociodemographic data were summarized using descriptive statistics, and qualitative analysis of the interview data was performed.

40 caregivers (95% female; mean ± SD age, 31.7 ± 5.0 years) of infants (65% female) 3–14 months CA were interviewed. Respiratory morbidities reported by caregivers post-NICU discharge included difficulty/changes in breathing (82.5%), bronchopulmonary dysplasia (60%), respiratory infections (60%), and apnea (32.5%). Infants with respiratory morbidities experienced medication use (92.5%), RTS (82.5%), hospitalizations (37.5%), and ER visits (35%). Table lists the top 3 self-reported negative impacts of each of these. Based on their own experiences, caregivers considered supplemental oxygen as the most burdensome treatment. They most wanted to avoid RTS (tracheostomy and home ventilator use), hospitalizations, and ER visits. Reduced need for oxygen, less frequent administration of medications, and reduced hospitalizations were considered to be the most meaningful treatment changes.

In this study we found that all of the respiratory treatment modalities explored (RTS, ER visits, hospitalizations, and use of respiratory medications) carried a negative impact and were burdensome. A reduction in the use of these treatment modalities would be a meaningful benefit to patients and their caregivers. It should be noted that the small sample size, drawn from only 3 countries, limits the broader generalizability of our results.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=cdf1ebdfb60b4154ad81e875268edaf9-MjAxOS0wNSM1Y2UyNyJ2YzcYjU4

IMAGE / TAB CAPTION: Table: Top 3 Respiratory Treatment Negative Impacts by Treatment Modality

COI: This study was funded by Takeda. S. P. Sarda, L. Han, and A. Mangili are employees of, and own stock/stock options in Takeda. E.J. Schwartz and M. Vanya are employees of ICON and performed contracted research for Takeda in connection with this study. K. Sorrells is an employee of Preemie Parent Alliance and performed contracted consulting in
connection with this study. The authors thank I. Probodh, PhD, of Excel Medical Affairs, who provided medical writing assistance funded by Takeda.
**ID:** 494  
**TITLE:** INTEGRATION OF MOLECULAR PROFILES OF PRETERM BABIES  
**AUTHORS:** Hanna Danielsson 1; Linn Fagerberg 2; Gunnel Hellgren 3; Nele Brusselaers 4; Mathias Uhlén 5 and Ann Hellström 6.  
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**CONTENT:**  
The dawn of new omics tools for analyzing clinical samples such as genomics, proteomics and metabolomics has opened up new possibilities to study both health and disease with significant clinical accuracy. Here, we have used this approach to analyze the molecular profiles of extremely preterm babies with a focus on protein profiles in blood. The results of the longitudinal sampling have been analyzed and integrated with perinatal variables and clinical outcomes.

We conducted in-depth analyses of molecular profiles during the first weeks after birth of preterm babies born in week 22 to 28. The Longitudinal Integrative Program of Preterm Children (LIPPC) described here combines classical clinical chemistry with extensive omics profiling, including the analysis of the plasma proteome, the plasma metabolome and gut microbiota composition. In total, 450 protein targets have been studied from 14 extremely preterm babies and the protein profiles that have changed during the first weeks after delivery has been identified and correlated with clinical metadata.

The results show dramatic changes in molecular profiles during the early weeks of life. The analysis confirms patterns of well-known proteins known to be involved in for example weight gain, but more interestingly many protein targets, not described in this context previously, were identified with significant changes in protein levels. Some different patterns (clusters) of protein profiles have been identified, involving more than 200 proteins with strong correlation in longitudinal protein profiles across the analysed preterm babies. Examples of proteins with increasing protein levels (MYOC) and decreasing protein levels (COLECT12) are shown in figure 1. MYOC (myocilin) is believed to have a role in cytoskeletal function. COLEC12 (Collectin subfamily member 12) is a scavenger receptor, a cell surface glycoprotein that displays several functions associated with host defence.

This longitudinal study shows dramatic changes across many protein targets in peripheral blood of preterm babies. These changes were most profound during the first days of life after preterm birth. Time after birth seems more significant than...
postmenstrual age with regard to the patterns of protein levels. The study has allowed us to study the prediction of clinical outcome of the babies based on the integration of the omics profiles.

**IMAGE / TAB:**
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=af36823fa32b9c444eb95f54c7413cf0-MjAxOS0wNSM1Y2UyNyY2YzczZTZi

**IMAGE / TAB CAPTION:** Fig 1. Two examples of correlation in longitudinal protein profiles among the analysed pre-term babies.

**COI:** None declared
ID: 497

TITLE: THE CONTINUOUS BODY WEIGHT LOSS AFTER BIRTH IS STRESSFUL FOR THE TERM NEWBORN

AUTHORS: De Bernardo Giuseppe 1; Giordano Maurizio 2; Berselli Gloria 3; Linetti Laura 1; Villani Paolo 1; Pagani Franca 4; Sordino Desiree 1; Buonocore Giuseppe 5; Perrone Serafina 5

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CONTENT:

Body weight loss after birth is a physiological event when it is lower than 10% during first 72 hrs and lower than 3±1,5% at 24 hrs of life. Low birth body weight is correlated to up regulation of hypothalamus-pituitary-adrenal axis function and increased levels of plasma cortisol.

A prospective single centre study was conducted at the Department of mother and child’s health, Poliambulanza Foundation, Brescia, to test the hypothesis that body weight loss after 24 hr from birth increases salivary cortisol levels in term newborns. Fifty-six healthy full term newborns with body weight appropriate for age and with body weight loss of 3±1,5% at 24 hrs from birth were consecutively enrolled. Newborns were fed exclusively with breastfeeding. Salivary cortisol level was measured at 48 hr of life by SalivaBio Infant’s Swab. Data were analysed by independent two samples t-test or Pearson’s correlation coefficient. Statistical analysis was carried out by IBM SPSS Statistics for Windows, v.25.

A significant positive correlation was found between salivary cortisol level and body weight loss after 24 hours, expressed as ratio between percentage of body weight loss at 48 hours and percentage of body weight loss at 24 hr (r=0,393; p<0,05; Figure 1). Newborns that at 48 hours of life lost 1,6 times more body weight compared to their body weight at 24 hours of life showed higher salivary cortisol level compared to those newborns who had maintained a more stable body weight between 24 hours and 48 hours of life (28,15±14,739 nmol/l vs 16,56±11,567 nmol/l; p=0,007).

Body weight loss after 24 hours of life is associated with higher levels of salivary cortisol in healthy term newborns. These data suggest encouraging the creation of donor human milk banks and to use this milk to reduce neonatal body weight loss while waiting for the increase in breastfeeding.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=9f4152bd971c6b2c9ae20582cb35b1b-MjAxOS0wNSM1Y2UyNjY2Yzc1MmYw

IMAGE / TAB CAPTION: Correlation between salivary cortisol levels and body weight loss in the first two days after birth

COI: None declared
ID: 499

TITLE: GUT TISSUE BIOMARKERS IN PRETERM INFANTS – WHAT IS NORMAL?

AUTHORS: Claire Howarth 1,2; Christian Mifsud 3; Simon Eaton 3; Jayanta Banerjee 4,5; Joan Morris 6; Narendra Aladangady 1,2

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CONTENT:

We previously established normal ranges of Near Infrared Spectroscopy (NIRS) measurements of regional tissue oxygenation in preterm infants. Measurement of tissue biomarkers of gut injury could predict antecedent Necrotising Enterocolitis (NEC). Although small observational studies have elucidated the importance of these tissue biomarkers, there is a paucity of data on normative values in preterm infants.

We aimed to establish normal ranges of tissue gut biomarkers for preterm infants over the first 7 weeks of life.

We examined 48 infants <30w gestation admitted to our tertiary level NICU (after ethical approval and informed consent) from Oct 2016 to May 2018. Exclusion criteria: birthweight ≤2nd centile, abnormal antenatal Doppler’s, major congenital anomalies or Twin to Twin Transfusion Syndrome.

Weekly urinary intestinal and liver fatty acid binding proteins (I-FABP, L-FABP), Trefoil Factor 3 (TTF3) and stool Calprotectin were measured and weekly clinical status recorded. 332 urine samples and 324 stool samples collected for biomarker analysis.

I-FABP, L-FABP and Calprotectin were measured using ELISA Kits. Creatinine was measured to standardise I-FABP, L-FABP and TFF-3 to account for changes in urine concentration between samples.

Median birthweight 884g (460-1600), median gestational age 26+3 weeks (23+0-29+6) and 52% female.

The geometric mean and 95% CI of values for each biomarker over the study period are in table 1.

Over the first 7 weeks of life no biomarkers were affected by presence of PDA, enteric feed volumes and haemoglobin. I-FABP and TFF showed no significant differences for each gestational age. L-FABP was significantly higher in 23-27 week gestation infants compared to 28-29 week gestation infants and in male infants. No other biomarker was affected by gender. Calprotectin significantly reduced in 24-26 week gestational age group infants as postnatal age increased.

Our results show a wide variation in normal ranges for urinary I-FABP, L-FABP, TFF-3 and stool calprotectin in preterm infants less than 30 weeks gestation which may limit their utility as clinical prognostic biomarkers. As far as we know normative ranges for these potential biomarkers in preterm infants have not been studied before.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=06c312249fbf5709b19f4918c222f32a-MjAxOS0wNSM1Y2UyNyY2Yzc2NGEx

IMAGE / TAB CAPTION: Table 1: Gut tissue biomarkers values for preterm infants <30 weeks gestation in the first 7 weeks of life.

COI: none declared
ID: 500

TITLE: DOES PATENT DUCTUS ARTERIOSUS AFFECT SPLANCHNIC OXYGENATION RESPONSE TO THE FIRST ENTERAL FEED?

AUTHORS: Silvia Martini 1,2; Silvia Galletti 1,2; Arianna Aceti 1,2; Francesca Vitali 1; Giacomo Faldella 1,2; Luigi Corvaglia 1,2

AFFILIATIONS: 1 Neonatal Intensive Care Unit, S. Orsola-Malpighi University Hospital, Bologna, Italy
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CONTENT:

Patent ductus arteriosus (PDA) is common in preterm neonates. Due to the fear of possible gastrointestinal (GI) complications, the presence of a haemodynamically significant PDA may delay the introduction of enteral nutrition in this delicate population. Near Infrared Reflected Spectroscopy (NIRS) provides a non-invasive, continuous monitoring of tissue oxygenation and an indirect estimation of regional perfusion. Current data on the influence of PDA on splanchnic oxygenation (SrSO2), however, are scarce. We aimed to evaluate whether SrSO2 patterns in response to the first feed and the subsequent rates of gastrointestinal (GI) complications differ in very preterm infants with different PDA status.

Preterm infants <32 weeks' gestation were enrolled before enteral feeding introduction. At first feed administration, a 3-hour continuous NIRS monitoring of SrSO2 and cerebral oxygenation was performed, and splanchnic-cerebral oxygenation ratio (SCOR) was calculated. According to their echocardiographic features at enteral feeding introduction, the enrolled infants were allocated into the following groups: pulsatile PDA (pPDA), restrictive PDA (rPDA), no evidence of PDA (noPDA). SrSO2 and SCOR patterns were analysed and compared between the groups. The occurrence of GI complications (i.e., necrotizing enterocolitis, intestinal perforation, feeding intolerance) was also evaluated and compared among the study groups.

Fifty infants (pPDA group, n=11; rPDA, n=11; noPDA, n=28) were enrolled. No significant difference in SrSO2 and SCOR patterns in response to first feed administration was observed between the study groups (Figure 1). The incidence of necrotizing enterocolitis, intestinal perforation and feeding intolerance was also similar in the 3 groups.

The presence of PDA, either with restrictive or hemodynamically significant features, does not affect splanchnic oxygenation response to first feed administration and is not associated with an increased incidence of gut complications in very preterm infants. These findings support the timely introduction of enteral nutrition in preterm infants with evidence of PDA.

COI: None declared.
ID: 503

TITLE: CARDIO-RESPIRATORY EVENTS IN PRETERM INFANTS DURING THE TRANSITIONAL PERIOD: CLINICAL FEATURES AND IMPACT OF NEONATAL CHARACTERISTICS.

AUTHORS: Silvia Martini 1; Topun Austin 2; Giulia Frabboni 1; Paola Rucci 3; Silvia Galletti 1; Francesca Vitali 1; Giacomo Faldella 1; Luigi Corvaglia 1

AFFILIATIONS: 1 Neonatal Intensive Care Unit, St. Orsola-Malpighi University Hospital, Bologna, Italy
2 Neonatal Intensive Care Unit, Cambridge University Hospitals, Cambridge, UK
3 Department of Biomedical and Neuromotor Sciences, Division of Hygiene and Biostatistics, University of Bologna, Bologna, Italy

CONTENT:

Cardio-respiratory events (CRE), defined as intermittent episodes of hypoxemia and/or bradycardia, are particularly common among preterm infants. It has been previously shown that CRE may result in transient brain hypoxia and hypoperfusion and, if persistent over the first weeks, may represent a possible risk factor for neurodevelopmental impairment and retinopathy of prematurity. The high cardio-respiratory instability that characterises the first 72 hours of life may influence CRE occurrence, with possible clinical implications. This study aimed to characterize CRE features in this transitional period and to evaluate the impact of neonatal and clinical characteristics on different CRE types.

Non-invasively ventilated newborn infants (gestational age [GA] <32 weeks or birth weight <1500 g) were enrolled. During the first 72 hours, heart rate (HR) and peripheral oxygen saturation (SpO2) were continuously recorded, and an echocardiogram was performed 12- to 24-hourly to assess the status of the ductus arteriosus. CRE lasting ≥10 sec were clustered into isolated desaturation (ID, SpO2<85%), isolated bradycardia (IB, HR<100 bpm or <70% baseline), combined desaturation and bradycardia (DB, occurrence of the two events within a 60-sec window). Generalized estimating equations were used to examine the impact of relevant variables (GA, antenatal Doppler status, ductal status, respiratory support, surfactant administration) on CRE types. Significance level was set at p<0.05.

A total of 815 events from 22 neonates (mean GA 30±2 weeks) were recorded and analysed. Of these, ID were 496 (60.9%), IB 123 (15.1%) and DB 196 (24%). Event duration differed significantly among the 3 types (p<0.01), being shortest for IB (median [interquartile range, IQR] 23.6 [16.3-33.5] sec) and longest for DB (52 [28.9-93] sec). Event type distribution was also significantly different among day 1, 2 and 3 (p=0.01). Compared with other CRE types, ID were more likely in the presence of a hemodynamically significant PDA (B 1.06 [95% confidence interval 0.18-1.93], p=0.01), whereas IB were less common (B -0.81 [-1.36; -0.26], p<0.01). DB were significantly higher in infants <30 weeks’ gestation (B 1.32 [0.62-2.02], p<0.01) and in nasal CPAP (B 1.94 [0.19-3.7], p=0.03). No effect of antenatal Doppler status or surfactant administration on CRE type was observed.

CRE occurring during the first 72 hours of life in preterm infants who do not require invasive ventilation are of different types, with ID being the most frequent. CRE types vary over time and are significantly associated with specific neonatal or clinical characteristics. This finding suggests different physiological mechanisms underlying CRE occurrence during the transitional period and may add useful information for their clinical management.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 504
TITLE: CLINICAL SEVERITY OF CARDIO-RESPIRATORY EVENTS DURING THE FIRST 72 HOURS OF LIFE: DO NEONATAL CHARACTERISTICS MATTER?
AUTHORS: Silvia Martini 1; Luigi Corvaglia 1; Giulia Frabboni 1; Paola Rucci 2; Francesca Vitali 1; Arianna Aceti 1; Giacomo Faldella 1; Topun Austin 3
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3 Neonatal Intensive Care Unit, Cambridge University Hospitals, Cambridge, UK

CONTENT:

Due to their cardio-respiratory instability, preterm infants are highly prone to cardio-respiratory events (CRE), which are defined as intermittent episodes of hypoxemia and/or bradycardia. These events have been shown to be associated with transient brain hypoxia and hypoperfusion and possible long-term neurodevelopmental sequelae. During the first 72 hours of life, the risk of neurological complications is highest; therefore, the occurrence of severe CRE during this period may be of clinical relevance. Hence, we aimed to assess CRE severity during the transitional period, and to evaluate whether different CRE types and neonatal characteristics may predispose to more severe events.

Newborn infants with a gestational age (GA) <32 weeks or birth weight (BW) <1500 g were enrolled. Congenital malformations and mechanical ventilation were exclusion criteria. Heart rate (HR) and peripheral arterial oxygen saturation (SpO2) were continuously recorded during the first 72 hours, and a heart scan was repeated 12- to 24-hourly to assess the ductal status. CRE ≥10 sec were classified as: mild (SpO2 80-84% and HR 80-100 bpm and duration <60 sec), moderate (SpO2 70-79% or HR 80-60 bpm or duration 61-120 sec) or severe (SpO2 <70% or HR 120 sec). Generalized estimating equations (GEE) were used to examine the impact of relevant variables (GA, antenatal Doppler status, antenatal steroids, ductal status, CRE type) on CRE severity. Significance level was set at p<0.05.

Of 815 events recorded from 22 neonates (mean GA 30±2 weeks), 333 (40.8%) were mild, 318 (39.1%) moderate and 164 (20.1%) severe. As shown in Table 1, the event severity differed significantly in relation to the type of CRE (p<0.001) and was highest for combined desaturations and bradycardias, defined as the occurrence of the two events within a 60-sec time window, compared to isolated desaturations or isolated bradycardias. This finding was confirmed by the GEE model results (p<0.001), which also documented a possible protective effect of antenatal Doppler impairment against severe CRE (OR = -0.25, 95% CI -0.489, -0.009; p=0.04). Conversely, GA, the presence of a hemodynamically significant PDA and antenatal steroids administration were unrelated with CRE severity.

According to the present results, one out of 5 CRE occurring during the first 72 hours in preterm neonates has severe characteristics; if desaturation and bradycardia occur simultaneously, however, this likelihood increases significantly. The fetal hypoxia/hypoperfusion ensuing from antenatal impairment of umbilical Doppler flow may play a role in decreasing neonatal susceptibility to severe CRE and may deserve further investigation.

IMAGE / TAB: https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=974839ee4b94a09e83a20dc97caad6ce-MjAxOS0wNSM1Y2UyNjY2Yzc4ZmI3

IMAGE / TAB CAPTION: Table 1. Event severity distribution among different types of cardio-respiratory events.

COI: None declared
ID: 509
TITLE: Survey of breast milk fortifier practices in a convenience sample of European tertiary neonatal units 2016-18.
AUTHORS: Caroline King
AFFILIATIONS: Imperial College Healthcare NHS Trust London

CONTENT:

Breast milk fortifier (BMF) use is extremely prevalent within tertiary neonatal units to help improve the growth of preterm babies. However there are no international guidelines on its use. To develop guidelines it is important to know current practice.

During 2016 to 2018 a convenience sample of consultant neonatologists working in tertiary neonatal units from mainland Europe were surveyed by email or face to face as to their practices around BMF, a validated proforma was used.

Thirty one units responded from 11 countries. Poland 6, France 4, Sweden 4, Germany 3, Norway 3, Spain 2, Italy 1, Turkey 1, Slovenia 1, Serbia 1, Slovakia 1, Greece 1, Denmark 1, Netherlands 1.
The lowest volume milk per kg BMF was started (number of units) was: 50 (2), 60 (3), 70 (6), 80 (9), 100 (7) 120 (2) (97% response rate).
Sixty four % reported babies to be 5-10 days old and 36% 11-15 days old when starting BMF (60% response rate).
Sixty % increased incrementally according to tolerance, and 40% started at full strength (90% response rate).
Sixty-five % stored fortified breast milk for 24-30 hours, 35% used it immediately (85% response rate).
Of the units storing milk 24-30 hours 58% had a milk kitchen.
Seventy eight % sometimes used a protein supplement, 22% never did (70% response rate).
Fifty five % never used an energy supplement, 45% occasionally did (55% response rate).

Although BMF was usually started at volumes below 100ml/kg, most units increased incrementally and cautiously according to tolerance. Most units which stored fortified milk 24-30hours used a dedicated milk kitchen. Many units use protein supplements in addition to fortifier suggesting current fortifiers are not considered to contain sufficient protein, however an energy supplement was rarely needed.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: none declared
ID: 511

**TITLE:** Neonatal outcomes following implementation of a Family Integrated Care bundle including a parent supporting mobile application in a UK neonatal service

**AUTHORS:** Aniko Deierl 1; Annie Aloysius 1; Karen Platonos 1; Ines Silva 1; Jayanta Banerjee 1,2

**AFFILIATIONS:** 1 Imperial College Healthcare NHS Trust
2 Imperial College London

**CONTENT:**

Imperial Neonatal service implemented a Quality Improvement program called Family Integrated Care (FIC) bundle named Integrated Family Delivered Care (IFDC) model including a parent supporting mobile application in our level 3 (Queen Charlotte’s and Chelsea hospital) and level 2 (St Mary’s Hospital) neonatal units. The aim was to improve parent experience, parent-infant bonding, parental mental health and infant health outcomes.

In collaboration with veteran parents’ focus groups a competency based, experience co-designed training and educational material for parents was created including the IFDC mobile application. Parents were supported to become primary caregivers for their baby from admission (starting at the intensive care nursery) through a competency based training, and parent led ward rounds were introduced. Care bundle was implemented in April 2017. IFDC care was open to all patients and families, but outcome data was collected and analysed after one year of implementation on infants participated in this care model and completed their entire care episode in our service with a gestational age (GA) at birth 14 days. Primary outcome was length of stay (LOS).

Over 14 month period, 89 families were recruited into IFDC care with full participation achieving primary caregiver role through competency based training; 37 infants completed their entire care in our units with a minimum LOS >14 days. GA and birth weight matched 57 control infants were selected from a retrospective cohort between January 2016 and March 2017 before the implementation of IFDC care. Median LOS was shorter for infants in the IFDC model, [41 (32-63) days compared to 55 (41-73) in the control group; p=0.022]. When LOS was analysed by level of care the special care days were significantly lower in the IFDC group [30 (21-41) compared to 40 (31-46); p=0.006]. This was more apparent in the infants born at <30 weeks’ gestation [35 (20-46) vs 49 (45-59) days (p=0.001)]. The rate of any maternal breast milk at discharge was high in both groups 34 (92%) and 54 (95%).

The Family Integrated Care bundle has significantly reduced length of stay in the neonatal unit for patients completing the entire care episode in our service which is more apparent in babies who were born at <30 weeks of gestational age and resulted high level of breastfeeding well above UK national levels.

**IMAGE / TAB:**

**IMAGE / TAB CAPTION:**

**COI:** Nil.
ID: 514

TITLE: Parent experience following implementation of a Family Integrated Care bundle in a UK neonatal service

AUTHORS: Aniko Deierl 1; Emilie Seager 1; Karen Platonos 1; Ines Silva 1; Jayanta Banerjee 1;

AFFILIATIONS: 1 Imperial College Healthcare NHS Trust, London, UK
2 Imperial College London, UK

CONTENT:

Imperial Neonatal service implemented a Family Integrated Care (FIC) bundle named Integrated Family Delivered Care (IFDC) model to improve parent experience, parent-infant bonding, parental mental health and infant health outcomes. The IFDC model provided structured material for training and support of parents and staff and the neonatal unit provided environment conducive of empowering families to be primary carers of their admitted infants along with psychosocial support. Ad-hoc spot and discharge questionnaires were designed to gather qualitative parent feedback about this model of care and to identify areas that work well and those that require further development.

The IFDC care bundle was implemented in April 2017, and feedback data was collected during the first 15 months after implementation. The spot questionnaires were completed by parents of infants who were participating in IFDC care model at random intervals during their stay. A total of 11 questions were asked (9 quantitative and 2 free text). A discharge questionnaire was provided to families to capture feedback at discharge; asking for detailed free text feedback on care received, ideas for improvement and three words to describe IFDC. Completion of these questionnaires was voluntary, and self-reported data was collected. Responses were anonymised and confidential. Descriptive analysis was performed along with thematic analysis of the free text answers.

During 14-month period, 50 spot questionnaires were completed. 84% of respondents were mothers, 10% fathers and 6% both parents. IFDC was described as: supportive, helpful, friendly, informative, educational, compassionate, kind, inclusive, empowering, humane and collaborative (Figure 1). 26 completed the discharge questionnaire: 81% mothers, 11% fathers and 8% both. Themes identified were: advantages of being involved in baby’s cares, values of cotside and group teaching sessions, feeling well informed, and value of parent-led ward rounds. Parents reported: ‘the project .. has given structure to my journey’, ‘the support and teaching received were outstanding. I feel more confident to go home’. Common theme for improvement was inconsistency in communication, “mixed messages from different staff” and “on how staff relay messages to parents”.

The findings from these spot and discharge parent questionnaires demonstrated the positive impact of IFDC model on families during their vulnerable time on the neonatal unit. This new care model was felt to be supportive, informative, educational, empowering and helpful; and majority of parents felt confident and empowered during their stay as well as at the time of discharge from the neonatal unit.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=dc8d4074f0e2c334f21d5f0a3a7673ae-MjAxOS0wNSM1Y2UyNjY2YzdjN2Rm

IMAGE / TAB CAPTION: Figure 1. Parent responses for question to summarize Integrated Family Delivered Care in three words.

COI: Nil
ID: 518
TITLE: Active discontinuation of antibiotics in near-term and term neonates with suspected early-onset sepsis
AUTHORS: Thomas Dretvik 1, Claus Klingenberg 2, Terje Selberg 3, Andreas Finnvåg 2, Anne Lee Solevåg 1, Ketil Størdal 3
AFFILIATIONS: 1 Paediatric Dept., Ahus University Hospital, Lørenskog, Norway
2 Paediatric Dept., University Hospital of North Norway, Tromsø, Norway
3 Paediatric Dept., Østfold Central Hospital, Kalnes, Norway

CONTENT:

The challenges of early diagnosis, combined with a potential fatal outcome if treatment is delayed, compels clinicians to empirically administer antibiotics, often for many days, to newborns at risk for or with only subtle signs of early-onset sepsis (EOS). Prolonged treatment with empirical antibiotics in non-confirmed EOS is associated with adverse clinical outcomes and leads to more antibiotic resistance. The aim of this study was to evaluate the effect of a quality improvement project aiming to reduce the duration of antibiotic therapy in neonates with suspected EOS, not verified after 36-48 h of treatment and observation.

We implemented a guideline across three Norwegian neonatal intensive care units (NICUs) giving advice to discontinue antibiotics after 36-48 h if sepsis was no longer suspected and the blood culture was negative in neonates ≥ 34 weeks gestation. We compared 14 months before (11,477 births) and 12 months (10,790 births) after guideline implementation. The main outcome measures were number of neonates who received intravenous antibiotic treatment in the first week of life, and duration of antibiotic therapy in all neonates commenced on antibiotics and among those not diagnosed with sepsis according to a) national criteria and b) the clinician. Data are presented as rates (%) or median with interquartile range (IQR). Statistical comparisons are with chi-square or non-parametric tests.

Among all live births ≥ 34 weeks gestation in the catchment areas, 283 received antibiotics (2.4%) before and 195 (1.8%) after guideline implementation (p=0.0018). Only 4 neonates (0.18/1000 live births) had culture proven EOS, all before guideline implementation.

Median (IQR) therapy duration for all neonates was 108 h (60-144) before (n=283), and 96 h (48-120) after (n=195) implementation (p= 0.011).

Median (IQR) therapy duration for neonates without sepsis, according to national criteria, was 84 h (48-109) before (n=196) and 72 h (42-98) after (n=140) (p= 0.038). However, 80 of these 140 (57%) received >48 h treatment after implementation. Median (IQR) therapy duration for neonates with no sepsis, according to the clinician, was 49 h (31-84) before (n=119) and 48 h (36-72) after (n=105) (p= 0.68). However, 59 of these 105 (56%) received >48 h treatment after implementation.

The duration of antibiotic therapy in neonates with suspected, but not confirmed EOS was reduced after guideline implementation. Still, more than half of non-infected neonates received empiric antibiotics > 48 hours. An unintended effect of the increased focus on a reduction of antibiotic therapy duration was that, after guideline implementation, a lower proportion of near-term and term infants received antibiotics in the first week of life.
ID: 522
TITLE: OUTCOMES OF A CONSISTENTLY ACTIVE APPROACH TO INFANTS BORN AT 22-24 WEEKS OF GESTATION
AUTHORS: Fanny Söderström 1; Erik Normann 2; Johan Ågren 3
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CONTENT:

While survival rates of extremely preterm infants are improving, active perinatal management of the most immature infants remains controversial due to a perceived risk for poor outcomes. On the other hand, the attitude towards active treatment might in itself influence outcome. The objective of this study was to evaluate survival, short-term hospital outcomes, and long-term neurodevelopmental outcomes in infants born at a center where all mother-infant dyads are provided active perinatal care irrespective of gestational age at birth.

Single center, retrospective cohort study including all infants born at 22-24 weeks during 2006-2015. Data on survival and short-term outcomes (retinopathy of prematurity, ROP; necrotizing enterocolitis, NEC; patent ductus arteriosus, PDA; intraventricular hemorrhage, IVH; bronchopulmonary dysplasia, BPD), and neurodevelopmental outcomes (cerebral palsy, CP; visual and hearing impairment; psychomotor delay) at 2.5 years were collected through chart review. For psychomotor evaluation, a full clinical assessment was used when data from formal testing were unavailable.

A total of 222 infants born at 22-24 weeks were included. Overall survival was 143 (64%): 23/44 (52%) at 22 weeks, 56/87 (64%) at 23 weeks, and 64/91 (70%) at 24 weeks. Among hospital outcomes, ROP and BPD were more common at 22 than at 23 and 24 weeks. Follow-up data at 2.5 years were available in 133 infants of whom 45 (34%) had adverse outcome. Psychomotor delay was found in 27%, and was more common in infants born at 22 weeks. No infants were blind, and visual impairment was less common in 24 week infants. While 2 needed hearing aid, no children were deaf. Ten children were diagnosed with CP of whom 3 were non-ambulant.

A consistently active approach to all infants irrespective of gestational age leads to survival rates that are not distinctly different across the gestational ages of 22-24 weeks. More than half of the infants were unimpaired at 2.5 years, suggesting that active management and increased survival do not result in higher rates of long-term adverse neurological outcome.

IMAGE / TAB:
a8f492a9b781f-MjAxOS0wNSM1Y2UyNjY2YzgwNmM5

IMAGE / TAB CAPTION: Table 1. Survival, hospital outcomes, and long-term neurodevelopmental outcomes.

COI: None declared.
ID: 532

TITLE: EFFECTS OF INFECTION AND VACCINATION ON T CELL POLARISATION IN PRETERM INFANTS AND ON NEONATAL CHRONIC LUNG DISEASE

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CONTENT:

Bronchopulmonary dysplasia (BPD) a chronic neonatal lung disease is the most common complication of extremely preterm birth and is underpinned by pulmonary inflammation. Previous studies have suggested the involvement of various cell types and soluble factors but have so far failed to reveal a dominant pathway that underpins disease progression. It remains unknown which T helper (Th) cell polarization, if any, contributes to the pathogenesis of BPD. Furthermore, the effect of inflammatory clinical events such as perinatal infection and vaccination on T cell polarisation in preterm neonates is also unknown.

Citrated whole cord and peripheral blood was collected from extremely preterm infants (born at 24-29 gestational weeks) on days 0, 1, 7 and 14, and additionally at 36 weeks corrected gestational age (CGA). Additional samples were collected from healthy term infant cord blood at birth and peripheral blood 4-16 weeks as well as healthy adults as controls. Following PMA+ionomycin- or vehicle-stimulation overnight cells were stained for multi-colour flow cytometry to enumerate Th1/2/17 and regulatory T cell (Treg) subset. Results were analysed against BPD status at 36 weeks CGA, perinatal infection and vaccination on T cell polarisation in preterm neonates is also unknown.

Th2-polarisation predominated in preterm (n=51) and term infants (n=20) ≤16 weeks of age, with ≤62% of CD4+ T cells Th2-polarised vs 2% in adults (n=5). Baseline Th1- and Th17-polarisation was low in all groups; inducibility of Th1- and Th17-polarisation developed at 16 weeks of age. Treg percentages were 5-fold higher in infants than in adults. Compared to infants without BPD, infants with BPD exhibited an up to 36-fold more Th2-polarised T cells. Chorioamnionitis or sepsis did not significantly change CD4+IL-4+ T cell abundance; however, early (d1) vaccination against hepatitis B increased Th2-polarisation by up to 4-fold.

Our study sheds light on the maturation of the immune system in preterm and term infants. Infection does not have a clearly defined effect, warranting subgroup analysis in future studies. However, early vaccination induces marked and sustained Th2-polarisation in preterm infants. Since the severe chronic lung disease BPD is strongly associated with Th2-polarisation, timing of vaccination practices in this population may require reconsideration.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 535

**TITLE:** COMPARISON OF NEONATAL OUTCOME AMONG SEVERE SGA(<3p), MODERATE SGA(3-10p), AGA IN ELBWIs.

**AUTHORS:** Jinwha Choi 1; Jisook Kim 2; So Yoon Ahn 3; Se In Sung 4; Won Soon Park 5; Yun Sil Chang 6

**AFFILIATIONS:** Korea university Guro Hospital, Seoul, Korea
Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

**CONTENT:**

The outcomes of small for gestational age infants in extremely low birth weight infants are controversial. Multiple criteria for small for gestational age have been used, including less than the 10th, 5th and 3rd percentile in weight, length or head circumference. This study evaluated to determine whether severe small-for-gestational age (SGA) infants among extremely low birth weight infants (ELBWIs; < 1,000 g) are at increased risk for morbidity, neurodevelopment impairment and catch-down growth compared with moderate SGA and appropriate-for-gestational age (AGA) infants focusing on subdividing SGA.

All ELBWIs who admitted to neonatal intensive care unit of Samsung Medical Center from January 2011 to December 2015 were included. Severe and moderate SGA were defined as birth weight < 3th percentile and 3-10th percentile for gestational age, respectively, based on Olsen growth curves. Maternal and infant characteristics, neonatal morbidity, neurodevelopment and growth data were compared among severe SGA, moderate SGA, and AGA groups. Neurodevelopmental outcomes were assessed via Bailey scales of infant development II (BSID-II). Growth outcomes were assessed via Z-score of body gauge at corrected age 12, 24 month, chronological age 36month, 4 year.

Among 336 ELBWIs, 59 (17%) infants were severe SGA, 36 (11%) were moderate SGA, and 241 (72%) were AGA infants. Severe SGA infants showed increased mortality during hospitalization compared with moderate SGA and AGA (35.6% vs 2.8%, p-value < 0.05; 35.6% vs 11.2%, p-value < 0.05). On multivariate analysis, mortality was greater for severe SGA than AGA infants (OR 7.62, 95% CI [3.65-15.93]), as was severe IVH (OR 3.13, 95% CI [1.47-6.67]), severe ROP (OR 2.26, 95% CI [1.06-4.81]). Severe SGA infants had a higher rate of early pulmonary hypertension (34% vs 14%, p-value < 0.05; 34% vs 15%, p-value < 0.05) and late pulmonary hypertension (10% vs 6%, p-value >0.05; 10% vs 2%, p-value < 0.05) With regard to neurodevelopmental outcome, severe SGA infants showed lower mental and psychomotor development index (Regression Coefficient - 5.3, 95% CI [-9.8 - -0.7], - 4.8, 95% CI [-9.6 - -0.1]). They also showed lower weight, shorter stature, and shorter head circumference at corrected age of 12, and 24 months compared with AGA infants at the same corrected age, so severe SGA had a more growth hormone treatment at 4 years compared with AGA(50% vs 4.8%, p-value < 0.05).

Severe SGA infants are at increased risk of mortality, severe IVH, severe ROP, pulmonary hypertension during NICU hospitalization, lower mental and psychomotor developmental index on BSID-II, and growth restriction at corrected age of 12 and 24 months compared with AGA infants. They may require special care including tailored nutrition, rehabilitation, and growth hormone treatment.

**IMAGE / TAB:**

**IMAGE / TAB CAPTION:**

**COI:** none declared
ID: 536

TITLE: SEX DEPENDENT CRP RESPONSE IN COOLED INFANTS WITH ADVERSE OUTCOME FOLLOWING NEONATAL ENCEPHALOPATHY

AUTHORS: Thomas Robb 1; Hemmen Sabir 2; Marianne Thoresen 1; Ela Chakkarapani 1

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CONTENT:

Hypoxic-ischaemic brain injury results in cellular inflammation. Cytokine responses are increased in infants with adverse outcome (death or disability), compared to infants with good outcome, following cooling for neonatal encephalopathy (NE). However, the relationship between adverse outcome and clinically used inflammatory markers; C-reactive protein (CRP), white blood cell count (WBC) and neutrophil count is not known. Furthermore, sex and risk factors for chorioamnionitis (rf-chorio) may influence inflammatory profiles. Therefore, we investigated whether clinical outcome, sex and rf-chorio were associated with the temporal course of inflammatory markers in infants cooled for NE.

Of 225 infants cooled for NE between 2006-2017 in a single centre, 39 were excluded due to lack of data, or additional diagnoses accounting for NE. In 186 infants (106 male), we recorded data on survival, sex, birthweight, Apgar10min, worst pH within 1 hour of life, meconium aspiration, rf-chorio (prolonged rupture of membranes >18hours, maternal fever >38°C, group B streptococcus vaginal colonisation), and CRP, WBC and neutrophil count 12 hourly until 168 hours (end of rewarming period). High CRP response was defined as median CRP(0-168hours) > 10mg/L. Bayley-III assessment was performed at 18–22 months. Adverse outcome was defined as death or Bayley-III cognitive/language composite score <85, or cerebral palsy (Gross Motor Function Score 3-5) or severe hearing/visual impairment.

Of 186 infants, 11 died and 157 underwent Bayley examination. 44/186 infants had adverse outcome. In the favourable outcome group, infants with rf-chorio had higher CRP values compared to infants without rf-chorio (fig 1A). CRP values were higher in infants with adverse outcome compared to infants with favourable outcome (fig 1B). In the adverse outcome group, females had a significantly lower CRP (fig 1C) and higher WBC and neutrophil count compared to males. In the adverse outcome group, females had significantly lower median CRP values (β: -29.2 mg/L, 95%CI:-48.1,-10.3), lower maximum CRP (β: -38.5 mg/L,95%CI:-67.2,-9.7) and a delay in reaching the maximum CRP value (β:18.6h, 95%CI:5.0, 32.2) independent of confounders. Logistic regression showed that in infants with high CRP response, male gender was significantly associated with adverse outcome (OR: 2.8, 95% CI 1.0, 7.5).

CRP response in newborns with adverse outcome following cooling for NE was found to be sex dependent. Females with adverse outcome had a lower CRP and higher white blood cell count response compared to males, independent of clinical risk factors for chorioamnionitis or severity of NE.

IMAGE / TAB:
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IMAGE / TAB CAPTION:

COI: None declared
ID: 543

TITLE: EARLY PRE-, PERI AND POSTNATAL VARIABLES ASSOCIATED WITH INFANTS DEVELOPING SEVERE RETINOPATHY OF PREMATURITY

AUTHORS: Chatarina Löfqvist 1,2; Eva M Andersson 3; Gunnel Hellgren 4; Karin Sävman 5; Lois EH Smith, 6, Ann Hellström 2

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CONTENT:

Retinopathy of prematurity (ROP) ROP is a multifactorial disease involving many factors. Low-gestational age, low-birth weight, sepsis, oxygen therapy, respiratory distress syndrome, and blood transfusion have been suspected to influence the incidence of ROP. In addition, postnatal circulating biomarkers such as growth factors and fatty acids have in clinical studies been strongly associated to ROP development. The goal of this project is to identify prenatal and perinatal variables together with early circulating biomarkers that best can be used together for prediction for ROP development.

Longitudinal (up to 10 measurements per infant) data, including clinical variables and biomarkers available from a cohort of 90 extremely preterm infants (born in gestational weeks 22-27), was analyzed. The variables were categorized into: 1. Birth characteristics; 2. Respiratory support; 3. Maternal factors; 4. Prenatal/Perinatal; 5. Serum/Plasma factors; 5. Comorbidities and Treatments. Within each category, multivariable logistic regression was used to assess which predictors that were associated with severe treatment-needing ROP. The variable with the strongest association in each category was then chosen for further multivariate analysis (SPSS 24.0).

Seventeen infants developed no ROP, 8 ROP stage 1, 22 ROP stage 2 and 31 infants ROP stage 3. Within the different categories we found that the following variables best discriminated between infants born extremely preterm who developed any (including severe) ROP compared with infants who developed no ROP. 1. Birth characteristics: Birth weight and sex; 2. Respiratory support: number of days with CPAP, Ventilator >7 days; 3. Maternal factors: Clinical notes on “Has the mother any relevant medical history during pregnancy”; 4. Prenatal/Perinatal: Antenatal steroids, Way of delivery, APGAR score 10 minutes; 5. Serum/Plasma factors: Brain-Derived Neurotrophic Factor Levels days 7 and 14, Adiponectin level days 1 and 7, Insulin-Like Growth Factor-1 levels at 28 days; 6. Comorbidities and Treatments. BPD, exposure to postnatal steroids.

We have identified a combination of clinical variables and biomarkers that might be used to safely and timely identify infants at risk for severe ROP needing treatment on an individual level. However, these variables need to undergo extensive statistical analyses to determine which can discriminate between preterm infants likely to develop severe ROP needing treatment and those likely to have normal vascular development at an individual level.
COI: None declared
ID: 546

**TITLE:** IMPACT OF PREECLAMPSIA ON CIRCULATING BIOMARKER LEVELS IN PRETERM INFANTS

**AUTHORS:** Ulrika Sjöbom 1, 2; William Hellström 1, 2; Gunnel Hellgren 2, 3; Anders K. Nilsson 2; Karin, Sävman 1, 2; Ann Hellström 2; Chatarina Löfqvist 2, 4

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**CONTENT:**

Biomarkers have become essential to clinical studies of extremely preterm morbidities. Yet there are no biomarkers which reliably or uniquely predict the subsequent clinical course. Development of morbidities depends on both pre- and postnatal factors. One known factor closely related to both frequencies of morbidities as well as variability in biomarker levels is gestational age (GA) at birth and birth weight (BW). Our hypothesis was that maternal factors would impact biomarker concentration measured in infants serum after birth. The specific aim of this project was to evaluate how preeclampsia (PE) influence the postnatal pattern of growth factors in extremely preterm infants.

Longitudinal data was collected from birth to postnatal day (PND) 28 in 90 extremely preterm infants (gestational age < 28 weeks at birth). Serum was analysed at PND 1, 7, 14 and 28 for Brain-Derived Neurotrophic factor (BDNF), Adiponectin (APN), Platelet Derived Neurotrophic factor-BB (PDGF-BB), Insulin-like Growth factor-1 (IGF-I) and Vascular Endothelial Growth factor (VEGF) with antibody based methods, (IGF-I- RIA and APN- ELISA (Mediagnost, Germany) and remaining analyses with ELLA (bio-techne, USA)). Biomarker levels as dependent variables were analyzed with linear mixed models (SPSS 24.0) using GA or BW, timepoint and PE as fixed variables. The purpose was to explore if PE significantly contributed to the variance in biomarker concentration adjusted for GA or BW and timepoint.

PE was defined as sustained elevation in blood pressure of >140 systolic and/or >90 diastolic, accompanied by proteinuria, after 20 weeks gestation in a previously normotensive woman. Thirteen infants were born from mothers with PE. Median age of infants born from mothers with PE was 26+0 weeks (range 23+4-27+9) and median birth weight was 689 grams (range 415-1240) and in control group median GA was 25+5 weeks (range 22+5-27+6) and median birth weight was 760 grams (range 420-1260). GA and BW contributed significantly to the development of all biomarkers except for VEGF. PE was found to significantly contribute (p<0.05) to variance in concentration of PDGF-BB and APN adjusted for GA and timepoint, significantly to variance adjusted for BW and timepoint for APN but not significant for PDGF-BB (p=0.067). PE was associated with lower concentration of APN and PDGF-BB (Figure 1).

Our results suggest the importance of including maternal factors when using early biomarker levels in prediction of preterm morbidities. Using biomarkers to create cut-off for individuals at risk for morbidities is challenging since results have a large variability, possibly influenced by both pre- and postnatal factors.

**IMAGE / TAB:**
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**IMAGE / TAB CAPTION:** Picture 1: Solid lines represent infants with preeclampsia, dotted lines represent controls. Blue colour represents logarithmic (base 2) concentration of Adiponectin (APN) [mg/L] and red colour represents Platelet Derived Neurotrophic factor-BB (PDGF) [ng/mL].

**COI:** None declared
ID: 548

TITLE: The effect of postnatal corticosteroid on brown adipose tissue in neonatal rat

AUTHORS: Yu-Shan Chang1,2; Shun-Yun Hou2; Shin-Yu Tsai2; Ying-Yi Chen2; Chyi-Her Lin1; Yau-Sheng Tsai2

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CONTENT:

Corticosteroids have been used to prevent or treat bronchopulmonary dysplasia in preterm infants. Early postnatal exposure to dexamethasone (Dex) has been shown to increase the risk of adverse neurodevelopmental outcomes. Dex was also shown to disrupt brown adipose tissue (BAT) thermogenesis in adult mice. The effect of immediate postnatal exposure to Dex on brown adipose tissue in neonatal rat is not known.

Rat pups were administered Dex or normal saline (Con) on postnatal day (PD) 1 to 3. Body weight, BAT weight, BAT histology and UCP1 protein levels were examined on PD4. BAT function was evaluated by cold exposure under 12°C for 6 hours. The impact of Dex on BAT mitochondrial morphology, membrane potential, fusion and fission were also analyzed.

Dex-treated rat pups, compared with Con, showed growth retardation, whitening of interscapular BAT, and higher mortality rate under cold environment. The expression of UCP1 protein was not significantly different between Con and Dex groups. Dex-treated BAT mitochondria showed decreased membrane potential. Under electron microscope, mitochondria were elongated in shape, showed electron-increased density and loss of normal cristae pattern. The expression of both mitochondria fission (DRP1 and MFF) and fusion proteins (OPA1, MFN1, and MFN2) were increased after Dex treatment. Dex treatment also increased translocation of fission (DRP1, MFF, and FIS1) and fusion proteins (OPA1 and MFN2) to the mitochondria. These results suggest that Dex treatment has a great impact on mitochondrial dynamics.

Postnatal exposure to Dex led to alternation of morphology and impairment of function of BAT mitochondria, resulting in BAT whitening and cold intolerance. Whether these effects persisted into adulthood and led to metabolic derangements requires further researches.

IMAGE / TAB:
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IMAGE / TAB CAPTION: (A) Experimental design, IP: intraperitoneal (B) Body weight and body length (C) BAT weight (D) Morphology of inter-scapular BAT (E) H&E staining (upper row) and UCP1 IHC staining (lower row) of BAT (F) Skin temperature change over time under cold environment (12°C) (G) Infrared thermo-imaging (H) Survival curves of Dex and Con groups under cold exposure (I) TMRM fluorescence staining (J) Mitochondria of interscapular BAT under electron microscope (K) Western blot of BAT mitochondria fission proteins (L) Western blot of BAT mitochondria fusion proteins (M) Mitochondria and cytosolic fractions of BAT mitochondria fission and fusion proteins

COI: None declared
ID: 549

TITLE: ORGAN DYSFUNCTION AS A PREDICTOR OF DEATH IN BLOOD CULTURE-PROVEN NEONATAL SEPSIS

AUTHORS: Eric Giannoni1, Philipp Agyeman2, Blandine Aubert1, Sabrina Goertz3, Sebastien Papis4, Martin Stocker5, Klara M Posfay-Barbe4, Ulrich Heisinger6, Sara Bernhard-Stirnemann7, Anita Niederer-Loher8, Christian R. Kahlert8, Giancarlo Natalucci9, Christa Relly3

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CONTENT:

In adults, sepsis is defined as a “life-threatening organ dysfunction caused by dysregulated host response to infection”. The operationalization of this definition is based on assessment of organ dysfunction through the Sequential Organ Failure Assessment (SOFA) score that evaluates the respiratory, cardiovascular, hepatic, coagulation, renal and neurological systems, using clinical data and laboratory results, to predict the risk of death. There is no widely accepted definition of neonatal sepsis. Robust characterization of organ dysfunction as a predictor of adverse outcome during neonatal infection could represent an important step towards a consensus definition of neonatal sepsis.

Newborns with blood culture-proven sepsis who were cared for in Swiss tertiary care hospitals between 9.2011 and 12.2015 were prospectively included. We defined early-onset sepsis (EOS) as infection occurring 48h after admission. We assessed the suitability of the 2005 international pediatric sepsis consensus definition, Pediatric Logistic Organ Dysfunction (PELOD)-2, and pediatric (p)SOFA score to identify infants who died ≤30 days after sepsis onset with area under the receiver operating characteristic curves (AUROC). Analyses were adjusted for gestational age, onset of sepsis, and sex.

We identified 444 episodes of blood-culture-proven sepsis in 429 infants, and excluded 5 episodes (1%) due to incomplete files. Eighty-seven (20%) episodes were EOS, 272 (62%) were HA-LOS, and 80 (18%) were CA-LOS. Forty-eight infants died within 30 days of sepsis onset, representing a case fatality ratio of 11%. Case fatality ratio was 18% (16/87) in EOS, 12% (32/272) in HA-LOS, and 0% in CA-LOS. Based on the 2005 pediatric consensus definition, 324 (74%) episodes were associated with an organ dysfunction, including 72 (83%) in EOS, 230 (85%) in HA-LOS, and 22 (28%) in CA-LOS. Organ dysfunction scores discriminated episodes with fatal outcome with an AUROC of 0.82 (95% CI 0.77-0.87) for the 2005 pediatric consensus definition, 0.9 (0.86-0.94) for PELOD-2, and 0.85 (0.8-0.9) for pSOFA, with adjusted AUROCs of 0.89 (95% CI 0.84-0.93), 0.92 (0.89-0.96), and 0.9 (0.86-0.94), respectively.

Organ dysfunction is a frequent complication of EOS and hospital-acquired LOS. Pediatric organ dysfunction scores applied to newborns with blood culture-proven sepsis can identify patients at higher risk of mortality. This supports the translation of Sepsis-3 into a neonatal-specific definition of sepsis, and highlights the importance of characterizing organ dysfunction in newborns evaluated for sepsis.
ABSTRACT BOOK
POSTER PRESENTATIONS

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 565  
TITLE: NATIONAL SURVEY IDENTIFIES NEED FOR TRAINING AMONG PERINATAL POST MORTEM CONSENT TAKERS  
AUTHORS: Hannah Wood; Jo Cookson; Asha Shenvi.  
AFFILIATIONS: Neonatal Intensive Care Unit, Royal Stoke University Hospital, University Hospitals of North Midlands, Stoke-on-Trent, UK. Staffordshire, Shropshire and Black Country Neonatal Operational Delivery Network (SSBC ODN), UK.  

CONTENT:  
All parents should be offered a post mortem examination of their baby. In 2016, MBRRACE-UK reported that post mortem was offered in 81.3% of neonatal deaths but consent was obtained in only 28.6%. Our network’s experience is similar with offer and uptake rates as low as 67% and 18% respectively in some units. Published evidence identifies multiple barriers to consent including issues related to training. In our region, pathology training days are too infrequent to meet demand. Lack of knowledge among consent takers impacts the uptake of post mortem.  

A national online survey was designed to gather information on health professionals’ current experiences of consent taking. The survey was hosted on the SurveyMonkey website between May and October 2018. Health professionals who were expected to obtain consent from paediatric, neonatal, obstetric, midwifery and bereavement communities were invited to participate. The survey was shared with health professionals by the Operational Delivery Networks, specialty training representatives and a link was available on the British Association of Perinatal Medicine (BAPM) website. The results of the survey were used to inform the development of a new perinatal post mortem consent e-learning training package.  

Survey responses were analysed from 122 health professionals. This included 80 (66%) paediatric and neonatal staff from across the UK neonatal networks, and 42 (34%) obstetric, midwifery and bereavement staff largely from the West Midlands region. Most agreed parents should be offered post mortem (94%). 43% have not been trained to take consent but 58% of this group already take consent. Those who have been trained listed 18 different types of training. A perinatal post mortem has not been observed by 51%. There was lack of consistency about what should be discussed with parents while obtaining consent. Confidence levels were variable with 28% feeling “not so confident” or “not at all confident”. Of this group, 11% are already consent takers. 82% felt more extensive and accessible training is needed.  

The uptake of perinatal post mortem remains low. Our national survey identified that the Sands prerequisites for consent takers are not being met and highlights the need for standardised training. We have developed a multi-model e-learning training package that will be freely available to consent takers. We anticipate this will improve health professionals’ ability to offer post mortem and subsequently impact uptake rates positively.  

COI: None declared
ID: S70

TITLE: CHANGES IN HEART RATE VARIABILITY IN THE HOURS LEADING UP TO CLINICAL DETERIORATION DUE TO LATE-ONSET SEPSIS; A RETROSPECTIVE COHORT STUDY

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CONTENT:

Late-onset sepsis (LOS, onset >72 hours after birth) is a major cause of morbidity and mortality among preterm infants. Early detection of LOS is important to improve outcome. However, clinical signs of LOS are often subtle and non-specific, delaying its diagnosis. Previous studies have shown that heart rate variability (HRV) holds potential to act as an early predictor of sepsis. Our aim was to characterize changes in various features of HRV, capturing autonomic regulation and transient heart rate decelerations, in infants diagnosed with LOS compared to controls.

We retrospectively included infants <32 weeks’ gestation with LOS proven by a positive blood culture (n=76) and controls without LOS (n=153) between July 2016 and November 2018. LOS and controls were matched on exact gestational age resulting in 30 LOS and 30 controls. A CRASH-moment (Cultures, Resuscitation and Antibiotics Started Here) for the LOS positive infants was defined by the time of starting antibiotics. Subsequently a virtual CRASH-moment was defined for each infant in the control group (T0-moment) using the postmenstrual age of a matched LOS infant. Three HRV-features were calculated and visualized 48 hours before and after CRASH- and T0-moments: standard deviation of normal-to-normal intervals (SDNN); percentage of decelerations (pDec) and extent of decelerations (SDDec).

In the LOS positive and control group, the mean (SD) gestational age and birth weight were respectively 28,8 (1,67) and 28,7 (1,68) weeks and 1162 (324) and 1252 (314) grams. There were no significantly differences (p>0.05). All HRV features show prominent changes prior to the CRASH-moment compared to controls (figure 1): SDNN increases by 50%, pDec reduces by 10% and SDDec increases by 100% compared to baseline, while controls show no differences of these features. These changes become significantly different for SDNN (p=0.002) and SDDec (p=0.002) in the period 3-6 hours before the CRASH-moment. For SDNN (p=0.005), SDDec (p=0.002) and pDec (p=0.003) these changes were also different in the period 0-3 hours before the CRASH-moment.

Clear changes in HRV features have been observed starting hours before the clinical diagnosis of LOS. The most prominent HRV changes were related to decreased overall HRV (SDNN) and transient episodes of bradycardia (pDec, SDDec), indicating instability of the autonomic regulation before LOS becomes clinical overt. These findings suggest that HRV holds the potential of predictive monitoring, which have to be validated in a clinical study.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=e77c9c6f54c06c823dd378c78f4e2d64-MjAxOS0wNSM1Y2UyNyY2Yzk0MTZl
IMAGE / TAB CAPTION: Figure 1. Time-series analysis of 3 HRV features in LOS positive (left panels) and control infants (right panels). Mean and SEM are shown. The vertical red line indication the CRASH- (Cultures, Resuscitation and Antibiotics Started Here) in the LOS or T0-moment in the control group. Note that there is an average moving window of 3 hours, i.e. the value denoted on a certain time moment is based on data three hours before. Statistical significance between LOS positive and controls (Wilcoxon sum rank test): (*) p<0.05 (**) p<0.01.

COI: None declared
ID: 572
TITLE: THE NEONATAL PRETERM BRAIN: A CONNECTOME ANALYSIS
AUTHORS: Joana Sa de Almeida 1; Serafeim Loukas 1,2; Lara Lordier 1; Alexandra Adam-Darque 1; François Lazeyras 3; Petra Hüppi 1
AFFILIATIONS: 1 Division of Development and Growth, Department of Pediatrics, University of Geneva, Geneva, Switzerland
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CONTENT:

Premature birth exposes the maturing brain to environmental stressors during a key period of development. Preterm infants have been shown to evidence later neurodevelopmental impairments, which might have their origin in structural brain alterations, englobing altered brain connectivity already present in the newborn period. Diffusion-weighted imaging is a non-invasive MRI method that allows in vivo visualization and quantification of white matter microstructure and structural connectivity. Using a whole-brain connectome analysis approach, we aimed to study the impact of prematurity on neonatal brain structural network organization.

13 full-term (FT) and 24 very preterm newborns (VPT) at term age underwent an MRI exam comprising T2-weighted and Diffusion-weighted image acquisitions. T2-weighted brain volumes were segmented and cortical brain parcellation was obtained by non-linear registration of ALL neonatal atlas propagated to each subject space. Structural networks were constructed using Mrtrix3 anatomically-constrained tractography with spherical-deconvolution algorithm and weighted per number of streamlines counts (SCw), fractional anisotropy (FAw) or SCw masked by FA (threshold 0.1) (SC*FAw). Graph analysis and network connectivity strength statistical comparison using FDR were performed to compare brain network organization of premature vs full-term newborns.

Graph analysis revealed that both FT and VPT infants’ brain networks presented a typical small-world organization. We identified 9 hubs in FT and 14 in VPT infants, with similar regions between both groups, mostly in basal ganglia, cingulate, insula and precuneus. In comparison to FT, VPT infants’ networks presented an increased characteristic path length, reduced global efficiency, reduced average closeness centrality and reduced nodal strength in 10 nodes, mostly located in frontal but also limbic and subcortical regions (Fig. 1A, 1B). Statistical comparison of connectivity strength between groups, using FDR analysis, revealed that, in comparison to FT, VPT infants presented 66 networks with significantly decreased connectivity strength, englobing mainly cortico-cortical and cortico-subcortical intra-hemispheric connections mostly in frontal and limbic and temporal regions (Fig. 1C).

Results show a preserved hallmark organization of the human brain connectome in both FT and VPT infants at term. VPT infants’ structural networks have a less optimal topological organization, resulting in a global reduced capacity to integrate information across brain regions and evidence alterations in subnetwork structural maturity mainly in frontal-subcortical and limbic networks.

IMAGE / TAB:
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**IMAGE / TAB CAPTION:** Fig.1. – A: 54 nodes with diminished closeness centrality in VPT infants in comparison to FT; B: 10 nodes with diminished nodal strength in VPT infants in comparison to FT. C: Representation of the 66 connections presenting diminished connectivity strength in VPT in comparison to FT infants, both at term age. Nodes are color coded representing the degree, from yellow (low degree) to red (high degree) colour range. For abbreviations, consult UNC Infant 0-1-2 atlases online documentation.

**COI:** None declared

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**Content:**

Data on tissue perfusion and oxygenation in preterm infants with patent ductus arteriosus (PDA) are still controversial. Near Infrared Spectroscopy (NIRS) could be a valuable tool for evaluation of regional perfusion and oxygenation of the brain (CrSO2) and renal tissue (rSO2). The aim of the study was to determine influence of PDA on the brain and renal perfusion and oxygenation using NIRS.

This is an observational study of the preterm infants with birth weight <1500g and gestational age 72 hours of age. Based on echocardiography findings two groups of patients have been classified: a persistent DA (PDA) and a closed DA. NIRS was used to assess CrSO2 and rSO2, calculating mean saturation values and fractional tissue oxygen extraction ratios (FTOE) during the 12 hours period. Statistical analysis was performed with SAS 9.2 program.

49 patients were enrolled in the study: 31 in the closed DA group and 18 in the PDA group. There were no difference in mean values of the CrSO2 and cFTOE in both PDA and closed DA groups: 78.29±1.82 vs 78.63±1.78 p= 0.25 and 0.16±0.03 vs 0.16±0.03 p= 0.57. But the mean values of the rSO2 were lower and rFTOE were higher in PDA group comparing with closed DA group: 74.58± 8.94 vs 67.03± 10.73 p=0.029, and 0.20± 0.09 vs 0.28± 0.11 p= 0.016.

NIRS can be used to determine the tissue oxygenation in preterm infants with PDA. Renal but not brain tissue oxygenation is effected by the PDA, showing decreased content and increased extraction of the oxygen.

**Image / Tab:**

**Image / Tab Caption:**

**COI:** None declared
ID: 587

TITLE: Acid base metabolism and cerebral oxygenation in term and preterm neonates during immediate transition after birth - an observational study

AUTHORS: Christian Mattersberger M.D a,b, Nariae Baik-Schneditz M.D.a,b, Bernhard Schwabberger, M.D.a,b, Georg M. Schmölzer, M.D., Ph.D.c,d, Lukas Mileder, M.D.a,b, Berndt Urlesberger, M.D.a,b, Gerhard Pichler, M.D.a,b

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CONTENT:

Background: Associations between blood-glucose-level and cerebral oxygenation (cerebral-regional-Oxygen-Saturation (crSO2) and cerebral-Fractional-Tissue-Oxygen-Extraction (cFTOE)) have been described in neonates. Aim of the present study was to investigate potential impacts of acid-base-metabolism on crSO2 and FTOE during immediate transition after birth.

Methods: Post-hoc analyses of secondary outcome parameters of observational studies were performed. Preterm and term neonates born by caesarean-section were included, in whom cerebral near-infrared-spectroscopy (NIRS) measurements were performed during immediate transition after birth and blood gas analyses (lactate (LAC), pH-value (pH), base-excess (BE) and bicarbonate (BC)) were measured from capillary blood sample taken between 15 to 20 minutes after birth. Routine monitoring was performed with pulse-oximetry (arterial oxygen saturation (SpO2) and heart rate (HR)). Correlation analyses were performed to investigate potential associations between crSO2, FTOE measured by NIRS at 15 minutes after birth and acid-base-metabolism were analyzed from the blood sample.

Results: 43 preterm neonates (GA: 34.0 weeks (24.0-36.7), BW: 1850g (640-3006) and 117 term neonates (GA: 38.9 weeks (37.0-41.4), BW: 3240g (2090-4466)) were included. Median crSO2 values at 15 minutes after birth were in preterm neonates 82% (16-95) and in term neonates 83% (54-95). Median FTOE values at 15 minutes after birth were in preterm neonates 0.13 (0.00-0.82) and in term neonates 0.13 (0.00-0.41).

In preterm neonates an increasing LAC and decreasing pH and BE were associated significantly with decreasing crSO2 and increasing FTOE. In term neonates no significant correlations were observed.

Discussion: In the present study we observed associations between acid-base-metabolism and cerebral oxygenation immediately after birth in preterm neonates, but not in term neonates.

IMAGE / TAB:
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IMAGE / TAB CAPTION: Basic demographic informations of the study population

COI: None declared
TITLE: THE STUDY OF TRANSITIONING HEMODYNAMIC INSTABILITY AND BRAIN INJURY CAUSED BY PRETERM BIRTH

AUTHORS: Reyin Lien 1, Chan-Chung Lee 2, Gao Yee 3

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CONTENT:

A healthy cardiopulmonary system is defined by its ability to adequately deliver sufficient oxygen to the tissue to meet metabolic demands. In the care of high risk neonates, ensuring a hemodynamic stability to provide sufficient oxygen to the brain, and so as not to cause any brain injury, is our ultimate goal. Yet, maintenance of neonatal circulatory homeostasis remains a real challenge, not only due to the complex physiology during postnatal transition and the inherent immaturity of the organs, but also due to the lack of reliable hemodynamic monitor to guide our management. Low blood pressure has been used to define shock. Yet with the flow distribution by diving reflex and the impact of local vasoactive molecules, cardiac output and blood pressure hardly address the real picture of end-organ perfusion, let alone oxygen metabolism. Our aim of this study was to apply currently available hemodynamic monitors, namely blood pressure, cardiac output, cerebral blood flow by color doppler measurement, brain tissue oxygen saturation, pulseoxymetry (for SpO2), and transcutaneous CO 2 monitor to investigate the influences of systemic and cerebral circulatory changes on brain injury after preterm birth.

Cardiac output was measured by electrical cardiometry AESCULON™ and compared with measurements from echocardiogram. ACA blood flow was measured by color Doppler. The transcutaneous PCO2 (tcPCO2) was measured using SenTec OxiVenTTM system. Brain tissue oxygenation (CrSO2) was monitored using near-infrared spectroscopy (NIRS) INVOSTM 5100C. The CrSO2 was recorded every five or six seconds. The cerebral fractional oxygen extraction (cFTOE) was calculated as formula: cFTOE=(SaO2 – rStO2)/SaO2. They were monitored continuously for 72 hours starting within three hours after birth. Transitional cardiovascular performance were also monitored daily for the first 3 days and continued until PDA closure or for a maximum duration of 7 days postnatally. Study period was from 2017/12 to 2018/4.

We found that CrSO2 has weak positive correlation with blood pressure SBP (r=0.255, p=0.004), DBP (r=0.267, p=0.002) and MABP (r=0.259, p=0.004). There was a strong negative correlation between CrSO2 and cFTOE (r=-0.798, p<0.001). cFTOE has a weak positive correlation to FiO2 (r=0.23, P=0.002). The tcPCO2 has a weak positive correlation to cETOE (r=0.181, p=0.015) and negative correlations to CrSO2 (r=-0.183, p=0.01).Infants with IVH had lower mean CrSO2 than infants without IVH (median 66.95, IQR (62.69, 72.27) vs. median 75.35, IQR (72.27, 81.97); p=0.001). VLBW infants who had lower mean CrSO2 within first 72 hours of life and developed PDA later was prone to failure of pharmacologic treatment of PDA (median 75.36, IQR (72.28, 82.36) vs. median 69.85, IQR (65.5, 76.8; p=0.113).

In our study, the correlations between CrSO2 and blood pressures are weak indicating systemic blood pressure does not represent organ perfusion. Infants with lower postnatal 72 hours CrSO2 were more likely to develop IVH and hsPDA, and also had higher risk of medical treatment failure for closure of PDA. Continuous cerebral NIRS monitor may help guide better management to ensure better outcome in VLBW preterm infants.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared.
ID: 591
TITLE: THE EFFECT OF ANTENATAL BETAMETHASONE ON NEONATAL RESPIRATORY MORBIDITIES IN LATE PRETERM INFANTS
AUTHORS: Nuran Üstün 1, Meryem Hocaoğlu 2, Abdulkadir Turgut 2, Sertaç Arslanoğlu 1, Fahri Ovalı 1
AFFILIATIONS: 1 Istanbul Medeniyet University, Medical Faculty, Department of Pediatrics
2 Istanbul Medeniyet University, Medical Faculty, Department of Obstetrics and Gynecology

CONTENT:

Late preterm infants (LPIs) account for approximately 75% of all preterm births and 8-9% of all births, with high respiratory morbidity. Antenatal corticosteroid (ACS) therapy in preterm infants born before the 34th week of gestation currently represents standard of care. However, a small number of studies have been conducted on the effect of glucocorticoids in late preterm infants, with contradictory results. The objective of our study was to evaluate the effect of betamethasone on respiratory morbidities in late preterm infants.

Late preterm neonates were prospectively enrolled in this study. Infants with major congenital anomalies, maternal diabetes or gestational diabetes, congenital infections, previous exposure to corticosteroids and multiple births, were excluded. Infants were classified into two groups: (1) study group: infants had received at least one dose of betamethasone (n=218) and (2) control group: infants did not receive betamethasone (n=288). The primary outcome measure was a composite respiratory morbidity outcome (RDS, TTN, mechanical ventilation or oxygen requirement). Other neonatal outcomes included admission to NICU, hypoglycemia, hyperbilirubinemia and length of hospitalization. Univariable and multivariable logistic regression analyses were performed.

Of 498 patients, 218 received at least one dose of betamethasone. The composite respiratory outcome was not significantly different between those who received versus those who did not receive betamethasone (1.33 95%CI [0.8-2.2] p=0.25). Additionally, there was no statistically significant difference in the rates of neonatal intensive care unit admission, hypoglycaemia and need for phototherapy (Table 1).

In late preterm infants, ANC exposure was not associated with lower incidence of respiratory morbidities.

IMAGE / TAB:

IMAGE / TAB CAPTION: Table: Results of the study. Data presented as numbers (percent) or means±standard deviation. CPAP continuous positive airway pressure; RDS respiratory distress syndrome; TTN transient tachypnea of the newborn; NICU, neonatal intensive care unit.
a: The presence of either RDS, TTN, mechanical ventilation or oxygen requirement.
Data adjusted for gestational age, gender, mode of delivery

COI: None declared.
ID: 598

TITLE: CAN SPLANCHNIC NEAR INFRA-RED SPECTROSCOPY BE USED AS A VALID TOOL IN NEONATOLOGY?

AUTHORS: Emilie Seager (first author) 1, Catherine Longley 1, Narendra Aladangady 2, Jayanta Banerjee 3

AFFILIATIONS: 1 - Imperial College Healthcare NHS Trust
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3 - Imperial College Healthcare NHS Trust and Imperial College London

CONTENT:

Near infrared spectroscopy (NIRS) measures the amount of oxygenated and deoxygenated haemoglobin, using venous, arterial and capillary haemoglobin in tissues, thereby measuring regional tissue oxygen saturation. NIRS was first demonstrated to be valuable in measuring brain oxygenation in 1977; it is routinely used to measure brain oxygenation in cardiac surgery and ITU. However, its usefulness in measuring gut perfusion remains to be proven. We undertook a systematic review to determine whether NIRS can be deemed a valid tool to measure regional oxygenation of gut tissue in neonates.

Pub Med and Embase databases were searched using the following terms: ‘preterm infants’, ‘NIRS’, ‘neonate’ and ‘gut oxygenation’. Where the title suggested relevance to the review the full article was reviewed to determine whether it was to be included. All clinical trials, observational studies and experimental animal studies that examined the validity of NIRS were included. Abstracts not in English and not relating to gut oxygenation were not included. This search was performed by two independent reviewers and the results then reviewed by two further independent authors.

A few studies have assessed the validity of NIRS measuring gut oxygenation (Table 1). The relationship between ileal blood flow, NIRS and liver tissue oxygenation has been well described; however, there is limited data regarding splanchnic NIRS and gut perfusion. Splanchnic NIRS has been compared to gastric pH by Kaufman et al who found a strong correlation between the two (r=0.79, p<0.0001). Fortune et al used abdominal NIRS to determine splanchnic perfusion in comparison to cerebral perfusion and demonstrated that the cerebro-splanchnic oxygenation ratio (CSOR) was highly predictive of intra-abdominal pathology such as necrotizing enterocolitis (NEC).

NIRS has been studied in detail in the neonatal population and can be used to monitor gut perfusion. Gut NIRS should be used as a tool in future randomised trials to underpin its use in clinical practice. Further research into normal values in different neonatal populations and a consensus on interpretation of results may facilitate adopting NIRS as part of routine, non-invasive bed side monitor in neonatal units soon.

IMAGE / TAB:
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IMAGE / TAB CAPTION: Table 1

COI: None declared
ID: 601
TITLE: LONG-TERM EFFECTS OF NEONATAL COMPLICATIONS ON BRAIN GROWTH AT 10 YEARS OF AGE IN CHILDREN BORN EXTREMELY PRETERM
AUTHORS: Hedvig Kvanta 1; Carmen Jimenez-Espinoza 2; Nelly Padilla 3; Ulrika Ådén (4)
AFFILIATIONS: Dept of Women’s and Children’s Health, Karolinska Institutet, Stockholm, Sweden.
Dept of Neonatology, Karolinska University Hospital, Stockholm, Sweden.

CONTENT:

Previous studies indicate that preterm children with surgery treated patent ductus arteriosus, IVH grade I-II and the lowest gestational ages have smaller brain volumes at term age (Lemmers 2016, Padilla 2015, Filian 2012). There is little known about the long term effect of these neonatal risk factors. The aim of this study was to investigate whether the volumetric differences seen at term age persisted when children were scanned with magnetic resonance imaging (MRI) at 8-11 years.

51 eligible extremely preterm (EPT) children born before week 27+0 in Stockholm between 2004 to 2007 successfully underwent MRI at age 8-11 (mean age 10.33). We excluded children with intraventricular haemorrhage (IVH) grade 3-4, periventricular leukomalacia at term age, severe white matter abnormalities and focal brain lesions. Scans were performed on a 3.0 Tesla General Electric system. T1-weighted images were pre-processed, automatically segmented into grey matter (GM), white matter (WM) and cerebro-spinal fluid (CSF). We also calculated cerebral parenchyma (CPAR=GM+WM) and intracranial volume (ICV=WM+GM+CSF). Volumes in cm³ were calculated for each tissue class. Groups were compared with Student t tests and multivariate general models for normally distributed variables.

Brain volumes for WM, GM, CSF, CPAR and ICV for children with IVH grade 1-2 (n=16) and no IVH (n=35) were compared considering relevant covariates, there were no differences in brain volumetry, see table 1. Brain volumes for WM, GM, CSF, CPAR and ICV between children with PDA ligation (n=16) and no PDA (n=15) were compared considering relevant covariates. We found significantly smaller brain volumes for ICV, WM and CSF for children with PDA ligation, when controlling for gestational age only the difference in CSF persisted, see table 1. Brain volumes for WM, GM, CSF, CPAR and ICV between children born 26 (n=25) were compared, there were no significant differences between groups, see table 1.

Considered covariates for each group analysis were age at scan, weight at 12, length at 12, head circumference at 12, gestational age and sex.

EPT born with perinatal risk factors associated with smaller brain volumes at term age showed no significant brain volume loss on a global level difference at 8-11 years when correcting for relevant covariates. This indicates compensation for volumetric brain loss along childhood. This does not rule out the presence of differences in brain organization, which requires other methods to be demonstrated.

IMAGE / TAB:
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IMAGE / TAB CAPTION: Table 1: Brain volumes for extremely preterm children with and without perinatal risk factors.

COI: None declared
ID: 602

TITLE: BRAIN GROWTH IN EXTREMELY PRETERM CHILDREN SCANNED AT TERM AGE AND AT LATE CHILDHOOD COMPARED WITH FULL TERM CONTROLS

AUTHORS: Hedvig Kvanta 1; Carmen Jimenez-Espinoza 2, Nelly Padilla 3; Ulrika Ådén 4

AFFILIATIONS: 1 Dept of Women’s and Children’s Health, Karolinska Institutet, Stockholm, Sweden.
2 Dept of Neonatology, Karolinska University Hospital, Stockholm, Sweden.

CONTENT:

Preterm born children have different brain growth patterns than full term born children. Extremely preterm children (EPT) have smaller grey matter brain volumes compared to full term controls at term age on a global and regional level (Padilla 2015). In very preterm born scanned at age 7 these volumetric losses persisted, the loss was most pronounced in the grey matter (Monson 2016). There is to our knowledge no study investing the global brain growth over time specifically in EPT children. We aimed to investigate whether the growth pattern in brain volumes is similar in EPT children compared with very preterm born over childhood.

51 EPT children born before week 27+0 in Stockholm between 2004 to 2007 underwent MRI at age 8-11 (mean age 10.33). 38 full term born were also included. We excluded children with intraventricular haemorrhage (IVH) grade 3-4, periventricular leukomalacia at term age, severe white matter abnormalities quantitatively defined and focal brain lesions. Scans were performed on a 3.0 Tesla General Electric system. T1-weighted images were pre-processed and then automatically segmented into grey matter (GM), white matter (WM) and cerebro-spinal fluid (CSF). We also calculated the volumes for cerebral parenchyma (WM+GM) and intracranial volume (WM+GM+CSF). Volumes in cm³ were calculated for each tissue class. We compared brain volumes of EPT children with full term controls.

Groups were compared using Student t tests and multivariate general models for normally distributed variables. Cohen’s effect size was calculated. 0.2 is considered a small effect size, 0.5 a medium effect size and 0.8 a large effect size. At term age brain volumes were smaller in EPT born than in controls and the difference was predominantly found in the GM (171 cm³ for EPT children and 177 cm³ for controls). At late childhood EPT children had significantly smaller brain volumes in the WM, CPAR and ICV. When adjusting for ICV we still found significant volume loss in WM. Cohen’s effect size was calculated at term age and at late childhood, see fig 1. The percentage growth from term age to late childhood for GM was equal in EPT children and controls (338 vs 337%) but percentage growth for WM was smaller in the EPT group compared to controls (203 vs 215%).

Our results suggest that brain growth over childhood is affected in extremely preterm children and that in late childhood, white matter substance is more affected than grey matter.

IMAGE / TAB: https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=28c14e91b030e938761d7506c58cf26a-MjAxs0wNM1Y2UyNjY2EyNTc1

IMAGE / TAB CAPTION: Fig 1: Effect size calculations at term age and late childhood for loss of white and grey matter volumes in extremely preterm born vs full term controls. There is a medium effect size of volume loss in white matter at late childhood for children born extremely preterm. *=significant difference between preterms and controls.

COI: None declared
ID: 613

TITLE: INTAKE OF UNPASTEURISED MATERNAL BREAST MILK, UNLIKE PASTEURISED DONATED BREAST MILK, IS POSITIVELY ASSOCIATED WITH POSTNATAL WEIGHT, LENGTH AND HEAD CIRCUMFERENCE GROWTH IN EXTREMELY PRETERM INFANTS

AUTHORS: Anna-My Lund 1; Magnus Domellöf 2; Ann Hellström 3; Elisabeth Stoltz Sjöström 4; Ingrid Hansen-Pupp 1

AFFILIATIONS: 1 Lund University, Skåne University Hospital, Department of Clinical Sciences, Lund, Paediatrics, Lund, Sweden
2 Department of Clinical Sciences, Paediatrics, Umeå University, Umeå, Sweden
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4 Department of Food and Nutrition, Umeå University, Umeå, Sweden

CONTENT:

The preferred choice of enteral feeds for preterm infants is unpasteurised maternal breast milk. If maternal milk is absent pasteurised donor milk is often offered as an alternative. The purpose of pasteurisation is to inactivate infectious agents, however important biological factors such as immunological components, growth factors and enzymes are reduced or destroyed in this process. Previous studies indicate that preterm infants receiving a greater proportion of maternal milk rather than pasteurised donor milk have a more favourable postnatal growth pattern. The aim of our study was to investigate the relationship between intake of maternal and donor milk and subsequent postnatal growth.

The study population originate from the Extremely Preterm Infant in Sweden Study (EXPRESS; 2004-2007) where infants had a gestational age (GA) <27 weeks (n=707). Data regarding neonatal morbidities were collected prospectively. For the first 28 postnatal days, daily intakes of breast milk, parenteral and enteral nutrition, were obtained retrospectively from hospital records and nutritional intakes were thereafter registered weekly (day 35, 42 etc.) until discharge. All available weight, length and head circumference (HC) measurements were obtained from hospital records. Infants with conditions known to affect enteral nutrition and growth were excluded. Finally, 456 surviving infants with complete breast milk data from birth to 32 weeks postmenstrual age (PMA) were included in the analyses.

Infants had a mean GA of 25.4 weeks, a mean birth weight of 778 g and a mean birth weight z-score of -0.78. Mean intake of maternal milk (ml/kg/d) from birth to 32 weeks PMA correlated positively and significantly with z-scores of weight (r = 0.230, p=<0.001), length (r = 0.132, p=0.008) and HC (r = 0.192, p=<0.001) at 36 weeks PMA and with change in z-score from birth to 36 weeks PMA for weight (r = 0.283, p=<0.001), length (r = 0.126, p=0.027) and HC (r = 0.256, p=<0.001). No such associations were found for donor milk milk. Mean total breast milk intake (i.e. maternal and donor milk combined) correlated positively and significantly with z-scores of weight (r = 0.342, p=<0.001), length (r = 0.224, p=<0.001) and HC (r = 0.307, p=<0.001) at 36 weeks PMA and with change in z-score from birth to 36 weeks PMA for weight (r = 0.420, p=<0.001), length (r = 0.264, p=<0.001) and HC (r = 0.437, p=<0.001).

An increased intake of unpasteurised maternal breast milk, as opposed to pasteurised donated breast milk, is associated with more favourable longitudinal growth outcomes of weight, length and HC until 36 weeks PMA in a Swedish population-based cohort of extremely preterm infants. All neonatal health care professionals should collaborate to promote and encourage an increased use of unpasteurised maternal breast milk within the preterm population.

IMAGE / TAB:
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IMAGE / TAB CAPTION: Relationship between mean intake of maternal, donor and total breast milk (ml/kg/d), respectively, from birth to 32 weeks postmenstrual age (PMA) and change in weight z-score from birth to 36 weeks postmenstrual age.

COI: None declared.
ID: 616

TITLE: LONG TERM NEURODEVELOPMENTAL OUTCOME OF ACUTE SYMPTOMATIC PERINATAL STROKE IN NEONATES

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CONTENT:

With an estimated incidence of 1/1600-3000 live births, perinatal stroke is the leading cause of hemiparetic cerebral palsy in childhood and thus contributes to lifelong disabilities. A better understanding of the relationship between the risk factors and outcome is therefore a major interest. Accordingly, our goal was to analyze patient characteristics of different clinical subgroups of term and late-preterm neonates diagnosed with perinatal stroke at Level III Neonatal Intensive Care Units in Budapest, Hungary.

We conducted a retrospective analysis enrolling 225 term (37-41 weeks of gestation) and late preterm (31-36 weeks of gestation) neonates with the diagnosis of perinatal stroke confirmed by MRI between 2007-2017. The Bayley Scales of Infant Development-II, the Brunet-Lézine test and the Binet Intelligence scales-V were used for follow-up at a mean age of 60 months (range 18-138 months, unless died earlier). Follow-up was available in 174 infants. Logistic regression models and Fisher exact tests were applied to test the associations between the outcome and a set of explanatory variables (late-preterm neonates, in utero stroke, cerebral sinovenous thrombosis (CSVT), congenital heart disease (CHD), mild-to-moderate asphyxia and infection).

Mean (±SD) Apgar scores at 1 and 5 minutes were 7.2±2.6 and 8.5±2.1, respectively. There was a male predominance (60%). Genetic or acquired thrombophilia was detected in 27 (38%) out of 71 screened neonates. Normal neurodevelopmental outcome was recorded in 39% of the infants. CSVT was a dependent predictor of death (odds ratio (OR) [95% confidence interval (CI)] = 18.2 [3.2,104.3]; p=0.001). Asphyxia (OR [95%CI] = 41.5 [3.0;567.2]; p=0.005) and infection (OR [95%CI] 12.3 [1.1;134.2] p=0.040) were significantly related to hearing impairment. In utero stroke was associated with the need for ventriculoperitoneal shunt placement (p=0.027), while infection was related to cognitive deficit (p=0.01). CHD had a significant association with death (p<0.001) and behavioral deficit (p=0.031). Finally, late-preterm neonates developed hemorrhagic stroke more frequently (86% vs. overall 54%; p<0.001).

Perinatal stroke adversely affects neurodevelopmental outcome in the majority of cases. Our findings suggest that a better understanding of the relationship among the risk factors, findings of imaging studies and long-term neurodevelopmental outcome may improve the potential for prevention, accuracy of diagnosis and the timely initiation of treatment and rehabilitation of neonates with perinatal stroke.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared.
ID: 621

TITLE: APNOEIC OXYGENATION TIME IN PRETERM NEONATES

AUTHORS: Dr Radhika Kothari 1; Dr Eoin O’Currain1,2,3,4; Dr Kate Hodgson 1,2,4; Dr Brett Manley 1, 2,5; Dr Joyce E O’Shea 6; Dr Lorraine McGrory 7; Dr Louise S Owen1,2,5; Dr Omar Kamlin 1,2,5; Dr Jennifer A Dawson1,2,5; Dr Marta Thio1,2,5; Prof Peter G Davis 1, 2

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CONTENT:

Clinical deterioration with desaturation or bradycardia is common during neonatal intubation attempts [1,2]. The NRP recommends a 20-second time limit for intubation attempts; however attempts often take longer. The time until onset of desaturation in neonates has not previously been reported. Kinouchi et al. [4] examined apnoea time in infants and concluded that SpO2 decreases to < 95% more quickly in younger ones. Patel et al. [5] measured the time until SpO2 <90% after apnoea in healthy children and showed a similar trend in age-related desaturation (94-214 sec). Aim of this study was to determine the apnoeic oxygenation time in preterm infants undergoing elective intubation.

This was an observational study of very preterm neonates born ≤32 weeks’ gestation undergoing elective endotracheal intubation at the Royal Women’s Hospital (RWH), Melbourne, Australia. Data were acquired from a previous randomised trial [6]. All infants received premedication for intubation. Continuous SpO2 and heart rate data were recorded using a pulse oximeter. Apnoeic oxygenation time was defined as the time from the last positive pressure or spontaneous breath, until desaturation (SpO2 <90%), in keeping with other studies [5, 7, 8]. Video recordings of the intubations were retrospectively reviewed and apnoeic oxygenation time was determined for the first intubation attempt only. Measurements of SpO2 and heart rate were recorded every 2 seconds during the apnoeic period.

Data from 119 patients were available from the original trial. Infants were excluded (n=41) if they did not have continuous saturation data, or if intubation occurred in the delivery room. The remaining 78 infants were included. The mean (SD) gestational age was 27 (2.2) weeks and birth weight 1022 (359) g. Median (IQR) age at intubation was 36 (10 – 312) hours. All but 5 neonates had SpO2 <90% during apnoea (73/78, 94%). The mean (SD) apnoeic oxygenation time was 25.3 (19.4) seconds. The mean (SD) time to desaturation <80% was 37.0 (21.9) seconds, and to desaturation <60% was 58.2 (20.2) seconds. Percentile charts were produced to demonstrate SpO2 changes with time after apnoea. No bradycardia <100 beats per minute was seen. There was no correlation between apnoeic oxygenation time and gestational age (r=-0.04, p=0.71), birth weight (r=-0.19, p=0.11) or starting FiO2 (r=-0.25, p=0.03).

To our knowledge this is the first study to report apnoeic oxygenation time in preterm neonates, and to characterise the changes in oxygen saturation and heart rate after apnoea. Apnoeic oxygenation time is substantially shorter in preterm neonates, compared with pediatric and adult patients. These data provide important clinical information for the development of clinical guidelines and studies to improve neonatal intubation safety.
IMAGE / TAB:
https://www.eiseverywhere.com/eeselectv3/v3/events/351149/submission/files/download?fileID=f75d6b9e8e6db53dc188e8575074bca2-MjAxOS0wNSM1Y2UyNjY2Y2E5YmVh

IMAGE / TAB CAPTION:

COI: None declared
ID: 622

**TITLE:** Predictors of growth parameters in preterm infants at discharge

**AUTHORS:** Kenneth Tan 1; Clare Hellyer 2; Caitlin Watson 3; Pramod Pharande 4

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**CONTENT:**

A recent unit feedback report from the ANZNN showed unsatisfactory 18 months growth for our infants <28 weeks gestation. Inpatient growth is predictive of growth and developmental outcomes in early infancy, circa 18-22 months. We aim to investigate discharge growth parameters (weight, head circumference (OFC) and length) of our infants <32 weeks gestation and identify risk factors. This is to assist in the development of nutritional intervention of this most vulnerable group of infants for growth failure. We aim to identify risk factors for poor growth for infants <32 weeks gestational age in our NICU.

The cohort of infants from 2014-2016 <32 weeks admitted to our NICU was identified and clinical and anthropometric data was abstracted. Infants were categorised into 3 GA bands (23-27, 28-29, and 30-31 weeks). The Fenton Z-scores for weights, OFC and length were calculated using the LMS method. The differences in z-scores at admission and at discharge for all three the parameters were calculated. Statistical software Stata 14 was used for analyses. T-test was used to compare change in z-scores of the growth parameters. Paired Multiple (linear) regression models was used to identify significant predictors.

635 infants (355 males) admitted, BW 1.3 ±0.4 kg, GA 28.4±2.2 weeks who stayed median 42(19-82) days. Z-score change (95% CI) in parameters shown in table below.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>23-37 weeks</th>
<th>28-29 weeks</th>
<th>30-31 weeks</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ weight z-score</td>
<td>-1.3 (-1.4,-1.1)*</td>
<td>-0.8 (-1.0,-0.7)*</td>
<td>-0.8 (-0.8,-0.7)*</td>
<td>-0.9 (-1.0,-0.9)*</td>
</tr>
<tr>
<td>Δ OFC z-score</td>
<td>-0.9 (-1.1,-0.8)*</td>
<td>-0.8 (-1.0,-0.6)*</td>
<td>-0.6 (-0.7,-0.5)*</td>
<td>-0.8 (-0.8,-0.7)*</td>
</tr>
</tbody>
</table>
| Δ length z-score  | -1.4 (-1.6,-1.1)* | -0.8 (-1.0,-0.6)* | -0.6 (-0.7,-0.4)* | -0.9 (-1.0,-0.8)* * p<0.001

Significant independent predictors (coefficient, 95%CI) for the two of the three parameters were:

- Weight: IUGR -0.27 (-0.43, -0.1) surgery -0.11 (-0.19, -0.03) NEC -0.3 (-0.43, -0.06)
- Length: IUGR -0.29 (-0.52, -0.05) TPN exposure -0.14 (-0.25, -0.02)

Every growth parameter z-score in our very preterm population were negatively affected at discharge, especially in the group <28 weeks gestation. Intrauterine growth restriction, NEC, surgery and need for TPN are important predictors for poor growth.

**IMAGE / TAB:**

**IMAGE / TAB CAPTION:**

**COI:** None declared
ID: 631

TITLE: AN 'OMICS' APPROACH TO INVESTIGATING THE EFFECTS OF ARGinine SUPPLEMENTATION OF PARENTERAL NUTRITION-DEPENDENT VERY PRETERM INFANTS

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CONTENT:

Our current parenteral nutrition (PN) formulation results in both overprovision of some essential amino acids (AAs) and underprovision of certain conditionally-essential AAs, including arginine. Arginine has a vital and versatile role in nutrition and metabolism and is involved in multiple metabolic pathways. Arginine deficiency results in growth failure in animal models and there is evidence that arginine depletion has negative effects on T-cell function and immune-signalling. This exploratory physiological study used transcriptomics and metabolomics to assess the impact of parenteral nutrition arginine supplementation on the immune system and metabolism of very preterm infants.

Very preterm infants born <29 weeks’ gestation and/or <1200g were eligible for parenteral nutrition (PN). The aim of the study was to investigate changes in gene expression and metabolomic profiles following arginine supplementation. Study infants received standard PN only or continuous intravenous arginine supplementation alongside standard PN until day 10 (D10) of life. Blood samples were taken on day 3 (D3) and D10 of life and analysed for AA levels, microarray and metabolomics. Plasma AA levels were measured using ion exchange chromatography. Gene expression was measured on Agilent SurePrint microarrays. Plasma metabolomics were analysed by NMR spectroscopy and the resulting spectra were manually phased, baseline-corrected, and the metabolites identified using Chenomx software.

26 infants with mean gestational age of 26+4 weeks’ and a mean birth weight of 855g were recruited. 8 infants received standard PN only (6% arginine), 12 received 12% arginine and 6 received 15% arginine. Plasma arginine levels were significantly higher on D10 of life in the supplemented infants (mean 72.8 v 45.5µmol/L, p=0.03). The microarray and subsequent qPCR validation experiments confirm significant up regulation from D3-D10 of B cell differentiation factors APRIL (p<0.01) and BAFF (p<0.05) and pathogen recognition receptors TLR2 (p<0.01) and TLR4 (p<0.01). Gene expression profiling indicates expression changes between infants with low versus normal plasma arginine levels to be similar to changes from D3 to D10 of life. We found different metabolomic profiles on D10 of life for infants with normal arginine levels following supplementation versus non-supplemented infants (Graph 1).

PN arginine supplementation can correct arginine deficiency. Supplemented infants with normal plasma arginine levels exhibit changes in immune pathways similar to the temporal changes seen from D3 to D10 of life. These gene expressions changes are consistent with the development of a functional immune system. Arginine supplemented infants with normal plasma arginine levels exhibit different D10 metabolomic profiles to unsupplemented infants.
IMAGE / TAB:
83c8503da91c-MjAxOS0wNSM1Y2UyNjY2Y2FjMjk5

IMAGE / TAB CAPTION:

COI: None declared
ID: 632
TITLE: Respiratory monitoring during newborn resuscitation using a laryngeal mask airway vs. facial mask: a quasi-randomized trial
AUTHORS: Nicolas J Pejovic 1 Francesco Cavallin 2 Allan Mpamize 3 Clare Lubulwa 4 Susanna Myrnerts Höök 5 Josaphat Byamugisha 6 Jolly Nankunda 7 Thorkild Tylleskär 8 Daniele Trevisanuto 9
AFFILIATIONS: University of Bergen
Department of Global Public Health and Primary Care
Bergen
Norway

CONTENT:

Mortality rates from birth asphyxia in low-income countries remain high. Safe and effective positive pressure ventilation (PPV) can improve outcome, but the optimal mode of PPV delivery remains unclear. Face mask ventilation (FMV) performed by midwives is the usual method of resuscitating neonates in such settings but may not always be effective. The i-gel is a cuffless laryngeal mask airway (LMA) that could enhance neonatal resuscitation performance. We aimed to evaluate the respiratory function of laryngeal mask airway (LMA) and face mask (FM) in asphyxiated infants resuscitated by midwives in a low-resource setting.

This prospective randomized clinical trial was conducted at the labor ward of Mulago National Referral Hospital, Uganda. After a brief training on LMA and FM use, infants with a birth weight >2000 g and requiring positive pressure ventilation at birth were ventilated by LMA or standard face mask by daily non-blinded block randomization. Resuscitations were video recorded. A NewLifebox monitor collected ventilation data through a flow sensor between bag and mask. Heart rate was obtained with a Laerdal NeoBeat dry-electrode electrocardiography (ECG) monitor. The primary outcome was mask leak (%) during the first 30 given breath.

Forty-six infants were included in the study, 23 in each group. Baseline characteristics were comparable between the two arms. Mean expiratory tidal volume was 8.2 ml/kg (SD 3.4) in LMA and 8.8 ml/kg (SD 5.8) in FM arms (p=0.66), while mean mask leak was 39% (SD 20) in LMA and 46% (SD 24) in FM arms (p=0.32) during the first 60 breaths. Peak inspiratory pressure (PIP) was 39.4 cm H2O (SD 7.6) in LMA and 34.5 cm H2O (SD 8.2) in FM (p=0.04). The mean number of given breaths was 87 (IQR 64-162) in LMA and 236 (IQR 60-593) in FM arms (p=0.15). HR rate was higher in LMA than FM arm (p=0.05) and increased faster during the first 60 breaths (p=0.0001). In 26 infants with HR100 bpm in LMA (median 13 seconds, IQR 9-15) with respect to FM arm (median 61, IQR 33-140) (p=0.0002).

Mask leak and expiratory tidal volume were similar with a cuffless LMA compared to the standard Face Mask. LMA provided higher PIP, shorter ventilation time and a significantly improved heart rate response. The results are relevant for both low and high-income settings since this is the first report of respiratory function and heart rate during resuscitation with LMA. An ongoing trial will address potential benefits on long-term outcomes.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=ed35799c3259556475e16afa159414f1-MjAxOS0wNSM1Y2UyNjY2Y2FjZmQz

IMAGE / TAB CAPTION: Newborn resuscitation by midwife using LMA

COI: None declared
ID: 637  
**TITLE:** ENDOTHELIAL MICROPARTICLES (EMPs) AND ENDOTHELIAL PROGENITOR CELLS (EPCs) AS EARLY BIOMARKERS OF CARDIOVASCULAR RISK IN PREPUBERTAL CHILDREN BORN PREMATURELY  
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**CONTENT:**  
Endothelial microparticles (EMPs) and endothelial progenitor cells (EPCs) are reliable, early biomarkers of endothelial dysfunction. It has been suggested that preterm birth is significantly associated with cardiovascular risk factors and endothelial dysfunction. EMPs and EPCs have not been studied, so far, in prepubertal children born prematurely. The aim of this study was to determine EMPs and EPCs in prepubertal children born prematurely and to assess possible correlations with cardiovascular risk factors.  

The study population consisted of 112 children, 8-13 years old (54 preterm and 58 fullterm, as controls). Anthropometric measurements (body mass index - BMI, waist/hip circumference - WHR), arterial blood pressure and blood biochemistry (glucose, insulin, and lipid levels) were assessed. Moreover, ultrasonographic measurements of interventricular septum thickness (IVSd), left ventricular internal dimension (LVIDd), mass (LVM) and mass index (LVMI), common carotid (cIMT) and abdominal aorta (aIMT) intima-media thickness, were performed. Circulating EMPs [CD62e(+) and CD144(+)] and EPCs [CD34(+)/VEGFR2(+)] and CD34(+)/VEGFR2(+)/CD45(-)] were quantified by flow cytometry. For statistical analysis, Student’s t-test, Mann-Whitney U-test, and correlation/multiple regression analysis were applied.  

In comparison with controls, children born prematurely presented with higher BMI (p=0.01), WHR (p=0.04), systolic (p<0.001) and diastolic (p=0.04) blood pressure, IVSd (p=0.006), cIMT (p<0.001) and aIMT (p=0.03). Circulating CD62e(+) and CD144(+) EMPs, CD34(+)/VEGFR2(+) and CD34(+)/VEGFR2(+)/CD45(-) EPCs were significantly higher in preterm compared to fullterm (p=0.01, p=0.005, p=0.02 and p=0.04, respectively). Circulating CD62e(+) EMPs correlated significantly with total cholesterol levels (rs=0.26, p=0.03), cIMT (rs=-0.3, p=0.02), aIMT (rs=-0.2, p=0.03) and LVMI (rs=-0.27, p=0.02). Furthermore, CD34(+)/VEGFR2(+) EPCs were positively correlated with systolic (rs=0.41, p=0.001) and diastolic (rs=0.4, p=0.003) blood pressure, insulin levels (rs=0.28, p=0.01), IVSd (rs=0.31, p=0.01), LVIDd (rs=0.27, p=0.03), LVM (rs=0.38, p=0.004), cIMT (rs=0.34, p=0.005) and aIMT (rs=0.32, p=0.01).  

Prepubertal children born prematurely demonstrate increased expression of endothelial microparticles (EMPs) and endothelial progenitor cells (EPCs), indicative of endothelial dysfunction and/or vascular damage, in comparison with fullterm born children. Significant correlations between EMPs and EPCs expressions and cardiovascular risk factors reflect possible endothelial injury and/or activation of vascular repair and remodeling.  

**IMAGE / TAB:**  
**IMAGE / TAB CAPTION:**  
**COI:** None declared
ID: 658

TITLE: CORRELATION OF VALIDATED MRI SCORING SYSTEMS IN NEONATAL ENCEPHALOPATHY

AUTHORS: T Hurley, 1-5 M O'Dea 1-7, KA Roche 5, E Jenkins 1, 5 L Kelly 5, A Byrne 8, E Molloy 1-8

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3. Rotunda Hospital, Ireland
4. Clinical Research Development Ireland, Dublin, Ireland
5. Department of Paediatric and Child Health, TCD, Dublin, Ireland
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8. Our Lady's Children's Hospital Crumlin, Ireland

CONTENT:

Predicting long term outcomes in neonatal encephalopathy (NE) remains challenging. Magnetic Resonance Imaging (MRI) is the gold standard of neuroimaging that best defines the nature and extent of brain injury in NE. There are a number of different validated MRI brain scoring systems to predict long term outcome in neonatal brain injury at term. The scoring systems have different levels of complexity and detail. The different patterns of injury seen on MRI have been correlated to neurodevelopmental outcome. These scoring systems have never been compared and it is unclear if any is superior.

Infants with NE, Sarnat Grade II and III, (n=35) were prospectively recruited into an observational study. All underwent therapeutic hypothermia (TH) and had early MRI scan (mean (SD) 8.9 (4.2) days). The MRI scans were scored by paediatric radiologists, blinded to patient outcome using three validated scoring systems – Barkovich, NICHD and de Vries. The relationships between the scoring systems were assessed using the Spearman rank correlation to assess the strength of association between them.

Adequate MRI images to complete assessment by all scoring systems were available for 31 patients. A high proportion of patients had normal scans using all 3 scoring systems – 13/31 Barkovich (13/31), NICHD (13/31) and de Vries (12/31) in keeping with previous validation studies of these scoring systems. There was a high level of correlation between all scoring systems. The strength of association between NICHD and Barkovich scores measured by Spearman rank correlation (SRC) was 0.9303 with a 95% confidence interval (95% CI) of 0.86 to 0.97 (Figure 1). Similarly the strength of association between de Vries and Barkovich scores measured by SRC was 0.93 with 95% CI 0.86 to 0.97. The strongest correlation found was between de Vries and NICHD scores, with a SRC of 0.96 and a 95% CI of 0.92 to 0.98. The p values for each comparison was <0.001.

There is high correlation between each of the scoring systems. They vary in complexity and consequently level of time and detail required to complete each one. Our study suggests that the Barkovich scoring system that requires the least time resource is as informative as the others. Correlation between the MRI scoring systems and with the infants neurodevelopment will be done when infants are aged 2.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=1d9c4d07d6f66f00ad236756accf562-MjAxOS0wNSM1Y2UyNjY2Y2IzNWQ3

IMAGE / TAB CAPTION: Figure 1. Relationship between MRI brain predictive scoring systems in NE. 1a. Relationship between NICHD and Barkovich Score. A significant correlation was observed by the Spearman rank correlation (r=0.93, 95% CI 0.86-0.97, p<0.001). 1b. Correlation between de Vries and Barkovich Score. A significant correlation was observed
by the Spearman rank correlation ($r=0.93$, 95% CI 0.86-0.97, $p<0.001$).  
1c. Correlation between de Vries and NICHD Score. A significant correlation was observed by the Spearman rank correlation ($r=0.96$, 95% CI 0.92-0.98, $p<0.001$).

COI: nil
ID: 660

**TITLE:** QUANTITATIVE EEG TO DETECT INTRA-VENTRICULAR HAEMORRHAGE IN VERY PRETERM INFANTS

**AUTHORS:** John M. O’Toole 1,2; Clodagh Walsh 3; Daragh Finn 1,4; Geraldine B. Boylan 1,2; Eugene M. Dempsey 1,2

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4 Cork University Hospital, Wilton, Ireland.

**CONTENT:**

Postnatal adaption to extra-uterine life for preterm infants presents many challenges. Up to 1 in 3 infants born <32 weeks of gestation may develop brain injuries, such as intra-ventricular haemorrhage (IVH). We aim to determine if quantitative analysis of the EEG, coupled with machine learning algorithms, can detect the presence of IVH on day one.

Continuous EEG was recorded within hours after birth for infants born <32 weeks of gestation. EEG epochs of 1-hour were pruned at 6 and 12 hours after birth. Epochs with poor signal quality were rejected from further analysis. A common channel to all EEG records, C3–C4, was analysed with quantitative EEG (qEEG). First, an automated method removed segments of the EEG distorted by artefacts. Second, a set of qEEG features were then extracted; these features included spectral power, range-EEG, and inter-burst intervals. Cranial ultrasound was performed within 48 hours of birth to determine the presence of IVH. qEEG features were combined to detect IVH (any grade) using a gradient-boosting machine. A leave-one-baby-out cross-validation scheme was used for training and testing.

Forty EEG epochs were available at the 6-hour time point and 43 were available at the 12-hour time point. Fourteen out of the 43 infants developed IVH. Preliminary analysis showed that relative spectral power at the 6-hour time point—with frequency bands 0.5–3 Hz, 3–8 Hz, 8–15 Hz, and 15–30 Hz—as the best-performing feature, with a maximum area under the receiver operator characteristic (AUC) of 0.72 (95% confidence interval, CI: 0.55–0.88). Cross-validation testing results for combing the 4 features of relative spectral power over the 2 time points yielded an AUC of 0.90 (95% CI: 0.80–0.99).

Machine learning methods using qEEG can detect IVH within 12 hours of birth. Automated analysis of the EEG could enable rapid identification of IVH and direct timely interventions to ensure the best possible outcomes for this high-risk population.

**IMAGE / TAB:**

**IMAGE / TAB CAPTION:**

**COI:** None declared
ID: 682

TITLE: EARLY PREDICTIVE BIOMAKERS FOR GRADE AND SEIZURES IN NEONATAL ENCEPHALOPATHY

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CONTENT:

Hypoxic-Ischaemic Encephalopathy (HIE), is a major cause of morbidity and mortality worldwide. One of the challenges we face today is predicting as early as possible the degree of the brain injury (HIE grade) and the risk of seizures after perinatal asphyxia. Clinical examination is often used to guide therapeutic intervention, however, an infant’s condition at birth does not always correlate well with the degree of the injury, nor with the risk for seizures. The aim of our study was to assess the ability of a combination of early biomarkers to predict HIE grade and the development of EEG confirmed neonatal seizures. Predictive ability was examined using machine learning techniques. This was a secondary data analysis from two European multicentre cohort studies (BiHiVe/ANSeR 1 and ANSeR 2 studies). Infants born >36 weeks gestational age (GA), needing continuous EEG monitoring for clinical concerns were included. Infants with a diagnosis of clinical and electrographic HIE were included in this analysis. All grades of HIE were included. All EEG recordings were assessed by a clinical neurophysiologist for grade of HIE and presence of seizures. The early features used for the analysis were: GA, birth weight (BW), occurrence of intrapartum complications, Apgar at 1, and 5 minutes, lowest cord pH, post resuscitation pH, base deficit and lactate, most intensive level of resuscitation at birth. Logistic regression was performed with repeated 10-fold cross validation.

266 infants with HIE were included in this analysis, 31.2% mild, 46.2% moderate and 21.1% severe. Mean (SD) GA was 40.05 ± 1.30 weeks, BW 3522.46 ± 601.03g, male:female ratio = 59.4%:40.6%. Mean Apgar scores were 2 and 4, at 1 and 5 minutes respectively, mean (SD) cord pH 7.03 ± 0.19, 63.2% needing PPV at 10 minutes; 79.3% received therapeutic hypothermia, 34.2% had electrographic seizures with a total seizure burden (TSB) 121.48 ± 130.26. HIE grade prediction was done using data from 254 infants with an overall accuracy (95%CI) of 0.54 (0.44 – 0.64). Seizures occurred in 131 infants (49.2%). After looking at the predictive ability of each feature individually, the best prediction was achieved with a combination of Apgar score at 5 minutes with the value of the post resuscitation lactate, which gave a PPV 67.57%, NPV 76.99%, and AUROC (95% CI) 0.7269 (0.66-0.80).

Our study shows that early clinical markers for neonatal encephalopathy are not reliable predictors of the grade of encephalopathy. A combination of these clinical markers improved the prediction of seizures, compared with individual feature prediction, but are not robust enough to guide treatment. Additional predictive power may require additional physiological or biochemical markers.

IMAGE / TAB:

IMAGE / TAB CAPTION:
COI: None declared
FRESH HUMAN MILK PROTECTS EXTREME PREMATURE INFANTS AGAINST BRONCHOPULMONARY DYSPLASIA

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CONTENT:

Improved survival rates in very premature infants were associated with a high prevalence of bronchopulmonary dysplasia (BPD), which may be due to lung immaturity, infection and other risk factors. Human milk contains a variety of nutrients and biologically active substances, these components can help preterm infants to enhance their innate immunity and antibacterial functions, provide antioxidants and anti-inflammatory molecules which could be very useful in preventing BPD. Our objective was to evaluate the protective effect of fresh human milk on the prevalence of BPD.

A retrospective cohort of preterm infants with gestational age between 24 and 28 weeks gestational age (GA) and exclusively fed with human milk, born from January 2014 to June 2018 was carried out. Placenta histology, antenatal and postnatal events were recorded and daily amounts of human milk (HM), fresh (FHM) or banked (BHM) intakes were prospectively calculated from birth up to 28 days after birth. BPD diagnosis and severity was diagnosed at 36 weeks postmenstrual age (PMA) as the need of supplemental O2 or ventilatory support. For statistical analysis Student t test and Chi square were run as appropriate. Logistic regression was performed with the variables that were significant in the univariate analysis. A p value lower than .05 was considered significant.

Clinical records were obtained from 161 of 210 (77%) infants who had histologic placental evaluation for chorioamnionitis. Patients who died before 36 weeks PMA were excluded, remaining a population of 110 preterm babies for this analysis. As expected, lower GA, body birthweight and mechanical ventilation were significant risk factors for BPD. Antenatal steroids, intrauterine growth restriction, gender or multiple birth were not different between groups. Risk factors and human milk intake are shown in the table. Persistence of patent ductus arteriosus, late onset sepsis and lower volumes of HM intake at 28 days were risk factors for BPD. In a multivariate analysis a lower volume of HM intake at 28 days was the only predictive variable for BPD (OR 6.99 CI 1.85-26.3, p=0.004). BPD patients who received more than 50 Pc (3430 ml/kg) of HM at 28 days had a lower proportion of FHM intake.

Persistence of PDA, late onset sepsis and a lower cumulative volume of HM at 28 days were risk factors for BPD development. Higher volumes of HM during first 28 days had a protective effect on BPD independently of other risk factors. In patients who had greater intake of HM at 28 days those who received a higher proportion of FHM did not develop BPD without difference in body weight or GA at birth.

IMAGE / TAB:
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IMAGE / TAB CAPTION:
COI: None declared
CONTENT:

Antenatal corticosteroid (ACS) use beyond 34 weeks of gestation is currently under debate. The biological plausibility of ACS use in women with Diabetic Mellitus (DM), particularly when undergoing elective cesarean section requires testing in representative cohorts. Recent randomized controlled trials of ACS use in late pregnancy excluded DM due to concerns about maternal dysglycemia. Similarly, evidence from observational studies is lacking. The aim of this study was to investigate the impact of exposure to ACS on the short-term neonatal outcomes in a population with a high prevalence of diabetes in pregnancy.

This was a population-based, retrospective analysis of data from the PEARL-Peristat perinatal registry- NPRP 6-238-3-059, funded by the Qatar National Research Fund (QNRF). Singleton live births, with no major congenital anomalies, were included. Maternal perinatal variables included the following: DM, hypertension, gestational age, mode of delivery, ACS, ACS ≤14 days before delivery, maternal age, and parity. Neonatal short-term outcomes included the following: Combined respiratory distress syndrome and transient tachypnea of the newborn (RDS/TTN), NICU admission, NICU admission for hypoglycemia, and low 5-minute Apgar score (<6). We tested the association of exposure to ACS and neonatal outcomes in a univariate and multivariate regression model, using IBM SPSS version 22.

Out of 13976 eligible mothers, a total of 3895 (28%) had DM, of whom 93% had gestational diabetes (GDM). Birth between 34-37 weeks of gestation, cesarean section, and exposure to ACS occurred in 864 (6.2%) and 4094 (29.3%), and 247 (1.8%), respectively. Exposure to ACS ≤14 days of delivery occurred in 52 (0.4%). Neonatal outcomes of RDS/TTN, NICU admission, NICU admission for hypoglycemia, and low 5-minute Apgar score occurred in 3.5%, 8.8%, 1.3%, and 0.1% of this cohort, respectively.

In univariate analysis, ACS was associated with RDS/TTN [OR (95% CI)]; [4.6 (3.18 - 6.72)], NICU admission; [4.0 (3.0 - 5.33)], NICU admission for hypoglycemia; [3.3 (1.70 - 6.22)], but not with low 5-minutes Apgar score; [3.0 (95% CI 0.41 – 23.29)]. In multivariate regression model adjusting for other perinatal factors, DM and ACS predicted risk for NICU admission but not for RDS/TTN. Table-1

Our data suggest an association between ACS use beyond 34 weeks in diabetic mothers and early neonatal morbidity, although the exposure rate of ACS was low. However, in a multivariate analysis neither ACS nor DM independently predicted RDS/TTN. It is unclear whether ACS in diabetic mothers has either maternal or neonatal benefits after 34 weeks. The safety and efficacy of ACS in diabetic mothers after 34 weeks needs to be determined in RCTs.
ID: 714
TITLE: INTRAOSSEOUS NEEDLE USE IN NEONATES IN THE UK
AUTHORS: Alexandra Scrivens* 1; Alexandra Doerr* 2; Adrian Sayers 3; Alessandra Glover 2; Faith Emery 4; Charles Christoph Roehr 1
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CONTENT:

Intraosseous (IO) devices form a mainstay of resuscitation in paediatric departments, but do not feature so prominently in neonatal units, possibly because most neonatal unit inpatients have an accessible umbilical vein or existing vascular access. However, this is not always the case. A literature search found 41 documented cases where IO needles were used in neonatal units, but only 75% of neonatal units have IO devices available.

Aim:
.To identify recent UK cases where IO access has been used or attempted in patients <28 days of age, or resident on a neonatal unit.
.To ascertain which devices were used, whether they were sited successfully and whether any complications occurred.

An online survey was sent out via trainee representatives to trainee paediatricians in the UK.

Ninety-three responses were received. Thirty-eight respondents (41%) had attempted IO access in the year 2017-8, 12 more than once. Of 65 attempts amongst respondents, 13 were on infants <28 days of age, or neonatal unit inpatients (Table 1). Of these 13 attempts, 10 (77%) were successful. Devices used were: EZ-IO® (12) and Cook needle (1). Complications occurred in 23% of cases (dislodged (2), extravasation (1), thromboembolism (1)).

This survey demonstrated that intraosseous needles have been used successfully in neonates. Whilst not a first choice form of vascular access, IO devices may be considered during neonatal resuscitation situations. Wider IO device training and availability on neonatal units may offer a rare but lifesaving alternative form of IV access in an emergency situation. Further work is needed to determine optimal position and type of IO device in infants.

IMAGE / TAB:
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IMAGE / TAB CAPTION: Table 1: Features of all IO attempts in neonates or neonatal unit inpatients. NNU – neonatal unit, ED – emergency department, PICU – paediatric intensive care, PW – paediatric ward, CGA – corrected gestational age (weeks)

COI: None declared
ID: 715
TITLE: THE FEASIBILITY OF TRANSCUTANEOUS ELECTROMYOGRAPHY OF THE DIAPHRAGM AS MONITORING TECHNIQUE IN THE DELIVERY ROOM
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CONTENT:

To assess cardio-pulmonary transition of (preterm) infants in the delivery room (DR), heart rate (HR) and oxygenation are monitored using either chest impedance (CI) and/or pulse oximetry (PO). However, CI and PO do not provide information on the respiratory effort of the patient, an essential factor to titrate the level of respiratory support. Electromyography of the diaphragm (dEMG) measures the activity of the diaphragm and might be helpful to determine respiratory effort. In addition, it measures HR and RR, so dEMG might improve monitoring compared to CI. However, first it needs to be established if dEMG provides accurate data on HR compared to standard techniques available in the DR.

Infants with a gestational age (GA) > 26 weeks, in need for cardio-respiratory support and monitoring, but without congenital anomalies, were enrolled. CI and PO (standard care monitoring), and dEMG measurement equipment was applied as soon as possible after birth and recorded during the cardio-respiratory stabilization. Time between device application and the first read out of the corresponding HR was calculated (Δt).

HR was calculated based on the dEMG signal and the raw CI waveform. Numerical HR, based on CI and PO data, was acquired from the patient monitor. All HR-readings were compared during periods of noise-free recordings using intra-class correlation coefficient (ICC) and Bland-Altman (BA) analysis, including the limits of agreement (LOA).

Fourteen preterm infants (GA 32.5 ± 3.0 weeks; birth weight 1743 ± 790 grams) were included in this ongoing study. Due to errors in data storage, for some patients not all CI tracings were recorded (missing n = 6 for raw CI and n = 1 for numeric CI), so groups size differed for HR-readings.

Time between device application and the first HR read out was equal for dEMG and raw CI signal (both with median (IQR): 10.1 (10.1-10.3) seconds). The median (IQR) Δt based on numeric CI was 12.0 (8.1-13.7) seconds. HR detection of PO was slower compared to dEMG and CI with a median of 35.9 (16.3-67.7) seconds.

Heart rate monitoring could be executed with high accuracy (all p < 0.01) with an ICC of 0.98 for dEMG vs. raw CI; 0.96 for dEMG vs. numerical CI; and 0.96 for dEMG vs. numerical PO. BA analysis showed the best agreement between dEMG and raw CI (mean difference (LOA): -0.5 (6.8) beats/minute).

This study suggests that dEMG monitoring during cardio-pulmonary transition in the DR is feasible and provides fast and accurate data on HR, similar to CI and faster than PO. Future studies should now investigate the additional value of dEMG in assessing respiratory effort and titrating respiratory support in the DR.
IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 724

TITLE: ANTENATAL CORTICOSTEROIDS AND OUTCOMES OF PRETERMS ACCORDING TO DIFFERENT GESTATIONAL AGES

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AFFILIATIONS: 1Division of Neonatology, Health Sciences University, Zekai Tahir Burak Women’s Health Education and Research Hospital, Ankara, Turkey.

CONTENT:

Antenatal corticosteroid therapy is known to reduce risks of respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), early sepsis and mortality in preterms. For this reason current guidelines recommend the administration of antenatal corticosteroids to women at risk of preterm delivery from 24 0/7 to 34 6/7 weeks’ gestation and agree on considering administration from 230/7 to 236/7. In this study we aimed to see whether there was any difference in the effect of antenatal steroids on outcomes of preterms according to different gestational ages at birth.

We conducted a retrospective cohort study of infants cared for at a single tertiary care neonatal intensive care unit during a 5-year period between 2013 and 2017. All infants, of 240/7 to 296/7 weeks’ gestation age, admitted for neonatal care were included. The demographic and clinical characteristics of the study infants were reviewed. The patients divided into two groups; exposed to no antenatal steroids (ANS) or partial course of ANS and exposed to complete course of ANS. The study groups were further divided into two subgroups according to gestational ages; <28 and ≥28 weeks’ gestation. The association of neonatal morbidities and mortality of preterm infants at each gestation week in two groups were compared.

A total of 820 premature babies were analysed. There was no difference in the incidence of RDS, among babies born between 24 and 25 weeks’ gestation in two groups. But there was a statistically significant reduction in RDS incidence among babies born between 260/7 and 296/7 weeks’ gestation age whose mothers had received complete course of steroids compared to those who had not, and this difference was evident at each week of gestation. Severe intraventricular hemorrhage, bronchopulmonary dysplasia, early sepsis, air leaks and mortality did not significantly differ among groups at each gestational weeks. There was a reduction in the incidence of IVH (13.9% and 22.3%, p=0.04) and mortality (23.6% and 39.6%, p=0.001) among babies born <28 weeks’ gestation who were exposed to antenatal steroids than those not.

Antenatal corticosteroid treatment is associated with improved survival and reduction of IVH in babies born <28 weeks’ gestation.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared.
ID: 730

TITLE: THE EFFECTS OF PREECLAMPSIA ON PRETERM MORBIDITIES IN VERY LOW BIRTH WEIGHT INFANTS

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CONTENT:

Preeclampsia is a common pregnancy complication that causes high morbidity and mortality in newborns. The aim of this study was to compare very low birth weight infants (VLBW) born to mothers with preeclampsia with VLBW infants born to normotensive mothers in terms of preterm morbidities.

We assessed retrospectively the medical records of all preterm infants who were born at 250/7 to 296/7 weeks between 2013 and 2017. Preeclampsia is characterized with high blood pressure (systolic BP ≥140mmHG, diastolic BP ≥90mmHG) and proteinuria. Each infant born to mother with preeclampsia was matched randomly with three infants born to normotensive mothers by gestational age and by same gender. Newborns with incomplete medical data, perinatal asphyxia and major congenital anomaly were excluded from the study.

Data analysis of 128 infants whose mothers had preeclampsia and 384 matched controls revealed a median gestational age of 28.5 (27.5–29.4) and 28.4 (27.5–29.4) weeks and a median birth weight of 935 (790–1170) and 1090 (916–1260) g, respectively (p=0.09 and p<0.001). The incidence feeding intolerance (55.9% vs 34.4%, p<0.001), small for gestational age (33.6% vs 10.7%, p<0.001) and postnatal growth retardation (60.9% vs 54.9%, p=0.02) were higher in preeclampsia group. Moreover, surfactant requirement (70.3% vs 57.3%, p=0.009) and need laser photocoagulation retinopathy of prematurity (ROP) (13.3% vs 7.3%, p=0.02) was more significant in preeclampsia group. Preeclampsia were an independent risk factor for ROP requiring laser photocoagulation and surfactant requirement (Table).

The incidence of surfactant requirement, retinopathy of prematurity, small for gestational age and postnatal growth retardation increases in VLBW infants born to a mother with preeclampsia in comparison with VLBW infants.

IMAGE / TAB:
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IMAGE / TAB CAPTION: Independent risk factors for RDS and ROP in infants of preeclamptic mothers

COI: None declared.
ID: 734

**TITLE:** VARIATIONS IN PRACTICE MAY BE EVIDENCE-BASED: APPLICATION OF MULTI-CRITERIA DECISION ANALYSIS TO TREATMENTS FOR PATENT DUCTUS ARTERIOSUS

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**CONTENT:**

Patent Ductus Arteriosus (PDA) is a common cardiovascular condition in preterm infants where considerable variation in management practices exists. In a recent network meta-analysis of treatments for hemodynamically significant PDA (hsPDA), authors identified ten treatments evaluated across eight outcomes. The study purpose was to evaluate how treatment decisions for hsPDA differ across decision maker preference sets and baseline event rates.

We re-analyzed a published network meta-analysis of pharmacological treatments for hsPDA. Stochastic Multi-criteria Acceptability Analysis (SMAA), a tool to support decision making across multiple outcomes, was conducted using ordinal preferences (e.g. Mortality > necrotizing enterocolitis) from clinicians (SM, MCY) and a “preference free” model. Sensitivity to baseline rates was explored through increasing or decreasing single event rates +/- 2-10%. Monte-carlo methods were used for parameter estimation in NMA and integration over the preference weight space with 30,000 iterations used for both. Outcomes included first rank acceptability (FRA), the vector of central weights required to prefer one treatment over another, and a confidence factor (CF) reflecting certainty in decisions.

Clinicians differed in outcome rankings, which influenced treatment recommendations and their uncertainty (SM: highest FRA = continuous IV ibuprofen (0.28), CF = 0.66; MCY: highest FRA = oral paracetamol (0.31), CF = 0.32). Central weights for the preference free model suggest that continuous IV ibuprofen is preferred when PDA closure is ranked low compared to mortality/NEC. Central weights for paracetamol are more balanced across all outcomes. Variations in baseline rates have a similar effect on recommendations. We developed a web-based application in which outcome rank preferences and baseline event rates can be customized to compute the first rank acceptability and confidence factor of the top ranked treatments.

These findings suggest that observed treatment variation may be the result of a rational synthesis of available evidence, local event rates, and outcome preference. The web-application can be useful tool to incorporate outcome preferences and local event rates into available evidence for decision-making.

**IMAGE / TAB:**
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=67e3e2f6b5a5923ceec693f9d2f5facc-MjAxOS0wNSM1Y2UyNjY2Y2QyZmJk

**IMAGE / TAB CAPTION:** Table 1. Central weights and confidence factors for the preference free model

**COI:** Mr. Disher is an employee of Cornerstone Research Group Inc. Cornerstone consults for various pharmaceutical and medical device companies.
Hypertension affects up to 20% of pregnancies worldwide and is associated with increased rates of intra-uterine growth restriction, placental abruption, preterm birth and fetal death. Some authors report lower rates of respiratory distress syndrome (RDS), bronchopulmonary dysplasia (BPD) and intraventricular hemorrhage (IVH) among infants from hypertensive mothers and attributed this to stress response, while others report increased BPD and IVH when the infants were SGA. Our objective was to examine whether antenatal corticosteroids impact infants with and without maternal hypertension differently.

We conducted a retrospective study of all infants (n=34,416) born between 22-32 weeks and admitted to Canadian Neonatal Network NICUs between 2010-2017. We excluded infants who were moribund (n=257), with major congenital anomalies (n=1212), or missing data on date of birth (n=8), antenatal corticosteroid use (n=933) or maternal hypertension (n=650). We examined antenatal corticosteroid use among mothers with and without hypertension, and the characteristics (birth weight, gestational age, sex, small for gestational age (SGA), singleton, cesarean section) of their infants. We compared mortality and major morbidity (IVH, retinopathy of prematurity, necrotizing enterocolitis, infection, RDS, BPD) using bivariate and multivariate analysis, and conducted a sub-analysis for SGA infants.

18.9% of the cohort (n=31,356) had maternal hypertension. Antenatal corticosteroid use among mothers with (H) and without hypertension (N) was 92.7% and 86.8% respectively (p<0.01). Infants from hypertensive mothers were more likely to be singleton, born by caesarean section, SGA and of higher gestational age. Table 1 shows outcomes of infants with and without maternal hypertension. On multivariate analysis, antenatal corticosteroids reduced the incidence of mortality (H-OR 0.44 (0.38, 0.50), N-0.44 (0.28, 0.69)) and severe IVH (H-OR 0.53 (0.47, 0.61), N-0.56 (0.35, 0.89)) for all infants, but reduced composite outcomes (mortality or major morbidity) (OR 0.73 (0.67, 0.80)), RDS (OR 0.69 (0.63, 0.75)) and BPD (0.85 (0.76, 0.94)) only for infants from non-hypertensive mothers. Antenatal corticosteroids did not reduce mortality or morbidity among SGA infants with maternal hypertension.

Antenatal corticosteroids reduced the incidence of mortality and IVH for all infants, but only reduced RDS and BPD for infants when mothers did not have hypertension, and did not reduce mortality or morbidity among SGA infants whose mothers had hypertension.

**IMAGE / TAB:**
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**IMAGE / TAB CAPTION:** Table 1: Outcomes of Infants with and without maternal hypertension

**COI:** None declared.
ID: 738

TITLE: GASTROSCHISIS AND THE PRE-FORMED SILO (PFS): EARLY PHYSIOLOGICAL PARAMETERS AND OUTCOMES

AUTHORS: Rebecca Lee 1; Niyi Ade-Ajayi 2, Theodore Dassios 3, Ann Hickey 4

AFFILIATIONS: King’s College Hospital, London, UK

CONTENT:

Validated severity of illness and risk-adjusted scores of morbidity and mortality often require collection of physiological data that may not be available or relevant in early care of babies born with gastroschisis (GS). The relationship between commonly recorded early physiological parameters and short-term outcomes has not previously been described in a cohort of GS babies, exclusively managed with gradual surgical reduction using a PFS as the intended choice of closure. Aims: To describe a population of infants with GS managed with PFS’s, and investigate the association between individual early physiological parameters with length of stay (LOS) and days of PN (parenteral nutrition).

A retrospective cohort study of babies with gastroschisis born between 1st January 2008 and 31st December 2017 in a single tertiary NICU was undertaken. Babies managed with a PFS were included in full analysis. Routinely measurable physiological parameters including pH, base excess, lactate and toe-core gap were recorded over the first 24, 48 and 72 hours. Total length of stay and TPN days were selected as outcome measures. Babies were stratified into ‘complex’ and ‘simple’ gastroschisis groups, and whether they had an episode of blood culture positive sepsis. Data presented as medians (IQR), or counts (%). Non-parametric analysis, correlation coefficient and chi-squared statistical analysis was utilised. Multivariate linear regression assessed the independence of confounding variables.

100 babies were identified of whom 91 underwent closure with PFS. Complete records for 77 infants were included for full analysis [38 male, gestation 36+6(35+3 – 38+0), birthweight 2458(1993 – 2757)g]. Survival was 100%. The worst median lactate was 4.2 (IQR 3.0 – 5.8), base excess -7.0 (IQR -5.55 – -9.35), and ‘toe-core’ gap was 3.4oc (IQR 3.0 – 4.2oc) over the first 72 hours. Metabolic acidosis (pH <7.26 and BE < -8.5 or greater) was present in 30% of infants. There was no correlation between individual physiological parameters and outcomes in all babies with gastroschisis, or in the complex / simple or sepsis / no sepsis groups. PN days and total LOS were higher in infants with complex gastroschisis and blood-culture positive sepsis, p= <0.001 respectively.

In a population of gastroschisis patients that were managed exclusively with PFS, early physiological parameters and blood measurements were not associated with a longer stay or duration of parenteral nutrition. Simple and complex gastroschisis stratification provides clearer early prognostication.

IMAGE / TAB:
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IMAGE / TAB CAPTION: Early physiological parameters and outcomes in patients with gastroschisis managed with Pre-formed Silo as choice of surgical closure.

COI: None declared.
TITLE: UNIVERSAL NEWBORN SCREENING FOR CONGENITAL CYTOMEGALOVIRUS INFECTION – RESULTS OF A PILOT TRIAL IN GERMANY

AUTHORS: Norbert Teig1, Emmanouela Dimitrakopoulou 2, Susanne Dettmers 1, Dariusz Michna 4, Angela Nagel 6, Susanne Wiegand 1, Stefan Volkenstein 2, Peter Kern 3, Stefan Niesert 5, Thomas Lücke 1, Stefan Dazert 2, Klaus Korn 6, Klaus Überla 6, Katrin Neumann 2

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CONTENT:

Congenital cytomegalovirus (cCMV) infection is the single most common cause of hearing loss in infancy. 90% of affected infants will exhibit no symptoms at birth. If detected early infants with cCMV infection could receive earlier and presumably more effective antiviral and audiological treatment. As there are no epidemiological data for Germany we conducted a pilot project in order to examine incidence of cCMV and the feasibility of a universal newborn screening program.

Between 2015 and 2017 we performed screening for cCMV infection in two German nurseries if parental consent had been obtained. Screening was done by CMV specific PCR from buccal swabs taken on the third day of life. If positive the infant was recalled for confirmatory testing by viral PCR of urine and blood. If congenital CMV infection was confirmed the infant was offered a systematic neuropediatric and audiological follow-up program.

Within three years 6099 newborns were screened for cCMV. 38 newborns (0.62%) had a positive screening result, in 20 of these newborns cCMV was confirmed by positive PCR from urine (incidence = 0.33%). False-positive rate was 47%. One of the newborns with confirmed cCMV infection had clinical symptoms at birth. Another three infants (15%) demonstrated distinctive features of blood chemistry (thrombocytopenia, increased transaminases) or brain ultrasound. Universal screening for congenital hearing loss was negative in all infants with cCMV infection. Costs for the program totaled 20 € per screened newborn.

Universal screening for cCMV infection was feasible and demonstrated high precision when compared to screening tests performed for inborn errors of metabolism. Within our cohort selective screening for cCMV guided by hearing screening would have missed 100% of all infected newborns. Due to the low incidence of cCMV infection in our cohort a much larger trial would be necessary in order to proof possible benefits of universal cCMV screening.

COI: None declared
ID: 749
TITLE: Melatonin and superoxide dismutase rich fetal nutrition by amniotic fluid
AUTHORS: Soyhan Bagci 1; Özlem Altuntas 1; David Katzer 1; Ebru Aileen Alsat 1; Brigitte Strizek 2; Heiko Reutter 1; Peter Bartmann 1; Andreas Müller 1
AFFILIATIONS: 1 Neonatology and Pediatric Intensive Care, Children’s Hospital, University of Bonn, Bonn, Germany
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CONTENT:
Antioxidant molecules have shown to play a protective role in the gastrointestinal system. Melatonin (MT) plays an important physiological role through specific receptors or directly in immune regulation, anti-inflammatory responses and oxidative stress. Human breast milk contains important enzymatic and non-enzymatic antioxidants such as superoxide dismutase (SOD) and MT. An embryo starts swallowing amniotic fluid (AF) as early as the tenth week of gestation. However, little is known about the antioxidative enzymes in AF, which is the first fluid to enter the gastrointestinal tract. The main purpose of the present study was to evaluate MT and SOD status in AF during fetal period.

AF samples from 76 pregnant women (Median gestational age (GA) (min.-max.), 38.0 Weeks (14.3-40.1)) were obtained during an amniocentesis or an elective caesarean section. Immediately postnatal, blood samples were collected from the umbilical vein (n=53). According to gestational age (GA), the samples were divided into three groups: Group 1 (n=15), samples obtained before 28.0 weeks of gestation, Group 2 (n=12), samples obtained between 28.0 and 36.9 weeks of gestation, and Group 3 (n=49), samples obtained after 37.0 weeks of gestation.

GA, melatonin concentration (MTc) and SOD concentration (SODc) of the newborns enrolled in the study are shown in Table 1. MTc in AF was found positive correlated with GA (Pearson correlation’s coefficient, r= 0.282, p<0.014), while SODc was not correlated with GA (R= -0.103, p=0.378). Compared to serum samples, MTc was statistically significant higher in AF (11.2 pg/ml (6.1-20.7) vs. 58.4 pg/ml (14.7-135.5), p<0.001). SODc was not statistically significant different between serum and AF (88 ng/ml (69-131) vs. 77 ng/ml (51-94), p=0.090). Neither MTc nor SODc in AF was significantly correlated with their concentrations in serum (p=0.810 and p=0.799, respectively).

Our results indicated that the gastrointestinal system of fetus is continuously exposed to MT and SOD throughout its prenatal development. Further studies are needed to show whether the deficit of MT and SOD due to premature birth influences the development of the gastrointestinal tract and increases the risk for development of necrotizing enterocolitis in preterm infants.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=67d12c2c0d6a1327e58a3dc83c1a0a13-MjAxOS0wNSM1Y2UyNjJ2Y2RiMDNI

IMAGE / TAB CAPTION: Table 1. Melatonin, and SOD concentrations in the amniotic fluid during pregnancy

COI: No
ID: 753

TITLE: FOLLOW-UP OF THE REPRODUCTIVE OUTCOMES OF ADULTS WHO WERE BORN VERY PRETERM AND/OR VERY LOW BIRTH WEIGHT FROM 28 TO 35 YEARS OF AGE

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CONTENT:

Adults who were born very preterm (VPT) and/or with a very low birth weight (VLBW) within the Project on Preterm and Small for Gestational Age Infants in the Netherlands (POPS) cohort of 1983, showed significantly reduced reproductive rates compared to the national Dutch population at 28 years of age (females 23.2% vs 31.9% and males 7.4% vs 22.2% at least one livebirth) [1]. This study aimed to follow-up the reproductive outcomes of this cohort at 35 years of age.

The participants of the POPS cohort were retraced in the year 2018. Participants who returned a signed informed consent form received a link to the online POPS35 questionnaire about their Quality of Life, Employment & Burn-out symptoms and Reproductive Outcomes. Reproductive outcomes included reproductive rate, pregnancy wish, fertility problems, pregnancy complication and perinatal outcomes of their offspring, for example recurrence of preterm birth. These outcomes were also collected in term controls obtained through Facebook and also compared to national statistics and perinatal registries.

In this ongoing study, 351 POPS35 questionnaires are currently completed (37% of 955 surviving POPS cohort participants). In addition, 376 controls competed the same questionnaire. Preliminary analysis showed no difference in reproductive rates (at least one pregnancy) between the POPS participants and controls (both around 50%). Nevertheless, compared to the national statistics, POPS participants reported a lower mean number of children at 35 years and among females a significantly higher incidence of HDP (25%) and placental pathology (7%) compared to the national perinatal registry (11% and 1.5%). All these outcomes were comparable between POPS participants and controls.

These preliminary results suggest catch up of the delay in reproductive rate in adults born VPT and VLBW between 28 and 35 years of age, but still some differences with the Dutch population remain. These results should be interpreted with caution as they are still preliminary and may be confounded by selection bias due to selective non-response of those most handicapped, low educated and of male gender.

REFERENCES:

COI: This study was done for EU-project RECAP (www.recap-preterm.eu), funded by the European Commission; Horizon 2020; Grant Number: 733280. The authors declare no conflict of interest.
ID: 755

TITLE: EVALUATION OF THE EFFECTS OF NEW BPD CLASSIFICATION BASED ON RESPIRATORY SUPPORT ON INCIDENCE OF BRONCHO PULMONARY DYSPLASIA

AUTHORS: Mehmet Buyuktiryaki1, Tuğba Alarcon-Martinez1, Bengu Karacaglar1, Gulsum Kadioglu Simsek1, Fuat Emre Canpolat, Cuneyt Tayman, H. Gozde Kanmaz Kutman

AFFILIATIONS: 1Division of Neonatology, Health Sciences University, Zekai Tahir Burak Women’s Health Education and Research Hospital, Ankara, Turkey.

CONTENT:

Bronchopulmonary dysplasia (BPD) is one of the most common respiratory morbidities of preterm newborns. The utility of commonly used BPD definitions are still controversial. Therefore, herein, we evaluate the effects of two different BPD classification: i) based on the National Institute of Child Health and Human Development (NICHD) and ii) based on requirement of respiratory support.

We assessed retrospectively the medical records of all preterm infants who were born at 250/7 to 296/7 weeks between 2013 and 2017. Based on recent BPD definition, patients were categorized according to the respiratory support provided at postnatal 36 weeks and independently from the required oxygen concentration. Newborns treated with low flow nasal cannula and newborns supported with high flow nasal cannula or any other non-invasive respiratory support were classified as mild BPD and moderate BPD, respectively. Patients under invasive mechanical respiratory support were classified as severe BPD.

Data analysis of 757 newborns revealed a mean gestational age of 28.1±1.5 weeks and a mean birth weight of 1024±241 g. According to NICHD and recent definitions, patients were evaluated and classified into mild BPD (%31.2-%0, respectively, p<0.001), moderate BPD (%9.2-%1.3, respectively, p<0.001) and severe BPD (%4.1-%1.2, respectively, p<0.001) (Table).

The evaluation of chronic lung disease in newborns with the recent BPD definition demonstrates a lower incidence of mild-moderate and severe bronchopulmonary dysplasia compared to previous NICHD classification. Further studies are needed for more sensitive and valid clinical classification to determine long-term outcomes, treatment and complications of BPD.

IMAGE / TAB:
https://www.eiseverywhere.com/eiselectv3/v3/events/351149/submission/files/download?fileID=2b55a0c944f9741d36a7334c0a4741cb-MjAxOS0wNSM1Y2UyNjY2Y2RkMjYy

IMAGE / TAB CAPTION: BPD weight ratings according to NICHD and new classification

COI: None declared.
ID: 763
TITLE: Fetal Deprivation Sequence
AUTHORS: Nicola Mullins 1; Catherine Harrison 2; Simon Newell 2
AFFILIATIONS: 1 Neonatal Department, Hull University Teaching Hospitals NHS Trust, Hull, UK
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CONTENT:

Intrauterine Growth Restriction (IUGR) as a consequence of substrate deficiency has many detrimental effects on the fetus. These effects present with a constellation of symptoms including thrombocytopenia, persistent lactic acidosis, hypoglycaemia, coagulopathy, renal and hepatic failure. However, this clinical presentation has not been formally classified making diagnosis challenging.

Aims:
1. To describe the detailed clinical sequelae of placental insufficiency.
2. To define a diagnostic classification for the proposed term “fetal deprivation”.
3. To aid correct diagnosis of fetal deprivation sequence (FDS) and enable a streamlined investigative and diagnostic approach.

Over a two-year period, on a large tertiary neonatal unit, seven cases of infants with multi-organ failure in the absence of an acute asphyxial event at the time of birth were reviewed. A review of the clinical notes and Badger database was utilised for data collection. A systems based approach was adopted. Maternal and obstetric history was reviewed in conjunction with birth history and the clinical features identified in the affected neonates. Placental histology and outcome was also incorporated in the review. Findings were then tabulated to identify common features.

The case review has identified common features of FDS. All cases were growth restricted and had reduced fetal movement reported. Lactate significantly elevated in all cases and if normalised achieved by day 4-6. All required 15% Dextrose or more to maintain normoglycaemia. All had platelets <30 and resistant to platelet transfusion. 6/7 cases required ventilator support but for <48 hours. 6/7 had deranged clotting remaining until day 7 of life. 5/7 required inotropic support due to cardiac dysfunction. 5/7 had renal dysfunction and 5/7 babies died.

The authors suggest that to fulfil a diagnosis of FDS all of the major criteria should be present with minor criteria strengthening the diagnosis. The suggested diagnostic criteria are proposed in figure 1. A detailed literature review has identified pathophysiological explanations for these criteria.

Our review shows that babies affected by FDS have multi-organ failure with relative “brain sparing” due to fetal substrate deprivation. Since collating this data, we have recognised the pattern of FDS in over 20 more term babies all fulfilling the criteria suggested for this diagnosis. This has helped rationalise investigations and management and enabled a thorough approach to follow-up including postnatal counselling for families.

IMAGE / TAB: https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=13119e61946e5b7bd2e9e08834c187fc-MjAxOS0wNSM1Y2UyNjY2Y2RmMjM0

IMAGE / TAB CAPTION: Figure 1– Proposed criteria for diagnosing Fetal Deprivation Sequence

COI: None declared
ID: 765  
**TITLE:** Neonatal Hyperinsulinism. Patient demographics and the need for Diazoxide.  
**AUTHORS:** Sai-Kalyani Kanthagnany 1, Dushyant Batra 2  
**AFFILIATIONS:** Neonatal unit, Nottingham University Hospitals NHS trust, Nottingham, UK  

**CONTENT:**

Hypoglycaemia in neonates is a common reason for neonatal unit admission. Persistent, severe and recurrent hypoglycaemia can lead to long term neurological sequelae due to brain injury. The presence of high levels of insulin results in hypoglycaemia, prevention of gluconeogenesis, suppression of fatty acid oxygenation and ketogenesis. Thus depriving the brain of its alternative fuels, resulting in cell damage. Several risk factors have been suggested. We conducted this study to find out the incidence of neonatal hyperinsulinism in our neonatal population and to assess the associated demographic factors.

Neonatal unit admission databases and laboratory databases were used to retrospectively identify patients who underwent hypoglycaemia screens in Nottingham, between January 2014 and January 2019. The criteria for hypoglycaemia screens were based on our local neonatal hypoglycaemia guideline (persistent hypoglycaemia, neuroglycopaenia or blood glucose < 1mmol/l). The diagnosis of neonatal hyperinsulinism was made when a neonate had detectable insulin levels (>2mU/L) in the presence of hypoglycaemia (blood glucose level <2.6mmol/L).

We divided the population into two groups. Group 1 were all hyperinsulinaemic and required treatment with Diazoxide and Chlorthiazide. Group 2 responded to conventional treatment with increased feed volumes, increased frequency of feeds and intravenous fluids. Both patient and maternal demographics were collected from patient databases.

Incidence of neonatal hyperinsulinism requiring treatment with diazoxide, in our tertiary neonatal unit over the last five years was 1 per 10,000 live births.  
In group 1, 59% had a z score for growth < -1.28 and 18 % had z scores above 1.28 (median -1.64, IQR 2.69). Birth gestation varied between 33-41 weeks. 28% of these neonates were born to mothers with pre-eclampsia. 50% were born to mums with British ethnicity while 27% to Indian or Pakistani ethnicity mothers. Median maternal BMI 24.5 (IQR 6.1). In group 2, 110 babies had hypoglycaemia screens sent, 55% were hyperinsulinaemic. 42% had a z score for birthweight < -1.28 (median -2.18, IQR 1.073). 15% had z scores >1.28 (Median 1.99, IQR 1.12). Birth gestation varied between 24-41 weeks. Only 26% were born to diabetic mothers and 19% to mothers with pre-eclampsia. 55% were born to British mothers and 20% to Indian or Pakistani mothers. Median maternal BMI 27.8 (IQR 8.5).  
The Indian and Pakistani ethnicity was over-represented in both groups potentially indicating higher incidence (7.2% of live births Indian/ Pakistani ethnicity, ONS).

The incidence of Hyperinsulinism (HI) in our population is 1 in 10000 live-births. Babies born small for gestational age and of South East Asian ethnicity seem to be at higher risk.17% of our hypoglycaemic babies who underwent hypoglycaemia screen, needed treatment with Diazoxide and Chlorthiazide. Surprisingly few had significant maternal history to suggest they were at risk of significant Hyperinsulinism.
ID: 768
TITLE: MIDWIFERY OR MEDICAL CLINICAL LEADER TO IMPLEMENT A NATIONAL GUIDELINE IN BABIES ON POSTNATAL WARDS (DESIGN): A CLUSTER-RANDOMISED, BLINDED, CONTROLLED, TRIAL.
AUTHORS: Jane Alsweiler 1
Caroline Crowther 2
Jane Harding 2
AFFILIATIONS: 1 Department of Paediatrics: Child and Youth Health, University of Auckland, Auckland, New Zealand
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CONTENT:

Neonatal hypoglycaemia is a common condition associated with developmental delay. Treatment of neonatal hypoglycaemia with oral dextrose gel has been shown to reverse hypoglycaemia and reduce admissions to intensive care unit for hypoglycaemia. A clinical practice guideline was written to guide the use of dextrose gel to treat neonatal hypoglycaemia in New Zealand. However, it is unclear what clinical discipline might most effectively lead the implementation. Our aim was to determine if midwives or medical clinical leaders are more effective at implementing a clinical practice guideline for oral dextrose gel to treat neonatal hypoglycaemia in babies on postnatal wards.

A cluster-randomised, blinded, controlled, trial. NZ maternity hospitals that care for babies born at risk of neonatal hypoglycaemia were randomised to having a local midwife or doctor lead the guideline implementation at that hospital. Randomisation was stratified by prior use of dextrose gel and by level of care of the maternity unit. Audits of dextrose gel use were done before, and three and six months after, implementation of the guideline. The primary outcome was the change in the proportion of eligible hypoglycaemic babies (blood glucose concentration <2.6 mmol/L, diagnosed in the first 48 hours after birth), treated with dextrose gel from before implementation to three months after implementation. Data were analysed by linear regression adjusted for the stratification variables.

Twenty four eligible maternity hospitals in New Zealand consented to participate, 15 hospitals had eligible babies at both time points for the primary outcome (7 randomised to midwifery led, 8 randomised to medical led implementation). 463 eligible hypoglycaemic babies were included in the analysis (292 midwifery led, 171 medical led implementation). There was an increase in eligible babies treated with oral dextrose gel from before implementation of the guideline to 3 months after implementation (122/153(80%) v 144/163(88%), OR(95%CI); 3.42(1.67-6.98), p<0.001). There was no difference in the primary outcome between hospitals randomised to midwifery or medical led implementation (percentage treated with gel, mean(SD); midwifery led: before 70(38), after 87(12); medical led: before 63(43), after 86(16); adjusted change in proportion (mean difference(95%CI); 19.3(-4.4-43.0), p=0.11)).

Implementation of a clinical practice guideline increased the use of oral dextrose gel to treat neonatal hypoglycaemia. Midwives and medical clinical leaders were equally effective at implementing this guideline for treatment of babies on the postnatal ward.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 775

**TITLE:** Congenital heart disease in Trisomy 21: A single centre experience

**AUTHORS:** Dr Alexander Yule  
Dr Sirisha Balmuri

**AFFILIATIONS:**  
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**CONTENT:**

Due to the association that Trisomy 21 (T21) has with congenital heart disease (CHD), prompt diagnosis of CHD and treatment is needed to prevent irreversible pulmonary vascular disease (PVD). In the UK, national guidelines have been developed by specialist interest groups for the management of a neonate found to have T21 including recommendations on the investigation of CHD and the use of echocardiograms. At Nottingham Children’s Hospitals, we’ve developed our own guidelines that are in keeping with these recommendations. The purpose of this audit is to determine whether as a team we are complying with our guidelines and highlight any improvements that can be made with our pathway.

A list of all neonates born with trisomy 21 within Queen’s Medical Centre and Nottingham City Hospital between January 2016 and December 2017 was collected for retrospective analysis. Data was collected from two computer programmes; NoTIS (clinic letters and results) and Digital Health Records (electronic copies of written notes). Data was collected for: demographics, grade of most senior person reviewing patient, date of 1st echocardiogram and ECG, echocardiogram diagnosis, time to follow up. Each patient was compared against our local guideline algorithm and then also compared against key aims from the national recommendations; that CHD is diagnosed or excluded by 6 weeks of age and all are discussed with a Paediatric Cardiologist / Paediatrican with a special interest in Cardiology.

In total 28 patients were identified. 61% had T21 identified during their neonatal period. CHD was very prevalent in the population with 27 out of 28 having some abnormality identified. The most common cardiac abnormalities were AVSD and PDA. 100% of patients had an echocardiogram performed during initial work up or at cardiac clinic follow up. The average time till first echocardiogram was 6.4 days. 18 out of 28 patients (64%) followed the local pathways. Non-compliance with local guidelines was commonly due to delayed referral to follow up.  Performance against national guidelines: 26 of 27 patients (one patient excluded as had immigrated to the UK aged 2 years) through current practice, had either a serious CHD identified or excluded within 6 weeks of birth. For review by a Cardiologist, 89% (24 out of 27) of patients had been reviewed by 6 weeks of age.

This audit has found that as a service, we are good at rapidly identifying CHD in the population of neonates with T21 and that the echocardiogram is the mainstay diagnostic tool. Serious CHD abnormalities are referred promptly to specialist services. Areas for improvement include the use of ECG’s as part of initial work up for all neonates with suspected T21. Further work will be to create a streamlined referral pathway for patients with CHD.

**IMAGE / TAB:**

**IMAGE / TAB CAPTION:**

**COI:** We have no conflict of interests to declare.
ID: 777

TITLE: NEO-TRAIN QUALITY IMPROVEMENT INITIATIVE TO IMPROVE EOSIN (EARLY ONSET SEPSIS IN NEONATES) CARE AS PER NICE RECOMMENDATION

AUTHORS: Anoj Oommen 1; Nitesh Singh 2; Kamini Yadav 3; Divya Saxena 4; Adam Bonfield 5; Marks Ainsworth 6; Ali Pamina 7

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CONTENT:

Neonatal sepsis is a serious systemic infection and a leading cause of neonatal morbidity and mortality. Recognizing neonates at risk of sepsis and early identification of sepsis followed by immediate treatment is key to reducing adverse outcomes.

National Institute of Clinical Excellence guidelines on neonatal sepsis recommends administration of antibiotics within 1 hour of suspecting sepsis. Achieving this target can be challenging in a busy NICU. Adult and pediatric services have addressed this by introducing 1-hour sepsis care bundles.

Aim:

Improve adherence to NICE sepsis standard for administration of antibiotics within 1 hour of suspecting sepsis and following antibiotic stewardship

A quality improvement methodology of process mapping and fishbone analysis was used to study workforce pathways and system tools to identify barriers. Four Plan-Do-Study-Act (PDSA) cycles were run in two six monthly blocks between 02/2017 to 07/2017 and 08/2018 to 01/2019.

Cycle 1: Baseline issues and QI strategy defined.
Issues identified: delay in time to treatment, measurement of second CRP, reporting of blood culture within 36 hours.

Cycle 2: Significant delay in transport and processing of blood culture were leading to delay in reports.

Cycle 3: Pareto chart based staff survey were used to understand aspects of human behavior. Incomplete documentation identified.

Cycle 4: Time of 36 hours blood culture reports not available for babies on postnatal ward.

1. The outcome improved the average time of antibiotic administration from 120 minutes to 90 minutes.
2. Early reporting of blood culture results of neonates from postnatal ward which helped in early discharge from the ward when cultures were negative.
3. Improved awareness among staff about the importance of completing sepsis screen within 1 hour.
4. Changes implemented to bring about early delivery of blood culture bottles to the lab.

ACTIONS IN EACH CYCLE:

Cycle 1:
Sepsis Screening Pit-stop was implemented. An educational initiative 'Neo Train' was started and posters displayed in clinical areas.

Cycle 2:
Persuasion of stakeholders: pottering services and microbiology department to obtain blood culture results within 36 hours.

Cycle 3:
Staff education undertaken. A sepsis booklet created and implemented.

Cycle 4:
Negotiation with microbiology department

A Plan-Do-Check-Act quality improvement initiative for service innovation was used to improve care pathway for babies with risk factors for neonatal sepsis.
2. Value stream mapping helped to identify barriers and potential key areas for improvement.
3. Key feature for the success of the Neo-train Quality Improvement initiative was its use of a multidisciplinary team approach to strategically design and deliver the implementation program.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=c2fc1f30502959f6426a84b2a7a66f5f-MjAxOS0wNSM1Y2UyNjY2Y2UxZTM4

IMAGE / TAB CAPTION:

COI: NONE DECLARED
ID: 788
TITLE: VENTILATION ON A LOW RESOURCE SETTING NEONATAL UNIT: JUST BECAUSE WE CAN, DOES THAT MEAN WE SHOULD?
AUTHORS: Aoife Hurley
AFFILIATIONS: Neonatal Unit, University Teaching Hospital, Lusaka, Zambia
Neonatal Unit, Leeds Teaching Hospitals Trust, Leeds, UK

CONTENT:

There is plenty of research on neonatal resuscitation in low to middle resource countries, but less about ongoing ventilation. Zambia's only tertiary Neonatal unit, based at University Teaching Hospital, Lusaka has four ventilators. The decision to intubate is clinical with oxygen saturations the only monitoring. The infant should be above 1kg with an available ventilator. There is no carbon dioxide monitoring, no blood gases, no chest Xray. Therefore we cannot monitor for hypocapnia or hyperoxemia in infants ventilated for a prolonged period. With the mortality rate of these patients unknown, is it right or safe to intubate and ventilate those infants without ways to safely monitor?

A retrospective review of intubated and ventilated patients persisting beyond the acute neonatal life support setting, over a three month period was undertaken in the NICU. Exclusion criteria for ventilation was infants less than 1kg, those with congenital abnormalities and ventilator availability. A proforma was filled out including gestation, weight, reason for intubation, intubator grade, tube size, premedication used, length of intubation, how they extubated and outcome. If applicable, those infants with Hypoxic Ischaemic Encephalopathy (HIE) had a score out of 22 on arrival and at discharge, a higher number is associated with poorer outcome. Primary outcomes looked at mortality, secondary at documentation of event, if premeditation or surfactant was given and self extubation rates.

In total 44 patients, with average weight was 2.5kg. Main reason for admission to NICU was HIE with 64%, main reason for intubation was respiratory distress 34% then apnoea 27%. Registrars were responsible for 55% of intubations. 75% noted ETT size, 5% documented number of attempts. No one was premeditated and 9% received surfactant. There was no documentation of ETT length or grade of view. 14% documented air entry as means to assess tube position, no other method documented of confirmation. Average length of intubation was 23 hours. 30% were planned extubations. 36% self extubated, 66% did not document planned versus self extubation. 27% were reintubated after extubation, with 8 (67%) of these due to self extubation. 25% survived to discharge. 68% died prior to discharge. Of those who had HIE scores performed on admission, the average was 12/22 and on discharge the average was 12/22.

Whilst this is a small cohort of patients, it gives some indication of outcomes of ventilated infants. The question remains an uncomfortable unanswered one, for which further work is needed. An intubation check list has been created to aid documentation, teaching of nursing and medical staff includes how to intubate, use of premedication, how to secure ETT and ventilation. We will re audit to see if these interventions have made any difference.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 790

TITLE: TREATED CASES OF RETINOPATHY OF PREMATURITY - 5-YEAR DATA FROM THE RETINA.NET ROP REGISTRY

AUTHORS: Johanna M. Walz 1,2; Sebastian Bemme 3; Moritz Daniel 1; Amelie Pielen 4; Helge Breuß 5; Daniela Süßkind 6; Viktoria C. Müller 7; Lars Wagenfeld 8; Ameli Gabel-Pfisterer 9; Sabine Aisenbrey 10; Katrin Engelmann 11; Antonis Koutsonas 12; Birgit Lorenz 13;

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16 University Eye Hospital Greifswald, University Hospital Greifswald, Germany

CONTENT:

Retinopathy of Prematurity (ROP) is a potentially blinding disease in very preterm children. The incidence of ROP requiring treatment is relatively low in Germany, a fact that makes it difficult to analyse treatment data and outcomes. In order to overcome this limitation, the German Retina.net ROP registry was founded in 2012 with the aim to jointly collect and analyse treatment patterns and outcomes from ROP patients.

In the present study, changes in treatment patterns between 2011 and 2015 were analysed. Data from all children born between 2011 and 2015 who were entered into the database at the 12 participating German centres were included in the analysis. This cohort represents about 10-15% of children treated for ROP in Germany during the observation period.

Between 2011 and 2015, a total of 150 children (292 eyes) were registered in the database. Among them, stage II, 3+ was the most prevalent indication for treatment. While gestational age and birth weight remained stable over the years, the treatment patterns changed significantly during this period: in 2011, only 10% of eyes were treated with anti-VEGF drugs (bevacizumab or ranibizumab). In 2014 and 2015, 56% and 30% respectively were treated with anti-VEGF drugs. In all years, almost all eyes with AP-ROP and Zone I disease were treated with VEGF inhibitors, while the majority of zone II disease received laser. Recurrences happened more frequently and later in the group treated with anti-VEGF drugs in comparison to laser (23% recurrence at a mean of 60 days vs. 17% recurrence at a mean of 23 days). Regarding the perioperative complications, there was no difference between the two groups.

The presented data demonstrate a shift in treatment patterns towards an increasing use of anti-VEGF drugs for ROP. There is a selection bias towards the use of anti-VEGF drugs especially in the more aggressive stages of ROP, which needs to be taken into account when interpreting the data, especially when evaluating the frequency of recurrences. The risk for late recurrences after anti-VEGF treatment is of particular clinical significance.
COI: S. Bemme: Novartis
K. Engelmann: Novartis, Bayer
A. Gabel-Pfisterer: Bayer
T.U. Krohne: Alimera Sciences, Bayer, Heidelberg Engineering, Novartis
B. Lorenz: Novartis, Bayer, Editas Medicine, Allergan Pharmaceuticals
A. Pielen: Bayer, Novartis, Sanofi-Aventis
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L. Wagenfeld: Bayer, Novartis, Alimera Sciences, Allergan
J.M. Walz: Novartis
T. Barth, M. Daniel, H. Breuß, D. Süßkind, V.C. Müller, S. Aisenbrey, A. Koutonas: none
ID: 794
TITLE: IMPROVING GUIDELINE COMPLIANCE AND DOCUMENTATION THROUGH AUDITING NEONATAL RESUSCITATION
AUTHORS: L. Root 1; H.A. van Zanten 2; M.C. den Boer 3; E.E. Foglia 4; R.S.G.M. Wilox 5; A.B. te Pas 6
AFFILIATIONS: 1,2,3,5,6 Division of Neonatology, Department of Pediatrics, Leiden University Medical Center, Leiden, The Netherlands
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CONTENT:

To improve the quality of neonatal resuscitation, several Neonatal Intensive Care Units started recording and reviewing interventions in the delivery room on a regular basis. In order to improve delivery room management in our unit, we implemented weekly audits in 2014. The aim of this study was to assess whether weekly auditing increased providers’ compliance with the resuscitation guideline and improved documentation of delivery room management.

Since 2014, neonatal care providers reviewed recordings of neonatal resuscitation during weekly plenary audits. In an observational pre-post cohort study, we studied a cohort of infants born before and after implementation of weekly audits. Video and physiological parameters recordings of infants needing resuscitation at the Neonatal Intensive Care Unit of Leiden University Medical Center were analyzed. Using a pre-set checklist, recordings were compared with the prevailing resuscitation guideline and corresponding documentation in the medical record.

In total 212 infants were included, 42 before and 170 after implementation of weekly audits, with a median (IQR) gestational age of 30 (27-35) vs. 30 (29-33) weeks and birth weight of 1368 (998-1780) vs. 1420 (1097-1871) grams. Providers complied more often to the guideline after weekly auditing was implemented (63% vs. 77%). Appropriate respiratory support, air conditions (dry vs. humidified air), fraction of inspired oxygen (FiO2), timely start of interventions and evaluation of delivered care improved. Total number of correctly documented items in medical records increased from 39% to 65%. Documentation of present providers, mode of respiratory support and details about transport to the Neonatal Intensive Care Unit were most obtained improvements.

Regular auditing using video and physiological parameter recordings of infants needing resuscitation at birth improved providers’ compliance with resuscitation guideline and documentation in medical records. When preconditions for a safe environment are met, regular auditing can be recommended.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 795

TITLE: A RANDOMIZED TRIAL ON MATERNAL PREFERENCES IN DECISION-MAKING FOR INFANTS BORN NEAR THE LIMIT OF VIABILITY

AUTHORS: André Kidszun 1; Daniel Matheisl 1,2; Susanne Tippmann 1; Julia Winter 1; Catharina Whybra-Truempler 1; Anja Fruth 3; Julia Inthorn 4,6; Seyed H. Mahmoudpour 5,7; Norbert W. Paul 6; and Eva Mildenberger 1

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CONTENT:

Best available numerical outcome estimates are traditionally considered to be of paramount importance for making shared decisions for infants born near the limit of viability. Nevertheless, it is unknown how probabilistic data affect parental choices. The primary objective of this study was to determine whether better or worse neonatal outcome estimates affect expectant mothers’ decision-making preferences. The a-priori formulated primary study outcome was the preference for life-sustaining treatments. Secondary questions explored individual characteristics and values associated with maternal preferences and the desired degree of participation in the decision-making process.

A single-center, randomized trial was performed from December 2017 to January 2019. In-patients with gestational ages (GA) between 28 0/7 to 36 6/7 weeks and impending premature birth were eligible for the study. Patients were randomly allocated to respond to either a case vignette of 60% or 30% survival rate. Case vignettes described an impending preterm birth at 23 6/7 or 22 6/7 weeks GA and were similar except from numerical data. For secondary research questions, a multivariate multinomial logistic regression was performed including six variables in addition to the case vignettes (education, religion, marital status, previous children, fertility treatment, and age). Investigators were blinded to group allocations. Significance was determined at an alpha level of 0.05.

64 participants completed the study and were included in the analysis. No difference was seen in the primary outcome as 15 of 32 participants in the 60% survival group versus 16 of 32 participants in the 30% survival group opted for life-sustaining treatments. Increasing age and having no previous child were independently associated with a preference for palliative care. Preference for palliative care was also associated with attributing greater value on quality of life than on survival. Irrespective of group allocation, the majority of participants preferred to be empowered by their physicians to be able to make the decision on their own.

For infants born near the limit of viability, numerical outcome estimates appear to have little effect on expectant mothers’ preferences for life-sustaining treatments. In contrast, individual characteristics and values appear to be of importance.
COI: None declared
ID: 796  
TITLE: DO SURFACTANTS IMPROVE NONRESPIRATORY OUTCOMES IN PRETERM BABIES? META-ANALYSIS AND REVIEW OF PHYSIOPATHOLOGICAL PLAUSIBILITY  
AUTHORS: Silvia Foligno, Daniele De Luca  
AFFILIATIONS: Division of Pediatrics and Neonatal Critical Care, Medical Center “A. Béclère”, South Paris University Hospitals, Assistance Publique–Hôpitaux de Paris (APHP) and South Paris-Saclay University, Paris – France  

CONTENT:  
While porcine seems to be superior to bovine surfactants in terms of respiratory outcomes, it is unclear if a surfactant can also improve non-respiratory outcomes in preterm neonates with respiratory distress syndrome. It is also unknown if there is any physiopathological mechanism linking surfactant therapy to these outcomes. We aim to fill these knowledge gaps.  
Systematic pragmatic review and meta-analysis following PRISMA guidelines. Animal or human translational studies about mechanisms linking surfactant replacement to non-respiratory neonatal outcomes were also systematically reviewed. We considered common non-pulmonary outcomes registered in neonatal intensive care units.  

Porcine surfactant is associated with lower incidence of PDA (OR:0.655; 95%CI:0.460-0.931);p=0.018;12 trials;1472 patients); prenatal steroids (coeff.:–0.009,95%CI:–0.03–0.009,p=0.323) and gestational age (coeff.:0.079, 95%CI:–0.18–0.34,p=0.554) did not influence the effect size. No significant differences were found between porcine and bovine surfactants on NICU stay (mean difference (days):–2.977; 95%CI:–6.659–0.705;p=0.113;8 trials; 855 patients),IVH of any grade (OR:0.860; 95%CI:0.648–1.139);p=0.293;15 trials;1703 patients),severe IVH (OR:0.852; 95%CI:0.624–1.163);p=0.412;10 trials;1097 patients) and NEC (OR:1.190; 95%CI:0.785–1.803); p=0.313;15 trials;1672 patients) and ROP (OR:0.801; 95%CI:0.480–1.337);p=0.396;10 trials;962 patients). Physiopathological mechanisms explaining the effect of surfactant have been found for PDA, while are lacking for all other endpoints (Tab.1).  
Porcine surfactant is associated with lower incidence of PDA than bovine surfactants. As there are no differences in terms of other non-respiratory outcomes and no physiopathological plausibility, these endpoints should not be used in future trials.  
REGISTRATION: PROSPERO n.CRD42018100906  

IMAGE / TAB:  
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IMAGE / TAB CAPTION: Table 1. Mechanisms linking surfactant replacement to non-respiratory neonatal outcomes, as per animal or human translational investigations. More details in the text. Abbreviations: ROS: reactive oxygen species; PVR: pulmonary vascular resistances; CBF: cerebral blood flow; PaCO2: arterial partial pressure of CO2; PDA: patent ductus arteriosus; IVH: intraventricular haemorrhage; ROP: retinopathy of prematurity; NEC: Necrotizing enterocolitis;  
COI: A/Prof. D. De Luca has received grants for research and educational projects from Chiesi Pharmaceuticals spa and ABBVIE inc. He also received travel grants from ABBVIE inc. He served as consultant and lecturer for both Chiesi Pharmaceuticals spa and ABBVIE inc. Finally, he was member of the advisory boards for both Chiesi Pharmaceuticals spa and ABBVIE inc. These companies produce two surfactants analysed in the paper, but they had no role in design and conduct of the study; collection, management, analysis and interpretation of the data; preparation, review, approval of the manuscript or decision to submit it for publication. The other author declares no competing interests.
ID: 801
TITLE: RISK FACTORS FOR NASAL-BILEVEL POSITIVE AIRWAY PRESSURE FAILURE FOR INITIAL RESPIRATORY MANAGEMENT IN PRETERM INFANTS
AUTHORS: Heekwon Son 1; Jaewook Ha 2; Mi-ji Lee 3; Eui Kyung Choi 4; Kyuhee Park 5; Jeonghee Shin 6; Byung Min Choi 7
AFFILIATIONS: 1 Paediatric Dept., Korea University Ansan Hospital, Ansan, Gyeonggi-do, Republic of Korea

CONTENT:

Non-invasive ventilation (NIV) has been increasingly used with the purpose of reducing the risk of adverse pulmonary outcome associated with invasive mechanical ventilation (IMV). Nasal bilevel positive airway pressure (n-BiPAP) has been introduced as an alternative to conventional nasal continuous positive airway pressure (nCPAP) in recent years. Superiorities of n-BiPAP in function of oxygenation and ventilation compared to nCPAP were reported in some studies, however, n-BiPAP failure had been reported in 12.9-26.6%. The aim of our study is to investigate risk factors for n-BiPAP failure for initial respiratory management in preterm infants.

A hundred and twenty two preterm infants (≥ 30 weeks of gestation and >1,250 gram of birth weight) who required respiratory support by n-BiPAP after birth were included. The success group included infants who were weaned from n-BiPAP in 7 days. The failure group included infants who required IMV despite the application of n-BiPAP.

The rate of n-BiPAP failure was resulted in 10.6% (13/122). Incidence of respiratory distress syndrome (RDS) (76.9 vs 24.8%, P < 0.001) and need for surfactant administration (69.2% vs 0%) were significantly higher in the failure group compared to the success group. Increased oxygen requirement, lower pH and higher pCO2 on blood gas analysis within 2 hours after commencing n-BiPAP were also shown in the failure group. However, significant differences were not found in gestational age and birth weight between the two groups. After adjusted for gestational age, incidence of RDS, and increased oxygen requirement during n-BiPAP support remained significantly associated with n-BiPAP failure.

N-BiPAP failure in preterm infants are expected when they have any evidence for RDS. Increased oxygen requirement during n-BiPAP support may also help to identify high-risk preterm infants for n-BiPAP failure. Strategies to avoid n-BiPAP failure should be investigated, and further multi-centered well-designed randomized studies are needed to access efficacy and safety of n-BiPAP for initial respiratory management in preterm infants.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 802

TITLE: COMPARATIVE EVALUATION OF APPROACH TO CARDIOVASCULAR CARE IN ASPHYXIATED INFANTS WITH HEMODYNAMIC INSTABILITY BETWEEN A LARGE CANADIAN VS HUNGARIAN REFERRAL CENTER

AUTHORS: Kata Kovacs 1, Regan Giesinger 2, Andrea Lakatos 3, Miklos Szabo 1, Agnes Jermendy 1, Patrick J McNamara 2,4

AFFILIATIONS:
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4 Hospital for Sick Children, Toronto, Canada

CONTENT:

Patients with hypoxic-ischemic encephalopathy (HIE) may present with hemodynamic instability. Therapeutic hypothermia (TH) improves neurodevelopmental outcome in asphyxiated newborns, but may worsen hemodynamic instability. Our primary aim was to compare the approach to management of hemodynamic instability and short term outcomes in asphyxiated infants at two high volume centers.

In this retrospective cohort study, we studied 176 term infants with HIE, who were admitted to the NICU of the Hospital for Sick Children, Toronto, Canada (Center A, n=86) or the 1st Department of Pediatrics, Semmelweis University, Budapest, Hungary (Center B, n=90) for TH between 2015 and 2017, and developed systemic hypotension (mean arterial pressure less than gestational age). Baseline neonatal demographics, indices of hemodynamic stability and details of hemodynamic interventions were compared. Short term outcome was evaluated based on MRI examinations. Adverse outcome was defined as perinatal death or brain injury in the basal ganglia and/or in the watershed area.

Baseline illness severity and HIE staging were comparable between groups. The average lowest systolic and diastolic blood pressure were similar (table). Interestingly 49% of the patients in Center A did not receive any cardiovascular support during TH, whereas only 3% remained untreated in Center B (p<0.001). The first line cardiovascular therapy was dobutamine (66%) in Center A vs dopamine in Center B (94%). The rate of hypertension after the initiation of cardiovascular support was 47% in Center A, while 69% in Center B (p=0.003). Other clinical outcomes (diuresis, convulsions, length of antibiotic treatment and invasive ventilation) were comparable. Adverse outcome was similar in the two centers (48% in Center A and 53% in Center B; p=0.45); however, the pattern of brain injury differed between centers and there was a trend towards increased injury in center A (table).

A more aggressive approach to cardiovascular care did not lead to better MRI outcomes, but was associated with increased rate of hypertension. Use of early comprehensive echocardiography may provide enhanced diagnostic precision enabling investigation of the relationship of heart function and systemic hemodynamics to brain injury.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileId=c747ab080ab45cd33fcc3b552eba6e5-MjAxOS0wNSM1Y2UyNjY2Y2VhZjNj

IMAGE / TAB CAPTION: Lowest blood pressure values and MRI outcome of the study population

COI: None declared.
ID: 813

TITLE: IMPACT OF MATERNAL ETHNICITY ON PERINATAL OUTCOMES OF SMALL FOR GESTATIONAL AGE INFANTS

AUTHORS: Nicole E Young1, Nalin Choudhary1, Kathryn Shearer1, Natasha Juchkov1, Stacey Ellery2, Miranda Davies-Tuck2, Atul Malhotra2,3,4

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CONTENT:

Maternal ethnicity has been linked to perinatal outcomes of premature infants. However, the relationship between maternal ethnicity and perinatal outcomes of small for gestational age (SGA) infants remains unclear. The objective of this study was to examine the perinatal and neonatal outcomes of SGA infants born to South Asian (SA)-born mothers, when compared to Australian or New Zealand (ANZ)-born mothers. A secondary aim was to compare the placental histological findings of SGA infants with those of ANZ infants.

Retrospective cohort study conducted at Monash Health, a large metropolitan hospital network in Melbourne, Australia. Maternal and neonatal data was collected for infants of all gestations, born SGA between 2013-2017 to SA or ANZ-born mothers. Rates of perinatal mortality and morbidities were measured including resuscitation and respiratory outcomes, conditions related to prematurity, and outcomes of term infants. Univariate and multivariate analysis was conducted to compare neonatal outcomes between groups. Secondary analysis of placenta macroscopic and histological findings between a subset of infants from the two groups was also done.

1018 SA and 959 ANZ SGA infants were included. SA babies were significantly older (median (IQR) 39(38-40) weeks) and heavier (2590(2310-2780) grams) compared to ANZ babies (38 (37-40) weeks) and 2480 (2059-2740) grams; p<0.001. There was no difference in perinatal mortality (0.5% vs. 0.9%; p=0.2). After correction for differences in demographics, SA SGA babies were 1.5 times more likely to develop neonatal hypothermia (CI 1.1 to1.8, p=0.001); but 2.5 times less likely to be born with a major congenital malformation (CI 0.2 to 0.6, p=0.001) and 1.5 times less likely to need gavage feeding (CI 0.4 to 0.9, p=0.02) as compared to ANZ SGA babies. There were also trends towards less need for resuscitation, and need for respiratory support in SA SGA babies. However, there were no significant differences seen on placental pathology in a subset of 171 SA infants and 140 ANZ infants.

Babies born SGA to south Asian mothers have a different perinatal and neonatal outcome profile as compared to SGA babies born to Australasian mothers. Reduced growth seems to be associated with a similar placental pathology, in these ethnically diverse populations. Further research into the influence of ethnicity on organogenesis and fat stores of SGA babies may be warranted.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 814  
TITLE: Physical stimulation of newborn infants in the delivery room: a retrospective analysis  
AUTHORS: Vincent D. Gaertner 1,2; Sophie A. Flemmer 1,2; Laila Lorenz 1; Peter G. Davis 1,3; C. Omar F. Kamlin 1,3  
AFFILIATIONS: 1 Neonatal Services, The Royal Women’s Hospital, Melbourne, Australia  
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CONTENT:  
Neonatal resuscitation guidelines recommend that newborn infants should be dried, warmed and stimulated within the first minute after birth to assist with the establishment of regular respirations. However, the mode, site of application and frequency of stimulations are not stipulated in these guidelines. Although stimulation is the most common intervention during neonatal stabilisation in the delivery room, its characteristics and effectiveness are insufficiently described. Thus, the aim of our study was to describe timing, frequency, different methods and effects of tactile stimulation of newborn infants.  

We conducted a retrospective observational study using video recordings of neonatal resuscitations performed at The Royal Women’s Hospital, Melbourne. The video captured the resuscitaire from above allowing to see the treating clinicians’ stimulations as well as the infants’ reactions. Four different types of stimulation (drying, chest rub, back rub and foot flick) were defined a priori and the frequency and infant response were documented. Data were summarised as medians (IQR) or as numbers (%). The difference in medians was assessed using a Wilcoxon test. Infants were grouped by gestational age (GA): infants <30 weeks’ gestation and infants ≥30 weeks’ gestation.  

A total of 120 video recordings were reviewed. 75 infants (63%) received at least one episode of stimulation and 70 (58%) infants were stimulated within the first minute after birth. The median (IQR) time to first stimulation was 19 (15–24) seconds. Stimulation was less commonly provided to infants <30 weeks’ gestation (median (IQR) number of stimulations: 0 (0–1)) than infants born ≥30 weeks’ gestation (1 (1–3); p<0.001). The most common response to stimulation was limb movement (71% of stimulations) followed by infant cry and facial grimace (37% and 36% of all stimulations, respectively). Truncal stimulation (drying, chest rub, back rub) was associated with more crying and movement than foot flicks.  

Less mature infants are stimulated less frequently than more mature infants and many very preterm infants do not receive any stimulation. If stimulation occurs, it is mostly performed within the first minute after birth. Truncal stimulation appears to be more effective than foot flicks and may be beneficial during neonatal transition. Further prospectively conducted studies investigating specific modes of stimulation are required.  

IMAGE / TAB:  
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IMAGE / TAB CAPTION: Number and timing of stimulations divided by gestational age. Part (A) shows infants <30 weeks’ gestation and part (B) shows infants ≥30 weeks’ gestation.  

COI: None declared
ID: 815

TITLE: Respiratory changes in term infants immediately after birth.

AUTHORS: Douglas A. Blank* 1,2; Vincent D. Gaertner* 1,3; Omar Kamlin 1,4; Kevyn Nyland 1; Neal Eckard 1; Jennifer Dawson 1,4; Stefan Kane 5; Graeme Polglase 2; Stuart Hooper 2; Peter Davis 1,4

AFFILIATIONS: * joint first author
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CONTENT:

Over 5% of infants worldwide receive breathing support immediately after birth. Studies have shown that exhaled carbon dioxide (ECO2) levels correlate with lung aeration and that increasing ECO2 precedes increases in heart rate and oxygen saturation in effectively resuscitated infants. The presence of ECO2 indicates airway patency, establishment of lung aeration, pulmonary blood flow, and pulmonary gas exchange. Monitoring ECO2 and exhaled tidal volume (VTe) may guide ventilation of the compromised newborn in the delivery room. Thus, our goal was to define reference ranges for ECO2, VTe, and respiratory rate (RR) immediately after birth in spontaneously breathing infants.

This was a single-centre, observational study at the Royal Women's Hospital in Melbourne, Australia. Healthy infants ≥36 weeks gestational age were eligible for participation. A combined CO2/flow sensor was used to record ECO2, VTe, and RR. An attached face mask was placed over mouth and nose of the infant as soon as the head was delivered and data was saved using a respiratory function monitor. Respiratory measurements were recorded continuously for the first 60 s after birth, then every 30-60 s from 1 to 10 min after birth. The measurements were repeated at one hour. In case of caesarean sections data was collected using a sterile technique. Distribution of the data was assessed and appropriate parametric and non-parametric statistic tests used for analysis.

We analysed 14,731 breaths in 101 spontaneously breathing infants ≥36 weeks gestational age (51 born via planned caesarean section and 50 born vaginally). It took a median (IQR) of 7 (4-10) breaths until ECO2 was detected. ECO2 quickly increased to a median (IQR) peak value of 48 mmHg (43-53) at 143 s (76-258) after birth, and decreased steadily to post-transitional values of 27 mmHg (24-30) by 7 min. There were no significant differences in ECO2 based on mode of delivery. VTe increased after birth, reaching a plateau of 5.3 ml/kg (2.5-8.4) by 130 s for the remainder of the study period. Individual maximum VTe was 19 ml/kg (16-22). RR values increased slightly over time and remained stable from minute 4 onwards. Median (IQR) RR values at 1 hour were 57 breaths per minute (48–66).

We demonstrated that ECO2 increases quickly in spontaneously breathing infants to peak values at 2–3 min after birth followed by a slow but steady descent to post-transitional levels. VTe and RR increased after birth, then plateaued in the first minutes after birth. This study may ultimately contribute to improved interventions in the delivery room by providing reference ranges of normal postnatal development of various respiratory parameters.
Exhaled carbon dioxide in millimetres of mercury (mmHg) over time (n=101). Median values and the 10th, 25th, 75th and 90th percentile are shown.

COI: None declared
ID: 818
TITLE: THE MANAGEMENT OF RESPIRATORY DISTRESS SYNDROME IN PRETERM INFANTS: THE CHANGING EXPERIENCE IN WALES
AUTHORS: Christopher William Course1, Mallinath Chakraborty1,2
AFFILIATIONS: 1: Welsh Regional Neonatal Intensive Care Unit, University Hospital of Wales, Cardiff, United Kingdom
2: Cardiff University, Cardiff, UK

CONTENT:
Respiratory Distress Syndrome (RDS) is the commonest diagnosis after premature birth, a result of structural and functional immaturity of the lungs. These preterm infants often require invasive and non-invasive respiratory support, supplementary oxygen and surfactant therapy. A proportion of these infants will go on to develop chronic lung disease of prematurity, with abnormal respiratory function and increased respiratory morbidity persisting through childhood and into adult life. There exists a wealth of high-quality evidence on optimal management of RDS. We aimed to describe trends in management before and after introduction of a national guideline in Wales on RDS management.

Anonymised, prospective data from all participating neonatal units (level two and level three) in Wales were collected in two six-month time periods in 2015 and 2018 for all inborn infants <34 weeks’ gestation using a standardised proforma. A national guideline for management of RDS in preterm infants was introduced in 2016 by the Wales Neonatal Network. Data collection included areas of antenatal management, delivery room stabilisation, invasive and non-invasive respiratory support, surfactant treatment and elements of supportive care. Univariate and multivariate methods were used to compare data between the two epochs. Odds ratios and 95% confidence intervals (CI) were adjusted for gestational age at delivery and level of unit of delivery. Statistical significance was set at p < 0.05.

Data on 225 infants from 2015 and 276 infants in 2018 was analysed. Mean gestational age and birthweight were comparable between the epochs (p > 0.05). Comparing care before and after introduction of the guideline, there was overall improvement in use of targeted tidal volume ventilation (aOR 7.94 [3.75,16.8]), caffeine therapy (aOR 2.49 [1.4,4.6]), oxygen therapy post-surfactant (aOR 2.16 [1.23,3.82]) and early use of parenteral nutrition (aOR 2.75 [1.66,4.58]). Areas of poorer management included use of high positive end expiratory pressures (aOR 0.58 [0.35,0.96]) and stabilisation in FiO2 <30% (aOR 0.29 [0.17,0.47]). Little variation was seen between level two and three units, although more mature infants had significantly higher rates of delayed cord clamping (DCC) (aOR 1.44 [1.23,1.68]), stabilisation on CPAP (aOR 1.85 [1.65,2.07]), and early enteral feeding (aOR 1.22 [1.12,1.32]).

We present novel data from Wales collected around the implementation of a new national RDS guideline. Significant improvements in management of RDS in preterm infants were seen, particularly regarding mechanical ventilation. Yet some practices such as DCC, struggle to be embraced. Despite large volumes of high-quality evidence, some elements of best practice are yet to be adopted consistently. Further work should focus on education and training.

IMAGE / TAB:
b1ea5ad82e2cf-MjAxOS0wNSM1Y2UyNjY2Y2YxMzYz

IMAGE / TAB CAPTION: Summary of main results with adjusted odds ratio comparing the 2018 cohort with the 2015 cohort. (* = statistically significant results)

COI: None declared.
ID: 820
TITLE: A COHORT COMPARISON OF LESS INVASIVE SURFACTANT ADMINISTRATION IN A RESOURCE RESTRICTED INSTITUTION
AUTHORS: Lizelle Van Wyk 1; Johan Smith 2; Pierre Goussard ; Netta (IJ) van Zyl 4
AFFILIATIONS: 1,2,4: Division Neonatology, Dept. Paediatrics & Child Health, University of Stellenbosch, South Africa
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CONTENT:
Surfactant replacement therapy is the standard of care for neonatal respiratory distress syndrome. Survival has been shown to improve with CPAP and InSuRE in ELBW infants at Tygerberg Hospital, South Africa; a resource-restricted tertiary level public hospital with limited ventilation facilities. At Tygerberg Hospital, the ELBW birth and mortality rate are 60.2 and 83.3 per 1000 live births, respectively. All ELBW infants are supported with CPAP and less invasive SRT, if required. Recently, InSuRE has been replaced by LISA and surfactant supply by the Department of Health, South Africa, has changed from Curosurf to Survanta. The effect of these changes on neonatal outcomes are unknown.

Methods: A retrospective, medical record, comparative analysis was performed. A historical cohort of InSuRe administration, utilizing Curosurf (June 2007 - May 2009), was compared to a contemporary cohort of LISA administration, utilizing Survanta (June 2015 - May 2016), in ELBW infants with RDS at Tygerberg Children’s Hospital. Respiratory data were collected and infants underwent neurodevelopmental assessment at 1 year of age. Short-term (CPAP failure and/ or death prior to 72 hours of life) and long-term (death and/ or abnormal neurodevelopmental outcome at 1 year of age) composite outcomes were compared between the cohorts.

31.7% (97/306) and 43.8% (111/253) of ELBW infants received surfactant replacement in the historic and cohort groups, respectively, with an overall survival of 62.5% to discharge. The contemporary cohort received less doses of surfactant (1 vs 1.34, p=0.0004) but at an earlier age (3.2 vs 5.6 hrs, p=0.0001). There were no differences in CPAP failure, death prior to 72 hours of life, all-cause mortality or neurodevelopmental outcomes between the groups. Neither short-term nor long-term composite outcomes were affected by the method/surfactant combination. Both cohorts had very low BPD rates (<2%). The NNT to prevent CPAP failure or early death was 30 with a 3.39% risk reduction. NNT to prevent all-cause mortality/ abnormal neurodevelopmental outcome was 18.1 with a risk reduction of 5.53.

SRT increased between the two cohort eras with smaller and younger ELBW infants receiving minimally-invasive SRT with persisting low incidence of complications. Neither short-term nor long-term complications were accounted for by the combined method/ type of surfactant of SRT. Less invasive SRT methods, InSuRE and LISA, combined with CPAP, in ELBW infants is an effective management strategy in a resource-restricted environment.
ID: 821

TITLE: NUTRITIONAL STATUS OF BABIES WHO DEVELOP BRONCHOPULMONARY DYSPLASIA: HOW CAN WE DO BETTER

AUTHORS: Irnthu Premadeva 1; Marika Lasokova 2; Amy Carmichael 3; Sateeshkumar Somisetty 3; Claudia Chetcuti-Ganado

AFFILIATIONS: Luton and Dunstable University Hospital

CONTENT:

Lung injury during fetal development has poor potential for recovery, making very preterm infants vulnerable to bronchopulmonary dysplasia (BPD). Undernutrition in their first few weeks of life impairs the canalicular-saccular stage of lung development and alters developmental programming through epigenetic modifications. The accumulation of calorie deficit is most prominent in the very low (VLBW) and extremely low birth weight (ELBW) babies and further perpetuates lung injury. The ESPGHAN recommendations provide guidance as to the target ranges of nutritional intake for optimal growth in preterm babies. There is no evidence for whether reaching these targets prevents BPD development.

Retrospective data was collected on babies born at a tertiary centre between 2014 and 2016 with a birthweight of less than 1.5Kg. Babies were excluded if they were transferred out or died before day 28 of life. The babies with a discharge diagnosis of BPD, defined as oxygen requirement or respiratory support at 36 weeks corrected gestation, were compared to those who did not. The ESPGHAN recommendations were used as the target range. We developed a nutritional calculator and the daily intake of fat, protein, carbohydrate and non-nitrogenous calories were obtained. The weight gain at day 28 was also compared between the two groups. Each baby’s background risk factors for developing BPD was collected as a surrogate marker of additional stresses that may increase calorie requirements.

A total of 28 babies were included in the analysis with n=14 in each group. The mean gestation and birth weight in the BPD and control groups were 27+4 and 1017g and 28+6 and 1018g respectively. Babies in both groups received similar protein and carbohydrate calories in the first 28 days. The protein intake for both groups was below the recommended range throughout the study period. A consistent lower intake of fat was noted in the BPD group which contributed to the overall lower non-nitrogenous calorie intake in this group. Higher rates of sepsis, blood transfusions, PDA requiring treatment, chorioamnionitis and longer days on mechanical ventilation were observed in the BPD group. Both groups had the same mean weight gain on day 28 of life. The control group received a higher volume of feed over the 28 days, maximally reaching 170.7ml/kg/day, versus 153.3ml/kg/day in the BPD group.

Optimisation of early postnatal nutrition as a strategy for reducing BPD rates in VLBW and ELBW babies, should take into consideration factors which increase metabolic demand. A lower fat intake creates a cumulative calorie deficit which is likely to contribute to lung injury. Weight gain is not a reliable marker of adequate nutritional intake. We recommend routine monitoring of fat, protein and carbohydrate intake as part of intensive care.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=6e27eb5a9fd3fa3379a282f14ac8773-MjAxOS0wNSM1Y2UyNjY2Y2yYmQ1

IMAGE / TAB CAPTION:

COI: None Declared
ID: 825

TITLE: USING RESISTIVITY INDEX TO PREDICT RESPONSE TO MEDICAL MANAGEMENT OF PATENT DUCTUS ARTERIOSUS IN EXTREMELY PREMATURE NEONATES

AUTHORS: Adam King, Lambri Yianni, Rahul Kachroo

AFFILIATIONS: Department of Neonatology, Queen Alexandra Hospital, Portsmouth Hospitals NHS Trust, UK

CONTENT:

Patent Ductus Arteriosus (PDA) is a common problem affecting preterm infants, with incidence increasing with the degree of prematurity. Both PDA size and flow velocities measured by echocardiography can be used to assess the haemodynamic significance and response to treatment. Flow velocity is known to be more consistently and reproducibly measurable than size. It is suggested that assessing PDA by using flow velocities, rather than size, PDAs can be more accurately and consistently assessed in a repeatable manner. This study looks at whether Resistivity Index (RI) can be used to predict the response to medical treatment in extremely preterm infants born at less than 28 weeks gestation.

All infants born at less than 28 weeks gestation in the calendar year 2015 were identified from the BadgerNet neonatal database at a large medical NICU in the UK. Paper notes and electronic records were reviewed to identify whether a PDA was diagnosed and what management was carried out. The size and flow measurements of the first echocardiogram confirming the diagnosis were taken from the patient notes; or were measured from the echocardiogram images saved on the local scanner. The RI for each case was then calculated using the formula RI = (systolic velocity – diastolic velocity)/systolic velocity. Comparison was made using a T test between the RI for those who did respond to medical treatment, and those who did not.

The database search identified 58 babies born <28 weeks’ gestation and 24 were diagnosed with a PDA. Each of the 24 patients had at least one course of medical treatment, of which 11 (46%) were successful, and the remaining 13 (54%) failed. The median gestation was 25+1 weeks (range 23+0-27+5), with a median birth weight of 663g (range 409-995g). A Kolmogorov-Smirnov test confirmed normal distribution of RI values. Median RI of infants who responded to medical treatment was 0.51 (range 0.44-0.71), which is significantly lower than median RI 0.62 (range 0.35-0.82) in those in whom medical treatment fails, p=0.045. On subgroup analysis, the RI was found to be statistically significantly lower in infants with birth weight ≤650g who respond to medical treatment: median RI 0.47 (range 0.44-0.51) compared to those who failed medical management: median RI 0.71 (range 0.57-0.82); p=0.007.

Whilst this is a small sample size, it does suggest the feasibility of using Resistivity Index as a parameter for assessment of PDA and its response to medical treatment in extremely premature neonates, with lower RI being positively associated with a response to medical management. This effect is even more pronounced at small birth weights.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None Declared
ID: 827

TITLE: PRE- AND POSTNATAL RISK FACTORS FOR PULMONARY INTERSTITIAL EMPHYSEMA IN PRETERM INFANTS ≤32 WEEKS OF GESTATION

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CONTENT:

Pulmonary interstitial emphysema (PIE) is one of the most severe respiratory complications in preterm infants belonging to the group of air leak syndromes. Typically mechanically ventilated extremely low birth weight infants (ELBWIs) with respiratory distress syndrome (RDS) are affected. We aimed to determine the association of further important pre- and postnatal risk factors (e.g. diabetes during pregnancy, preeclampsia/HELLP, intrauterine growth restriction (IUGR), antenatal steroids (ANCS), gender) which are well accepted to increase the risk of the preterm infant for BPD and long-term pulmonary sequelae with the occurrence of PIE as well as their contribution to severe complications.

n=226 preterm infants ≤32 gestational age (GA) discharged between 2016-2017 from the neonatology of the Justus Liebig University of Giessen with chest x-ray examination within the first 5 days of life were retrospectively classified as non-PIE (n=142) or PIE (n=37) with the subgroup of severe PIE cases (n=12). Additionally, PIE cases were matched with 37 non-PIE cases by GA, birth weight (BW) and gender. Pre- and postnatal risk factors were identified by univariate analysis (SPSS Statistics 25). Data presented as median (interquartile range) and differences assessed for statistical significance using the Mann-Whitney U rank sum test or χ² test as appropriate.

Previously known risk factors including GA and BW and the association of PIE with adverse outcome parameters of intraventricular hemorrhage (IVH) and mortality were confirmed, but PIE did not impact the frequency of BPD (PIE 54.1% vs. 59.4% non-PIE). Pre-eclampsia/HELLP (PIE 24.3% vs. non-PIE 8.1%) was identified as additional risk factor (p≤0.05). In PIE cases, severe impairment in lung gas exchange correlated with the presence of RDS (PIE 51.3% vs. non-PIE 24.0%), the need for invasive mechanical ventilation (MV) (PIE 54.1% vs. non-PIE 29.7%) and the higher maximum inspired fraction of oxygen (FiO2) (PIE 0.50 (0.40-0.72) vs. non-PIE 0.37 (0.25-0.53)), but PIE was not fostered by differences in ventilator settings (PIP, PEEP). Any diabetes during pregnancy, chorioamnionitis, antenatal corticosteroid use (ANCS) and male gender had no significant effect on the incidence of PIE.

Pulmonary interstitial emphysema (PIE) is a severe complication in infants born ≤32 GA that poses a high risk for adverse outcome in preterm infants. We identified pre-eclampsia/HELLP as important additional risk factor for PIE that should be included in future risk calculations to identify infants at high risk for PIE directly after birth.

COI: None declared.
ID: 835

**TITLE:** Alterations in Umbilical Cord Blood messenger RNA Expression in Neonatal Hypoxic-Ischaemic Encephalopathy and Long-Term Outcome

**AUTHORS:** Marc Paul O'Sullivan1,2,3; Sophie Casey 1,2; Mikael Finder 4; Deirdre Twomey 1; Caroline Ahearne 1; Gerard Clarke 1,5,6; Boubou Hallberg 4; Geraldine B.Boylan 1,2; Deirdre M. Murray 1,2,3

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**CONTENT:**

Hypoxic-ischaemic encephalopathy (HIE) remains an important cause of neonatal death and long-term neurological disability. It remains challenging to classify infants eligible for therapeutic hypothermia (TH) within the short postnatal therapeutic time window of 6 hours. No objective and robust biological marker is available in the clinical setting. The purpose of this study was to explore the predicted downstream messenger RNA (mRNA) targets of validated microRNA in the whole blood across our two independent BiHiVE cohorts and to assess their ability to predict grade of HIE and neurodevelopmental outcome.

This study included two cohorts. The discovery cohort recruited full-term infants with PA at birth to the BiHiVE1 study in Cork, Ireland (2009-2011). Encephalopathy grade was defined using early EEG and Sarnat score. The BiHiVE2 multi-centre validation study (2013-2015) recruited full-term infants in Cork and Karolinska Huddinge, Sweden, the study recruited infants with PA along with healthy control infants using identical recruitment criteria to BiHiVE1. Umbilical cord blood was processed and biobanked in Tempus tubes at delivery. Infants were assigned a modified Sarnat score at 24 hours. Candidate mFZD4 and mNFAT5 were measured using quantitative real-time polymerase chain reaction. The outcome was assessed at 2-3 years using the Bayley Scales of Infant Development III.

126 infants were included in the analysis. BiHiVE1 included 55 infants(controls n = 16, PA n = 19, HIE n = 20) and BiHiVE2 included 71 infants(controls n = 22, PA n = 25, HIE n = 24). Both cohorts had a mean age = 40 wks[IQR = 39-41 wks] and included 82 males/44 females. In HIE severity, mFZD4 levels were increased in severe HIE(RQ = 2.98 (IQR = 2.23-3.68)) vs both moderate HIE (1.05 (0.81-1.20)), P = 0.003, and mild HIE(0.88 (0.46-1.37)), P = 0.004. Neurodevelopmental outcome was available in 56 infants. mNFAT5 levels were increased in severely abnormal(1.26 (1.17-1.39)) vs normal outcome(0.97 (0.83-1.24)), P = 0.036, and in severely abnormal(1.26 (1.17-1.39)) vs mildly abnormal outcome(0.96 (0.80-1.06)), P = 0.013. mFZD4 levels were increased in severely abnormal(2.51 (1.60-3.56)) vs mildly abnormal outcome(0.97 (0.75-1.34)), P = 0.026 and normal outcome(0.74 (0.48-1.49)), P = 0.004.

Altered mFZD4 expression was observed in umbilical cord whole blood of neonates with severe HIE; both mNFAT5 and mFZD4 expression were increased in infants with a severely abnormal outcome at 2-3 years. These mRNA could aid current measures as early objective prognostic markers of HIE severity at delivery.

**IMAGE / TAB:

IMAGE / TAB CAPTION:
COI: None declared
**ID:** 841  
**TITLE:** DO PROPHYLACTIC PLATELET TRANSFUSIONS REDUCE BLEEDING RISK IN PRETERM NEONATES WITH SEVERE THROMBOCYTOPENIA? A TIME-DEPENDENT PROPENSITY SCORE MATCHED COHORT ANALYSIS.  
**AUTHORS:** Susanna F Fustolo-Gunnink 1-2, Karin Fijnvandraat 2-3, Hein Putter 4, Isabelle M Ree 5, Camila Caram-Deelder 1, Peter Andriessen 6, Esther J d’Haens 7, Christian V Hulzebos 8, Wes Onland 9, André A Kroon 10, Daniel C. Vijlbrief 11, Enrico Lopriore 5, Joha  
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**CONTENT:**  
In a recent randomized trial in preterm neonates, platelet transfusions given at a platelet count threshold of 50x10^9/L were associated with increased risk of major bleeding and/or mortality when compared to a threshold of 25x10^9/L. Adult studies have suggested that lower thresholds or even no prophylaxis policies are safe in some patient groups. We aimed to assess in preterm neonates with severe thrombocytopenia whether prophylactic platelet transfusions reduce risk of bleeding and/or mortality when compared to therapeutic transfusions.  

We included neonates with a gestational age <34 weeks and a platelet count <50x10^9/L in seven Dutch neonatal intensive care units. We developed a dynamic propensity score to estimate the probability for a neonate to receive a platelet transfusion at two hour time-intervals. Neonates who received a transfusion were matched to neonates who did not, but had a similar probability of receiving a transfusion. We assessed a composite of major bleeding and/or mortality within three and ten days from each transfusion, using conditional weighted logistic regression.  

We included 640 neonates. The odds ratios for major bleeding and/or mortality within three and ten days for the transfusion versus the no-transfusion groups were 1.27 (95% confidence interval (CI) 0.77 – 2.08) and 1.16 (95% CI 0.74 – 1.80), respectively.  

In preterm neonates with severe thrombocytopenia, prophylactic platelet transfusion events were not associated with reduced risk of bleeding and/or mortality when compared to similar clinical situations where platelet transfusions were withheld. These findings suggest that the clinical benefit of prophylactic transfusion in neonates may be limited.
Outcomes for platelet transfusion events versus no platelet transfusion events within the time-dependent propensity score matched cohort.

COI: None declared
ID: 844

**TITLE:** DELIVERY ROOM CUDDLES FOR EXTREMELY PRETERM BABIES: A QUESTIONNAIRE SURVEY OF MOTHERS’ VIEWS, EXPERIENCES, AND MEMORIES

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**CONTENT:**

Parents of extremely preterm babies are rarely allowed a delivery-room cuddle (DRC). Urgent NICU admission is usually considered the immediate priority after stabilisation of such newborns. Many weeks can pass before parents first get to hold their babies. This period is inevitably very traumatic for mothers and may affect bonding/milk expression. Our unit strives to facilitate the DRC between mothers and their preterm infants after the initial stabilisation but before NICU admission. Yet there is scant data on parents’ experiences of the DRC practice. We aimed to survey views of mothers of extremely preterm babies born at <27 weeks’ gestation who had experienced a DRC in our centre.

We reviewed electronic medical records of all extremely preterm babies born at <27 weeks’ gestation who were admitted to our NICU in the 13-year period 2006–2018. We identified all inborn babies who had received a documented maternal DRC at birth recorded in their admission notes. We identified still-living children, and invited all non-bereaved mothers (n=24) who had received a facilitated DRC to participate in a structured web-based questionnaire survey asking about their reflections on, and memories, experience, and valuation of their DRC. This study was a service evaluation of a routinely-offered practice and did not require any formal ethics approval.

12 (50%) of 24 invited mothers completed the survey. Of respondents, most (80%) vividly remembered their DRC and rated it very important to them as a new mother. Feelings commonly recalled about the first DRC included initial relief/reassurance (50%), intense pride and love (50%), and being initially scared at the prospect of holding their tiny baby (33%). 75% of mothers reported being able to get a photograph/video recording of their first cuddle. The vast majority (92%) considered it very important that neonatal doctors/nurses should try to offer mothers of newborn very preterm babies a DRC before their baby is removed to NICU.

Free-text comments included:
“...it meant the world to me to have those few seconds bonding with my beautiful boy”
“It was incredibly important as I did not get to hold my son again for 2 weeks as he was too sick. That cuddle helped to initiate my breast milk...”.

Cuddling the human newborn is instinctive and invaluable for all parents, and parents of extremely preterm infants are no exception. Most mothers given the chance to briefly cuddle their baby in the delivery room before the NICU admission greatly valued the experience. The DRC may enhance bonding and breast milk expression and should be facilitated for all mothers and fathers with their babies, wherever possible, irrespective of birth gestation.
ID: 846

**TITLE:** NEONATAL NOISE EXPOSURE AND NOISE REDUCTION DURING NEONATAL TRANSPORT: NOISE PROTECTION DURING NEONATAL HELICOPTER TRANSFERS

**AUTHORS:** Nurul Aminudin 1; Jan Franta 2; Ann Bowden 3; David Corcoran 4; Afif El-Khuffash 5; Naomi McCallion 6

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**CONTENT:**

Air transport provides for distant and time-critically ill and premature neonates. Air transfers can expose neonates to noise levels that may compromise health such as noise-induced hearing loss, autonomic disturbances, behavioural and cognitive instability. The current recommended safe environmental sound pressure levels (SPL) should not exceed 45dB (decibel) in neonatal intensive care units (NICU) or 60dB during transport. We measured noise during helicopter transfers and quantified the efficacy of noise protective equipment in a mannequin study. We also investigated the effects of noise protection equipment on oxygen saturation and heart rate of neonatal patients on helicopter transfers.

In the mannequin study, a 4-channel sound level meter (Svan958-A®) connected to 3 microphones measured SPL in decibel-A (dBA) from the external ear, inside the incubator and outside (helicopter cabin) during practice air transfers. This was repeated with the use of noise protective ear muffs (NPEM) and active noise canceling headphones (ANC). Similar methods were used for patient studies, using NPEM and ANC with additional pulse oximetry recording. All patients had noise protection during the single journey air transfers. The demographic data were collected on all subjects. SPL was continuously recorded from 3 positions along with the simultaneous recording of heart rate and oxygen saturation. All data were analysed using specialist software and SPSS v.25® was used for statistical analysis.

Noise (dBA) was represented as peak SPL (Lpeak) and total sound energy (Leq). The mannequin study: Mean Lpeak during transfers was 87±5 (ear), 98±15 (incubator) and 98±9 (outside) and mean Leq was 74±5 (ear), 86±14 (incubator) and 86±10 (outside). 100±14% of cabin noise was detected at the mannequin ear, 85±10% was detected with NPEM and only 68±13% was detected with ANC. Paired sample t-test compared SPL of cabin with noise protection with p values <0.001 for Lpeak and Leq. The patient study: Noise protection was applied during the whole flight. 4 patients were recruited (2 NPEM and 2 ANC). NPEM group experienced harmful Lpeak of >85dBA 82% of the time vs 36% in ANC group. O2 saturation were lower at SPL >85dBA in NPEM group (92 vs 85, p<0.001) but higher in the ANC group (85 vs 94, p<0.001). Heart rate was lower if SPL >85dBA in both; NPEM (166 vs 137, p<0.001) and ANC (127 vs 106, p<0.001).

Noise represented in Sound Pressure Level (SPL) measured at the patient ear during helicopter transfers exceeds safe levels and reached dangerous and hazardous levels >50% of the time. These cause changes to heart rate and oxygen saturation. The application of noise protection helps reduce noise exposure with ANC being an effective modality in reducing neonatal noise exposure during helicopter transfers. Further studies are currently in progress.

**IMAGE / TAB:**
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=8a671f490d186bbf5fe7c4dc1376036c-MjAxOS0wNSM1Y2UyNjY2ZDBhN2RI

**IMAGE / TAB CAPTION:** The application of Noise Protective Ear Muffs (NPEM) for a neonatal helicopter transfer.

**COI:** None declared
ID: 848

TITLE: SURGICAL INTERVENTION IN NEONATES WITH NECROTISING ENTEROCOLITIS: A RISK STRATIFICATION SCORE

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CONTENT:

Necrotising enterocolitis (NEC) is the commonest surgical condition affecting premature infants. It still carries a significant morbidity and mortality despite advances in neonatal intensive care. Early risk stratification of infants who will require surgery for NEC is important as this enables more informed parent counselling, a higher index of clinical suspicion of the need for surgical intervention and/or prompt transfer to a surgical centre. Stratification would also reduce unnecessary neonatal transfers and improve neonatal cot utilisation in surgical centres.

Part 1 of the retrospective study was undertaken of a prospectively-collected electronic neonatal database (Badgernet) including all neonates with NEC modified Bell Stage 2 between 2009 – 2015 in one centre. Data on patient demographics, clinical parameters, specific laboratory findings through the episode of illness (serum white cell count, platelet count, C-RP and albumin), abdominal radiographs, surgical status and death were recorded. Multivariate analysis was performed to identify significant factors and a scoring system was developed.

Part 2 of the study collected the same data between 2016 - 2018. Data from the second part was used to validate the scoring system developed in part 1.

Part 1 of the study included 133 infants. Analysis of the data identified factors significantly associated with surgery. Factors included in the final model were: male gender, extremely low birth weight (<1000g), serum albumin < 20g/L on day 2, platelet count < 100 x 109/L on day 2, white cell count < 5 x 109/L on day 2 and C-RP > 20mg/L on day 2. A final risk scoring system was developed with maximum total score of 10. A score of 6 or more indicates the probability of need for surgery is > 70% and has a predictive value with AUC=71.8%.

Part 2 of the study included 64 infants. The identified score variables for these infants were entered into the scoring system to predict the need for surgery. Predicted outcomes were compared with the actual outcomes for this set of infants. A risk score of 6 or more out of 10 in the proposed scoring system has a predictive value of 71.8% for need for surgery with a positive predictive value (PPV) of 83.3% and negative predictive value (NPV) of 80.5% (p =0.004).

The scoring system is a tool for stratifying need for surgery for an infant with NEC modified Bell stage 2. It should be used as an adjunct to clinical assessment and judgement and is not designed as a clinical substitute. To validate this further, we plan to conduct a prospective observational study with larger smile size in conjunction with the London Neonatal Transport Service.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared.
ID: 849

TITLE: FLOWS AND FUNCTION OF THE INFANT FLOW NEONATAL CPAP DEVICE

AUTHORS: Thomas Drevhammar 1; Niclas Berg 2; Snorri Donaldsson 3; Kjell Nilsson 4; Baldvin Jonsson 5; Lisa Prahl-Wittberg 6

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3 Department of Women’s and Children’s Health, Karolinska Institutet, Stockholm, Sweden
4 Retired Senior Consultant in Anaesthesiology and Intensive Care, Östersund, Sweden
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CONTENT:

Continuous Positive Airway Pressure (CPAP) was first described by Gregory in 1971 as a non-invasive respiratory support of preterm infants. The first dedicated variable flow system for nasal use was developed by K Nilsson and G Moa in Sweden, later known as Infant Flow. Compared to other systems it was pressure stable with a low resistance to breathing and low imposed work of breathing. The Infant Flow type of geometry has been used in a new system for neonatal resuscitation (rPAP) with a marked reduction in resistance to breathing. The aim of this study was to describe the flow and function of the Infant Flow geometry using simulated breathing and computational fluid dynamics.

To resolve the flow characteristics within the Infant Flow device during the breathing cycle, the 3D unsteady and incompressible Navier-Stokes equations were solved. A breathing flow profile of a 3.4 kg healthy infant was applied at the position of the nasal prongs. At the jet inlet, constant flows of 3.4 and 5 L/min, corresponding to CPAP pressure in the range of 3 – 9 cm H2O, were imposed along with a constant pressure boundary condition at the outlet boundaries. The results were presented for analysis as videos of the complete breath cycle and examples of expiration and expiration.

The simulation fully resolved the flow phenomena occurring in the Infant Flow geometry using breath flow profile recorded from an infant. The high resolution needed to resolve the field requires extensive computational power. The CFD simulations for the breathing cycle and the geometry (time plus three dimensions) were calculated and selected cross sections of inspiration and expiration presented in figure 1. The main flow feature during inspiration was support by gas entrainment and mixing. During expiration the jet deflected towards the exhaust with unstable impingement of the jet at the opposing edge. The results confirm the previously suggested function of a high velocity jet that deviate during expiration and produce a fluidic flip.

The Infant flow device was designed thirty years ago and a similar design has recently been used in a new resuscitation system. The delivered CPAP has low resistance to breathing, pressure stable CPAP and low imposed work of breathing. We have previously shown that on these aspects, the design still has an advantage over other CPAP system. The Infant Flow supports inspiration by gas entrainment and expiration by impingement at the opposing edge.

IMAGE / TAB:
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IMAGE / TAB CAPTION: Figure 1: Top row display early developments of the Infant Flow geometry (initially called Jet Piece). The left prototype was the first used in an infant. To the right the is the EME Infant Flow device similar to the devices manufactured today by other companies. The Infant Flow geometry (initially called Jet Piece) with schematic
drawing of the internal geometry including dimensions. The internal design of the CPAP generating part has remained unchanged. Examples of flows within the Infant Flow geometry during breathing (available as video).

**COI:** Kjell Nilsson is one of the inventors of Infant Flow. Thomas Drevhammar and Kjell Nilsson have invented a new resuscitation system based on a geometry similar to Infant Flow. Pilot results have been presented at the World Congress of Biomechanics 2018, Dublin.
ABSTRACT BOOK

POSTER PRESENTATIONS

ID: 851

TITLE: THE HEMOSTATIC PROFILE OF VERY LOW BIRTH WEIGHT MULTIPLES AT BIRTH: A THROMBOELASTOGRAPHIC-BASED OBSERVATIONAL STUDY

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CONTENT:

Twinning rate is increasing worldwide, ranging between 1.3 and 1.6% in high-income countries. Preterm twins are at higher risk of mortality and morbidity than singletons. Compared to dichorionic (DC) twin pregnancy, monochorionicity (MC) has a negative impact on gestational age-specific mortality, especially in case of twin-to-twin transfusion syndrome (TTTS), which complicates 10% to 15% of MC pregnancies. The hemostatic profile in multiples is largely unexplored. The aim of this study was to investigate the effect of a) birth order and b) monochorionicity complicated by TTTS on the thromboelastographic (TEG) profile of very low birth weight (VLBW) multiples at birth.

This is an ancillary study of a larger prospective observational study aimed at defining TEG in healthy VLBW infants at birth. For the purpose of this study, we enrolled (July 2015–June 2018) consecutive VLBW (birth weight ≤1500 grams) multiples. We collected a venous blood sample in the first day of life to perform blood count, PT, aPTT, fibrinogen and recalcified native blood TEG assay (TEG® 5000 Haemoscope): reaction time (R, minute) and maximum amplitude (MA, millimeter). We compared the TEG profile between: a. first-born vs second (third)-born twin in mono-diamniotic multiples; b. donor vs recipient in monochorionic pairs complicated by TTTS, whose diagnosis was made based on ultrasound criteria. Delayed cord clamping (30 seconds) was implemented in 2017 in our level-III NICU.

We analyzed 33 sets of multiples (n=68), consisting of 14 DC-diamniotic and 17 MC-diamniotic twin pairs, 1 trichorionic-triamniotic and 1 MC-triamniotic triplet. Table 1 shows demographic and hemostatic variables of the study population. At birth the median (min-max) TEG values were: R 5.8 min (2–19), MA 65 mm (34–81) in the first-born and R 5.7 min (1.5–23), MA 64 mm (31–80) in the second (third)-born, respectively. In MC twin pairs with TTTS, the median (min-max) TEG values were: R 6.6 min (2-15), MA 59 mm (31-64) in the donor and R 7.4 min (2-19), MA 57 mm (34-61) in the recipient. TEG parameters for both DC and MC multiples were in the normal range, compared to institutional reference intervals for healthy VLBW singletons. No infants had polycythemia or anemia. Delayed cord clamping (DCC) was applied in a restricted cohort of patients, based on institutional practice (table 1).

Multiple pregnancy does not influence the hemostatic profile of VLBW multiples. TEG trace was comparable between first and second (third) order multiples and between donor and recipient of monochorionic sets, complicated by TTTS. The role of DCC in the hemostatic balance should be determined. Further research is required to validate our findings.

IMAGE / TAB: https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=0a76faa111fa1022c4406acba03a5809-MjAxOS0wNSM1Y2UyNjY2ZDBjZDZI
IMAGE / TAB CAPTION: Table 1. Baseline characteristics and hemostatic profile of the study population at birth.

COI: None declared
ID: 852  
**TITLE:** POST-SURGICAL RESIDUAL INTESTINAL ANATOMY AS A PREDICTOR OF INTESTINAL FAILURE IN NECROTIZING ENTEROCOLITIS  
**AUTHORS:** Laetitia Bessalah1, Fabio Fusaro2, Roberto Tambucci1, Bénédicte Van Grambezen1, Dominique Hermans1, Antonella Diamanti2, Pietro Bagolan2, Olivier Danhaive1  
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**CONTENT:**

Besides acute mortality and morbidity during the neonatal period, necrotizing enterocolitis (NEC) can lead to chronic intestinal failure (IF) due to short bowel syndrome (SBS) following extensive intestinal resection, and requiring prolonged parenteral nutrition (PN). Despite this significant burden and its potential implication for care orientation during acute phase, there is a gap of knowledge in predicting the need for prolonged PN in post-NEC SBS, and a critical need for clinical predictors. We aim to assess to role of post-surgical residual intestinal anatomy in predicting long-term PN dependency.

Study design: retrospective cohort study in two level-4 pediatric institutions - St-Luc University Hospital (UCL), Bambino Gesù Children’s Hospital (OPBG) - during a 19-year period (1999-2018). Inclusion criteria: infants of any gestational age, advanced NEC (Bell stage IIIA/B) diagnosed at =6 weeks from birth to 6 months of age. We examined the correlation between post-surgery residual intestinal anatomy and PN duration. Clinical data were collected from local databases and medical records. In a representative prevalence sample (UCL), IF occurred in 3 infants, representing 8.3% of Stage III NEC (n=36) and 1.9% of all-stage NEC cases (n=160).

16 subjects were identified, with a male/female ratio of 57%, gestational age 24-38 weeks (median 31 – interquartile range 5), birth weight 675-2540 g (med 1554 - IQR 790). Chronic PN duration was 120-5338 days (med 331 - IQR 267). 1 infant died of late complications (sepsis) (4.4 months of life), 1 is currently on chronic PN (4.9 years at last follow-up), 14 were successfully transitioned to full enteral feedings at age 6.0-20.9 years (med 8.3 – IQR 9.8). Residual small bowel length was 3-95 cm (med 47.5, IQR 40.7). Regression analysis showed that residual small bowel length correlated with PN duration (r² = 0.33 – p=0.011) (figure). PN duration was 120-900 days (med 227, IQR 248) with preserved ileo-caecal valve (ICV+), and 240-1234 days (med 406, IQR 337 when absent (ICV-) (p=0.32). Association between colonic preservation and PN weaning could not be analyzed due to data heterogeneity.

Despite the limitation of this retrospective study, our data support that residual small bowel length is inversely correlated with PN duration. Future studies involving larger cohorts and longer follow-up are warranted in order to define and refine the prognostic value of residual intestinal anatomy for IF and digestive autonomy in NEC survivors.

**IMAGE / TAB:**
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=59b4b5097529a9fd89933619135a3b08b-MjAxOS0wNSM1Y2UyNjY2NzQ2ZDBkNWI2

**IMAGE / TAB CAPTION:** Duration of parenteral nutrition (days, logarithmic scale) as a function of residual intestinal length (cm) in 16 NEC survivors with IF. Linear regression statistics performed with Origin software (www.originlab.com).

**COI:** None declared
ID: 853
TITLE: Neurodevelopmental outcomes in extremely low birth weight (<500 grams) preterm infants
AUTHORS: Gayatria Athalye-Jape 1; Mei’En Lim 2; Mary Sharp 3
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CONTENT:

Survival of extremely preterm infants has significantly improved with advances in contemporary neonatal care; however, survival and outcomes of infants born with birth weight <500 grams remain poor. We aimed to review short and long term outcomes in preterm infants born with a birth weight of <500 grams. This retrospective study from Western Australia’s sole tertiary perinatal centre included all preterm infants born at 22 weeks gestation or more and weighing 500g or less between January 2001-December 2017 and admitted to the NICU at King Edward Memorial Hospital, Perth, Western Australia (WA).

Short term outcomes such as prematurity related complications (NEC, ROP, IVH, PVL, sepsis, epilepsy), mortality and long term follow up data (up to 5 years of age) were reviewed. Cognitive levels 2-3 or >3 Standard Deviations (SDs) were assigned moderate or severe disability. The most recent assessment was used for cognitive outcomes (Griffiths Scales of Child Development, Bayley Scales of Infant and Toddler Development, Wechsler Preschool and Primary Scale of Intelligence). Cerebral palsy (CP) assessed by Gross Motor Function Classification System (GMFCS) level greater than 2 was included in moderate to severe disability. Hearing loss requiring amplification bilaterally was assigned moderate disability and vision worse than 6/60 in best eye severe disability.

There were 92 admissions to neonatal intensive care and of these, 78/92 (84.7%) were small for gestational age. Survivors (46/92, 50%) to age five had median gestation of 24 weeks (22-30) and median birth weight of 427.5 (380-500) grams. Prematurity related complications were common, with only one infant who survived without any medical complications. Follow-up was available from 41 of 46 (89%) infants. At a median age of 5.06 years, standardized cognitive assessments showed that (29/41) 70% scored <1SD below the mean; 12/41 (29%) scored 1-2SD below mean, 9/41 (22%) scored 2-3SD, and 8/41 (20%) scored 2. One had moderate hearing loss requiring hearing aids in both ears and none were blind. Most remained with weight (32/41 infants, 78%) and height (27/41 infants, 66%) <2 SD below normal.

Half of infants with a birthweight under 500g admitted to NICU survived. Almost all survivors had medical complications in the NICU. However, 54% were free from moderate to severe disability as defined at up to 5 years. Growth remains a concern and needs further monitoring.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared.
ID: 855

TITLE: Integration of obstetrics and level 2 neonatology: an infrastructure to facilitate parent empowerment

AUTHORS: Mireille Stelwagen 1, Anne van Kempen 2, Alvin Westmaas 3, Yvonne Blees 4, Fedde Scheele 5.

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Prof. Dr. Fedde Scheele (MD, PhD), Professor in Health Systems Innovation and Education at VU University Amsterdam, Gynecologist and Dean Teaching hospital OLVG, Amsterdam, The Netherlands

CONTENT:

Empowerment of parents is beneficial for the quality of healthcare for newborns and parents. Family Integrated Care (FIC) is described to support parent empowerment in NICUs. A prerequisite for parent empowerment is closeness between the parents and their newborn. Single Family Rooms (SFR) and co-care should facilitate closeness and FIC. It is not yet common practice to provide co-care in the same room for mothers and newborns who both need specialized care for a prolonged period of time. The object of the study was to explore the conditions which were fulfilled by designing and implementing a fully integrated Mother-and-Child Center to optimize parent empowerment in neonatal level 2 care.

The study was conducted between September 2016 and April 2017 at the new Mother-and-Child Center, OLVG hospital Amsterdam. The current rate of births in this center is 3000 per year, around 1300 newborns a year receive level 1 or 2 neonatal care, 70 of these premature receive post-intensive-care. Using a case study research approach. Selecting and analyzing all available policy reports and other related documents that were produced during the transition process between April 2010 and October 2014. Supplemented with in-depth, semi-structured interviews, which were transcribed. Data collection and thematic analysis were alternately conducted using MaxQDA 2007. The categories that emerged were assigned to the themes, the main categories and the three levels of a model of patient empowerment.

The following themes were identified. At the healthcare system level, ‘Joint vision and goal’, ‘Integration of three wards into one ward with SFR’, ‘Organization of the healthcare team in SFR’ and ‘New equipment’. At the healthcare providers level, ‘Training for extension of professional goals’, ‘Intensifying coaching of parents’, ‘Implementing patient centeredness’. At the patient level, ‘Options and experiences of parents’. The change process started with the Obstetrics and Neonatology units developing a shared vision. The SFR made it possible to organize the healthcare provision of the two specialties geared around mothers and newborns. Training programs for health personnel and a new nurse position, the specialized Mother & Newborn nurse, were implemented for co-care. The medical visiting rounds were planned at the SFR with parents, including open visiting hours for family/friends.

The design and implementation of a infrastructure for obstetrics and neonatology to facilitate parent empowerment consist of Family Integrated care and co-care in Single Family Rooms by a fully integration of the units obstetrics and neonatology. Our case study demonstrated that the design showed a good fit with the model for patient empowerment of Bravo. This infrastructure therefore appears to be able to optimize and promote parent empowerment.
COI: Non declared
ID: 859
TITLE: EDUCATIONAL PROGRAMME TO PREVENT HYPOTHERMIA IN A LOW RESOURCE SETTING NICU
AUTHORS: Aoife Hurley 1
Kunda Mutese- Kapembwa 2
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CONTENT:

Hypothermia is defined as <36.5 degrees and is a challenge in the LMIC as well as high income countries. Data from the NHS improvement Academy shows that over 60% admissions to neonatal units are term babies and this number is increasing despite a reduction in term births. The commonest reasons are hypoglycaemia, jaundice and respiratory symptoms which was the commonest 25%. ATAIN data 25% of babies admitted with respiratory symptoms had a temp<36.5. Maintaining an optimal thermal environment can reduce term admissions for hypoglycaemia and respiratory symptoms. The NICU at University Teaching Hospital Lusaka is Zambia's only tertiary NICU, with up to 100 inpatients and 20 admissions daily.

It was observed by staff that the majority of infants are admitted to UTH NICU hypothermic, with little measures in place to prevent this. The aim of the project was to establish the incidence of admission hypothermia in the baby unit in UTH. To introduce an educational programme to prevent hypothermia with an aim to reduce the incidence of temperatures <36.5. Data collected from admission book over a 6 month period from October 2018 to March 2019. Temperatures collated into hypothermia < 36.4, normal 36.6 - 37.5 and high temperatures > 37.5. All babies included.

The intervention was 3 half study days in April 2019 to midwives from labour ward postnatal ward and NICU nursing staff. Attended by more than 60 staff. Teaching after weekly meeting to medical and nursing staff on NICU.

Over the pre intervention study period there were 2263 admissions of which 1905 had an admission temperature recorded. Between 52-68% admissions per month had an admission temperature of <36.5.

Post intervention in April there is a reduction in hypothermic babies and a rise in normothermic babies across total admissions seen in figure 1 attached.

In line with the NHSI work, we looked at term babies who were hypothermic. Gestational age is variably calculated and documented in Zambia, so we used a birth weight of 2.5kg as a surrogate identifier of term.

After the intervention programme, there was a reduction in the hypothermic term babies admitted to the unit.

We also looked at primary reason for admission in all the hypothermic babies of the pre intervention study period, these admission diagnoses are in line with the ATAIN work in the UK.

A simple educational programme has been shown to reduce the number of term admissions by reducing the number of hypothermic babies.

Ongoing work includes maternal education and information regarding simple measures to alleviate hypothermia. Posters will be used in the labour ward, postnatal areas and mothers area.

IMAGE / TAB:
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IMAGE / TAB CAPTION:
COI: non declared
TITLE: GASTROINTESTINAL EFFECTS OF AN INHALED PDE4 INHIBITOR IN VENTILATED PRETERM LAMBS EXPOSED TO CHORIOAMNIONITIS

AUTHORS: Charlotte Van Gorp 1, Barbara Ottensmeier 2, Kimberly Massey 1, Tim Wolfs 1, Boris W. Kramer 1, Steffen Kunzmann 2, 3, Matthias C. Hütten 1, 2

AFFILIATIONS: 1 Neonatology, Department of Pediatrics, Maastricht University Medical Center, Maastricht, The Netherlands
2 Neonatology, University Children’s Hospital, University of Wuerzburg, Wuerzburg, Germany
3 Neonatology, Department of Pediatrics, Bürgerhospital and Clementine Children’s Hospital, Frankfurt, Germany

CONTENT:

Bronchopulmonary dysplasia (BPD) remains a therapeutic challenge in neonatology. New substances like phosphodiesterase (PDE) inhibitors, which have successfully been tested in clinical trials of pulmonary diseases of adulthood, have potential therapeutic benefits for BPD. However, when given enterally, adverse effects mainly in the gastro-intestinal tract limit the clinical use. Inhalation might therefore be the preferable way of administration. We tested an inhalable PDE4 inhibitor in a triple hit lamb model of prematurity, Ureaplasma parvum-induced chorioamnionitis and mechanical ventilation. We hypothesized that inhaled PDE4 treatment would not induce gastrointestinal inflammation.

21 preterm lambs were in utero exposed for 7 days to Ureaplasma parvum chorioamnionitis, and surgically delivered preterm at 129d (term 150d). 16 animals were subsequently intubated, ventilated for 24 hours and received a nebulized PDE4 inhibitor twice in a higher dose (10 µg/kg, “IPDE10”), a lower dose (1 µg/kg, “IPDE1”), or no treatment (“Control”). Five lambs were sacrificed immediately after birth (“NOVENT”). Paraffin-embedded ileum sections were stained for CD3 and MPO and positive cells were counted in 5 random high power fields. PCR for mRNA of inflammatory cytokines was performed on homogenates of deep frozen ileum samples.

Histological evaluation of the ileum of PDE-inhibitor treated animals showed no significant increase of CD3 positive and MPO positive cells when compared to ventilated and unventilated controls. Inflammatory cytokine mRNA levels of IL-1, IL-6, IL-8 and TNF alpha showed a distinct pattern of inflammation in the high-dose group.

Our first analysis reveal dose-dependent, potentially adverse effects of inhaled PDE4 inhibitor on the gut of ventilated preterm lambs exposed to chorioamnionitis. Further analysis is performed to correlate pulmonary and intestinal effects.

IMAGE / TAB: 

IMAGE / TAB CAPTION:

COI: This study was supported by a grant from Deutsche Forschungsgemeinschaft (DFG-KU1403/6-1). No other potential conflicts of interest to declare.
ID: 868

TITLE: Renal outcome in former ELBW children at 11 years: a pooled analysis in search of covariates

AUTHORS: Maja Gilarska 1; Anke Raaijmakers 2, 3; Zhen-Yu Zhang 4; Jan A. Staessen 4; Elena Levchenko 2, 3; Małgorzata Klimek 1; Andrzej Grudzień 1; Katarzyna Starzec 1; Karel Allegaert 2 5; Przemko Kwinta 1

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4 Studies Coordinating Centre, Research Unit Hypertension and Cardiovascular Epidemiology, Department of Cardiovascular Sciences, University of Leuven, Leuven, Belgium.
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CONTENT:

A great number of studies examine the association between being born as extreme low birth weight (ELBW) infant, and subsequent kidney size and function later in life. However, the number of cases versus control (term equivalent age) in published cohort studies is low and multicenter cooperation to pool data together to obtain more accurate results is crucial.

We performed a subject level meta-analysis to pool data from Cracow (64 cases/34 controls) and Leuven (93 cases/87 controls). We assessed and analyzed cystatin C estimated glomerular filtration rate (eGFR), ultrasound kidney length and blood pressure (BP) in 11-years-old children born with extremely low birth weight (ELBW, birth weight < 1000 grams) compared with controls born at term. The prevalence of hypertension (HT) and prehypertension (preHT) in both groups was also analyzed.

The study group comprised 157 former ELBW children (gestational age 23-33 weeks and birth weight 430-1000 g) and 123 born at term. Former ELBW children had lower mean eGFR (100.62±16.53 ml/min/1.73m2, vs. 111.89±15.26 ml/min/1.73 m2; p<0.001), smaller absolute kidney length (8.56±0.78 cm vs. 9.008±0.73 cm; <0.001) and higher systolic (111.8±9.8 vs. 107.2±9.07 mmHg; p=0.01) and diastolic (68.6±6.8 vs. 66.3±7.7 mmHg; p=0.03) blood pressure. Lower renal size in former ELBW children was positively associated with lower birth weight, shorter gestational age, and with the severity of perinatal complications (intraventricular hemorrhage, length of stay, mechanical ventilation and oxygen therapy, postnatal steroids).

ELBW is associated with lower eGFR and a higher systolic and diastolic blood pressure. Within ELBW cases, birth weight, gestational age and perinatal complications were associated with lower renal size.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: the leuven study has been supported by the Safepedrug initiative (IWT-SBO)
ID: 871

**TITLE:** Chorioamnionitis as a Risk Factor for Bronchopulmonary Dysplasia: A Meta-analysis and Meta-regression

**AUTHORS:** Eduardo Villamor-Martinez 1, María Álvarez-Fuente 2, Amro M. T. Ghazi 1, Mohammed A. Kilani 1, Pieter Degraeuwe 1, Luc J. I. Zimmermann 1, Boris W. Kramer 1, Eduardo Villamor 1

**AFFILIATIONS:** 1 Department of Pediatrics, Maastricht University Medical Center (MUMC+), School for Oncology and Developmental Biology (GROW), Maastricht, the Netherlands. 2 Hospital Ramón y Cajal, Madrid, Spain

**CONTENT:**

Bronchopulmonary dysplasia (BPD) remains one of the major complications of very preterm birth. Inflammatory and infectious events are suggested to play a key role in the initiation, progression, and severity of BPD. The inflammatory response may have been initiated in utero, in the setting of chorioamnionitis (CA). We aimed to perform a systematic review, meta-analysis, and meta-regression of clinical studies exploring the association between CA and BPD.

PubMed/MEDLINE and EMBASE databases were searched. Studies were included if they examined preterm infants and reported primary data that could be used to measure the association between exposure to CA and the presence of BPD. A random-effects model was used to calculate odds ratios (OR) and 95% confidence intervals (CI). Sources of heterogeneity were determined by subgroup and meta-regression analyses.

We found 3,168 potentially relevant studies, of which 158 met the inclusion criteria (185,676 infants). Meta-analysis showed that CA exposure was significantly associated with BPD28 (OR 2.10, 95% CI 1.76-2.51), and BPD36 (OR 1.29, 95% CI 1.16-1.42). The association between CA and BPD remained significant for both clinical and histological CA. Exposure to funisitis was not significantly associated with a higher risk of BPD when compared to exposure to CA in the absence of funisitis. In addition, we found significant differences between CA-exposed and CA-unexposed infants in GA, BW, and other infant characteristics. CA was not significantly associated with RDS (OR 1.10 95% CI 0.92-1.34) but multivariate meta-regression with backward elimination revealed that a model combining difference in GA and odds of RDS explained 64% of variance in the association between CA and BPD36 across studies.

Our results confirm that preterm infants exposed to CA have a higher risk of developing BPD, but the pathogenic effect of CA on BPD may be modulated by the effect of CA on GA and risk of RDS.

**IMAGE / TAB:**
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**IMAGE / TAB CAPTION:** Figure 1. Meta-analysis of the association between chorioamnionitis (CA) and bronchopulmonary dysplasia (BPD), grouped by definition of CA. k: number of studies; PMA: post-menstrual age.

**COI:** None declared
ID: 874

**TITLE:** BILIRUBIN BINDS TO LIPID RAFTS

**AUTHORS:** Ningfeng Tang 1; Min He 1; Cynthia F. Bearer 1

**AFFILIATIONS:** 1 Division of Neonatology, Department of Pediatrics, University of Maryland School of Medicine, Baltimore, MD, 21201, USA

**CONTENT:**

The mechanism of bilirubin neurotoxicity is poorly understood. Bilirubin has previously been reported to bind to phospholipids. We hypothesize that bilirubin binds specifically to the phospholipids in lipid rafts, microdomains of the plasma membrane critical for signal transduction, and inhibits their function. To test this hypothesis, we measured the binding of bilirubin to lipid rafts.

Our objective was to determine the location of bilirubin in the fractions of sucrose density gradients that separate lipid rafts from non-lipid rafts in lysates of cerebellar granule neurons.

Cerebellar granule neurons were isolated from postnatal day 5 rat pups and cultured overnight in neurobasal media with B27 additive (K5). Media was replaced with 100 μM human serum albumin in K5 with or without 5 μM bilirubin and incubated for 1 hour. Cell lysates made using 1% Triton X100 were added to sucrose density gradients followed by ultracentrifugation to isolate lipid rafts (LR) from non-lipid rafts (N). Ten 1 ml fractions were taken from the gradients, and aliquots dot blotted for bilirubin (B) and for GM1 ganglioside, a marker for lipid rafts. In some case, methyl beta-cyclodextrin (MBCD) was added to cell lysates prior to addition to sucrose density gradients.

In the absence of bilirubin addition to cell culture (B-), there was no immunoreactivity in the dot blot for bilirubin. Addition of bilirubin to the cultures (B+) resulted in bilirubin reactivity only in fractions with co-reactivity for GM1 ganglioside (Fisher Exact test: B immunoreactivity present yes/no, LR vs N, p<0.03). In lysates treated with MBCD to chelate cholesterol and eradicate lipid rafts, bilirubin reactivity was found in all fractions of the sucrose density gradient.

Bilirubin binds preferentially, if not exclusively, to phospholipids in lipid rafts. The binding of bilirubin to lipid rafts may disrupt lipid raft function and be one possible mechanism for bilirubin neurotoxicity.

**IMAGE / TAB:**

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**IMAGE / TAB CAPTION:** Figure: Panel A. Dot blot showing presence of GM1 ganglioside (GM1) in fractions of sucrose gradients indicating the presence of lipid rafts. Addition of Bilirubin (B) had no effect on the distribution in the presence or absence of methyl beta cyclodextrin (MBCD). In the absence of MBCD, GM1 was only in fractions 1 - 6 of the gradient. Addition of MBCD reduced GM1 reactivity and faint reactivity was found in all fractions. Panel B: Dot blot of the same experiment as in Panel A, but developed with antibody to bilirubin. In the absence of added bilirubin (B-), no immunoreactivity is found. In the presence of added B without MBCD, bilirubin immunoreactivity is found only in the fractions corresponding to GM1 immunoreactivity. Addition of MBCD to cell lysates in the presence of bilirubin resulted in bilirubin reactivity throughout the gradient. (n=4, Fisher Exact test: B immunoreactivity present yes/no, LR vs N, p<0.03).

**COI:** None declared.
ID: 876
TITLE: IMPACT OF INTRAAMNIOTIC INFECTION ON SHORT-TERM NEONATAL OUTCOMES IN PRETERM INFANTS
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2 Neonatology Department. Hospital Sant Joan de Déu. BCNatal | Barcelona Center for Maternal Fetal and Neonatal Medicine. Hospital Sant Joan de Déu and Hospital Clínic, Universitat de Barcelona. Spain.
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CONTENT:
Intraamniotic infection (IAI) is a common cause of spontaneous preterm delivery, perinatal mortality and long-term morbidity. Some guidelines for the management of women with preterm labour (PTL) and/or premature rupture of membranes (PROM) include amniocentesis to rule out IAI in amniotic fluid (AF).

The aim of this study was to evaluate the influence of IAI in short-term neonatal outcomes in preterm infants less than 35 weeks of gestational age (GA).

Prospective cohort study (2009-2018) including women without clinical chorioamnionitis, with an amniocentesis at admission to rule out intraamniotic infection (IAI) and delivered a preterm infant<35 weeks of GA. IAI was defined as a positive aerobic/anaerobic amniotic fluid (AF) culture for bacteria or yeast, or Ureaplasma spp. and Mycoplasma hominis in mycoplasmas culture or by sequencing of the small-subunit ribosomal RNA gene. Three subgroups were identified according to the results of the AF: (1) negative, (2) isolated Mycoplasma/Ureaplasma and (3) Others (gram-positive or gram-negative bacteria or Candida). Short-term neonatal outcomes were compared among the groups. A multivariate analysis was carried out to predict morbidity and mortality of the newborn regardless of GA.

345 women were studied, mean birth GA 29±3.3. Groups: 1) Negative (n=235; 68.1%), 2) Ureaplasma/Mycoplasma (n=60; 17.4%) and 3) Other microorganisms (n=50; 14.5%). No differences were found in antenatal management and maternal outcomes. Worse neonatal outcomes were more frequent in case of IAI, p<0.001. Group 3 showed shorter latency to delivery (5±9 vs 16±18, p<0.001) and lower GA at birth (28.3±3.8 vs 31.4±3.1, p<0.001). Multivariate analysis showed no differences in mortality or bronchopulmonary dysplasia. Group 3 was associated to higher intubation in delivery room (OR=3.1 (CI95% 1.25–7.55), p=0.015) and early onset sepsis (OR=8.47 (CI95% 3.67–19.5), p<0.001). Group 2 was related to less respiratory distress syndrome (OR=0.28 (CI95% 0.10–0.75), p=0.012), patent ductus arteriosus (OR=0.28 (CI95% 0.08–0.95), p=0.041) and retinopathy of prematurity (OR=0.23 (CI95% 0.55–0.95), p=0.042).

Preterm infants born after IAI exhibit worse short-term neonatal outcomes but, except for early onset sepsis, GA was the main predictor of neonatal mortality and morbidity. Ureaplasma infection was related to less neonatal complications than other microbes infection. The amniocentesis in women with PTL or PROM may give a valuable information to neonatologists in order to adequate family’s information and optimize future neonatal care.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 878
TITLE: ULTRA-HIGH FIELD MAGNETIC RESONANCE IMAGING: SAFETY AND FEASIBILITY IN NEONATES.
AUTHORS: Annink K.V. 1,2; Wijnen J.P. 3; Dudink J. 1,2; Groenendaal F. 1,2; Alderliesten T. 1,2; Visser F. 3; Lequin M.H. 3; Luijten P. 3; Hendriksje J. 3; Blanken N. 3; Jansen F.E. 4; Benders M.J.N.L.* 1,2; van der Aa N.E.* 1,2
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CONTENT:

A high number of neonates admitted to the NICU is at risk of brain injury. Cerebral MRI is the gold standard to assess brain injury and maturation, and to predict long-term neurodevelopmental outcome. Currently, in neonates MRIs are performed with a magnetic field strength of 3 Tesla (T). In adults however, a growing number of studies have shown the added diagnostic value of 7T MRI including improved quality of arterial spin labelling (ASL), susceptibility weighted imaging (SWI) and magnetic resonance spectroscopy (MRS). The aim of the study is to investigate the safety of 7T imaging in neonates and to assess the feasibility of obtaining good quality images at 7T.

In this prospective study, 5 of the planned 20 infants have been examined. Clinically stable infants can be included if they have a clinical indication for MRI between term (equivalent) age and 3 months of (corrected) age. They will undergo 7T MRI immediately after their routine 3T MRI scan (Philips, Best, the Netherlands). Prior to the study, power deposition (as quantified by the specific absorption rate (SAR)) was simulated in a baby model. Safety will be determined by measuring the infant’s vital parameters, temperature and comfort scales before, during/between and after MRI. Since this is the first time that 7T MRI will be performed in neonates, the 7T scan protocols will be developed and optimized whilst scanning the first patients.

The global SAR and peak local SAR levels did not exceed the SAR levels in the adult head for the same settings. Scanning at maximum permissible SAR for normal operation, results in an average SAR deposition of 0.94 W/kg in the baby model in centre position.

So far, five preterm born infants were scanned at term equivalent age. No major adverse events occurred and the vital parameters and comfort scales were not statistically different before, during and after 3T and 7T MRI scans. Importantly, no increase in temperature was observed. It was feasible to obtain good quality imaging at 7T. SWI showed better visualisation of the deep venous circulation (Figure 1). Proton MRS showed additional metabolite peaks at 7T compared to 3T, such as N-acetyl aspartyl glutamate. Phase contrast angiography and T2-weighted imaging were of comparable quality, T1-weighted imaging still needs to be improved.

7T MRI was demonstrated to be safe in the first five neonates scanned at term equivalent age with no major adverse events. It was feasible to obtain good quality proton MRS and SWI which provided additional information at 7T. In the following months more neonates will be included whilst further improving the protocol. Demonstration of safety and feasibility in neonates paves the way for larger cohort studies.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=c9f21f7b8324f47d1d420a5acf853374-MjAxOS0wNSM1Y2UyNy1y2ZDE3MWFh
IMAGE / TAB CAPTION: Figure 1. A: SWI image at 3T MRI in a preterm born neonate at term equivalent age. B: SWI image of the same patient at 7T MRI. At the 7T MRI more details of the deep venous circulation are visible.

COI: Fredy Visser is as well an employee of the UMC Utrecht as of Philips. The other authors have no conflict of interest to declare.
**ID:** 879  
**TITLE:** Neglected and desperately needed: nutritional support for preterm survival in low-income countries  
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**CONTENT:**

Neonatal mortality represents 45% of under-5-year-old deaths worldwide and malnutrition contributes to half of those deaths. In Benin, like in other Sub-Saharan African countries, prematurity (35%), neonatal infections (26%) and birth-related events (28%) explain 90% of all neonatal deaths. Exclusive breastfeeding at 6 months is only 40% and the availability of breastmilk for hospitalized newborns is limited. Preterm infants are particularly at risk of complications due to malnutrition. Kangaroo Mother Care is recommended by WHO. We report on interventions done during the “Breath of Life-Benin” (BOL) programme to improve the nutritional status and survival of hospitalized preterm infants.

BOL-Benin is a multifaceted program targeting the main causes of neonatal mortality. It was developed and implemented by our Global Development Alliance and co-funded by USAID Benin (2015-2017). Interventions to reduce mortality due to prematurity included, amongst others, emphasis on early nutrition with mother’s own breast milk and continuous Kangaroo Mother Care (KMC). We report the survival (number and percent), length of stay (days) and weight gain/loss (grams and percentage below/above birth weight) observed in preterm infants admitted to the neonatal unit and KMC unit, according to birth weight (BW) categories (1000-1249 grams (g), 1250-1499 g, 1500-1749 g and 1750-1999 g), in the 2 largest neonatal units of Benin, before and after BOL.

Approximately five thousand newborns are admitted each year between the 2 neonatal units, 60% of them being preterm infants, with approximately 2/3 inborn and 1/3 outborn. Before BOL, skin-to-skin care was limited to breastfeeding attempts for more mature infants. Survival was dismal below a BW of 1250 g and uncommon below 1500 g and malnutrition was present in virtually all preterm infants surviving beyond a week of age. Following BOL interventions, preterm survival increased significantly for infants with BW below 1500 grams. Despite earlier feeds initiation, increased breast milk ratio and protein supplementation, preterm infants cared for in the neonatal unit exhibited poor weight gain. Preterm infants cared for in the KMC unit 24h/day demonstrated constant weight gain, significantly improved survival (beyond 95% for infants 1000-1999 grams) and earlier discharge home.

BOL interventions improved survival of preterm infants but malnutrition remains a concern in the neonatal unit. KMC increased survival and weight gain of low BW infants. Future efforts to improve preterm infants’ outcome in low-income countries should emphasize on KMC and consider involvement of families at bedside to palliate understaffing in the neonatal unit. Parenteral nutrition and milk fortification may be needed in very low BW infants.

**IMAGE / TAB:**

**IMAGE / TAB CAPTION:**

**COI:** None declared
**ID:** 881  
**TITLE:** Towards the End of Kernicterus in Sub-Saharan Africa?  
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**CONTENT:**

The burden of neonatal jaundice is the highest in countries with low socio-demographic index. Acute Bilirubin Encephalopathy (ABE) and kernicterus but remains a serious problem in low- and middle-income countries (LMIC), in part due to a high prevalence of G6PD deficiency. Bhutani (2013) estimated that more than 100,000 term or late preterm death and above 60,000 kernicterus are due to severe jaundice annually, with predominance in Sub-Saharan Africa (SSA) and South Asia. We describe the evolution of ABE in Benin (SSA) after our Global Development Alliance increased the availability of phototherapy lamps and dispensed an education program to prevent neonatal jaundice complications.

BOL-Benin is a multifaceted program targeting the main causes of neonatal mortality and morbidity, including neonatal jaundice. It was developed and implemented by our Global Development Alliance and co-funded by USAID Benin (2015-2017). Interventions to reduce complications from neonatal jaundice, namely death and ABE, included the provision of high intensity phototherapy lamps and an education program regarding clinical presentation of jaundice, ABE, as well as therapeutic modalities, to physicians and nurses in charge of newborns in neonatal units. We report the effect of BOL on severe complications from neonatal jaundice in the 3 main neonatal units of the country.

Preliminary data analysis show that clinical ABE and neonatal death attributed solely to severe jaundice have virtually disappeared from the inborn neonates admitted to one of the 3 largest neonatal units of the country, totalling close to 7000 admissions with close to 5000 inborn per year (only 2 cases reported in the past 3 years). High intensity phototherapy was initiated immediately following clinical recognition of jaundice on the chest or upper abdomen of the newborn (Kramer’s scale), up to the availability of a serum bilirubin level below phototherapy threshold when parents could afford the test, or up to clinical resolution of the jaundice when test could not be performed. Unfortunately, ABE and death from jaundice remained frequent in the population of outborn newborns, due to late recognition of the jaundice in the community and late referral for treatment.

Our program offering technical support and education has massively reduced ABE and death from severe jaundice in the inborn portion of hospitalized newborns. Considering the low cost of phototherapy equipment, our program should be easily reproducible in other LMICs. Community interventions to increase awareness of neonatal jaundice complications need to be held in those countries to eradicate completely the sequelae of neonatal jaundice.

**IMAGE / TAB:**

**IMAGE / TAB CAPTION:**

**COI:** None declared
ID: 893
TITLE: Compositional changes associated with the improvement of pulmonary surfactant performance under whole body hypothermia
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CONTENT:

WBH (33.5°C) is an effective treatment for neonates with encephalopathy due to perinatal asphyxia, but has also several biological effects on neonatal lungs. For instance, we previously demonstrated a reduction in both lung inflammation and secretory phospholipase A2 activity in cooled neonates [1,2]. At the same time, we observed a temperature dependent improvement of pulmonary surfactant (PS) activity after 72h of WBH [3]. Since in vivo DPPC turn-over does not seem to vary during cooling [4], we investigated whether other compositional changes could explain this temperature- and time-dependent improvement of PS performance.

5 asphyxiated neonates without lung disease received nonbronchoscopic BAL before and after 72h of WBH [5]. Large aggregates (LA) of PS were precipitated (1h at 40,000 g) to test: 1) the amount of surfactant proteins SP-B and SP-C by western blot analysis, and 2) the percentage of lipid classes and subclasses by lipidomic analysis (UPLC-TOF). Total proteins (TP) and phosphatidylcholine (PC) amount were also measured by colorimetric methods.

No changes in TP and total PC were obtained. SP-B amount did not vary, but a significant decrease in SP-C content was observed after 72h of WBH [pre=72(70-74)%; 72h=0(0-18)%, p=0.027]. At this time point, the percentage of some unsaturated PC (unPC) species significantly decreased, promoting a simultaneous increase in DPPC proportion [unPC(34:2): pre=12.1(11.3-12.6)%, 72h=9.7(8.5-10.8)%, p=0.039], [unPC(34:3): pre=2.4(2.0-2.7)%, 72h=0.85(0.6-1.0)%, p=0.018], [DPPC: pre=41.8(39-45)%, 72h=45.8(45-46)%, p=0.051].

The boost in PS activity under WBH may be partially explained by a better exclusion of less active lipid species from large surfactant membranes at 33.5°C, promoting a simultaneous increase in DPPC proportion.


COI: no conflict of interest
ID: 895

TITLE: An in vitro model to understand the improvement in lung surfactant activity during whole body hypothermia

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CONTENT:

Pulmonary surfactant (PS) is a lipid-protein complex that reduces the surface tension at the respiratory air-liquid interface of alveoli, minimizing the work of breathing[1]. The composition and structure of PS are directly responsible for its mechanical properties in a healthy lung or under pathological conditions. We previously demonstrated that PS activity improves after 72h of Whole Body Hypothermia (WBH) in neonates with and without lung injury[2,3]. PS performance is significantly better when samples are tested under cooling condition (33.5°C). To better understand the molecular mechanisms at the basis of this temperature-dependent improvement, we designed a surfactant in vitro model.

We combined synthetic lipids and porcine surfactant protein-B(SP-B), preparing 2 protein/lipid mixtures characterized by higher or lower surface active properties: 1) DPPC (35% w/w), POPG (35% w/w) and SP-B (1% w/w) in the presence of POPC (30% w/w) or 2) DPPC (35% w/w), POPG (35% w/w) and SP-B (1% w/w) in the presence of a lower surface active lipid, namely DOPC (30% w/w). We studied their biophysical activity upon breathing-like conditions at the Captive Bubble Surfactometer, analyzing each sample in triplicates (8 mg/mL of phospholipid) at both 37°C and 33.5°C.

We did not find any significant differences along compression-expansion dynamics in the performance of the more active mixture containing POPC [37°C: minimum gamma=13 +/- 4 mN/m; 33.5°C=16 +/- 2 mN/m]. Conversely, we obtained a significant decrease in surface tension, testing the mixture with DOPC at 33.5°C [37°C: minimum gamma=18 +/- 2 mN/m; 33.5°C=7 +/- 2 mN/m, p<0.001].

Conclusions: Our in vitro data suggests that the improvement in PS activity upon WBH may partially depend on a better and preferential exclusion from the air-liquid interface of less active phospholipids during expiration.


IMAGE / TAB:

IMAGE / TAB CAPTION: 

COI: no conflict of interest
ID: 896
TITLE: IMPACT OF INTRAAMNIOTIC INFLAMMATION AND INFECTION ON SHORT-TERM NEONATAL OUTCOMES AFTER PREMATURE RUPTURE OF MEMBRANES
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CONTENT:
One of the main risks associated with premature rupture of membranes (PROM) is intraamniotic inflammation and/or infection, increasing the probability of preterm birth and early onset sepsis (EOS). Some guidelines for the management of women with PROM include performing an amniocentesis to rule out inflammation and infection in amniotic fluid (AF). The aim of this study was to evaluate the influence of intra-amniotic inflammation and/or infection in short-term gestational and neonatal outcomes, in pregnant women with PROM before 34 weeks of gestational age (GA) and their offspring.

Prospective cohort study (2009-2018) including women with PROM until 34 weeks of GA, with an amniocentesis at admission to rule out infection. Clinical chorioamnionitis (Gibbs criteria) and multiple gestations were excluded. Three subgroups were identified according to the presence of infection or inflammation. Infection (MIAC) was defined based on AF cultures results. Inflammation (IAI) was based on interleukin (IL)-6 levels. Culture results and glucose in AF were available and used for clinical making decision, while IL-6 wasn’t (just for research purpose). Pregnancy and short-term neonatal outcomes were compared according to the characteristics of AF. Multivariate analysis was carried out to predict the morbidity and mortality of the new-born regardless of GA and prenatal management.

213 women studied, mean GA at PROM 30±3.7. Groups: 1) No IAI nor MIAC (29.1%); 2) sterile IAI (40.7%); 3) MIAC (30.2%). Ureaplasma sp. (58%) was the microbe more frequently isolated, anaerobes (22%), Streptococcus (16%), gram-negative bacteria (9%), Candida (7%). There were 6.1% stillbirths. No differences were found in antenatal management, spontaneous onset of labour, mode of delivery or maternal outcomes between groups. Group MIAC: shorter latency to delivery (median 6 vs 11w, p=0.044), lower GA (29.0±3.8w vs 32.3±2.4, p<0.001), higher mortality (14.5% vs 1.9%, p=0.005), EOS (21.3% vs 5.8%, p=0.04) and BPD (27.7% vs 9.4%, p<0.01). Multivariate analysis adjusted by GA showed no differences in mortality (OR=1.51 (CI95% 0.47–4.84) p=0.485) or EOS (OR=2.85 (CI95% 0.68–11.9) p=0.151). 45 women (22.5%) were induced at 34 w. None of these newborns developed infection or needed antibiotic.

Gestational age was the main predictor of neonatal mortality and morbidity in gestations with PPROM before 34 weeks, but latency to delivery is highly influenced by the presence of infection in AF. The performance of amniocentesis in women with PROM allows us to give a more reliable information to the family. Termination of pregnancy at 34 weeks gestation in women with PROM and without intraamniotic infection could be avoided.
COI: None declared.
ID: 902

TITLE: ELEVATED SERUM INTERLEUKIN-10 IS ASSOCIATED WITH INCREASED SEVERITY OF ENCEPHALOPATHY AND ADVERSE 2-YEAR OUTCOMES IN UGANDAN INFANTS WITH NEONATAL ENCEPHALOPATHY

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CONTENT:

Traditional biomarkers that predict neurodevelopmental outcome in neonatal encephalopathy (NE) are not widely available in low-income countries. Cytokine levels predict outcome in NE, however studies have focussed on infants in high income settings and are limited to small numbers, excluding those with co-existing infection.

Infection and inflammation are independent risk factors for NE in Ugandan infants[1]. In this cohort, we aimed to characterise the cytokine profile that predicts longer-term outcomes. We hypothesised that IL10 levels predict NE outcome, based on findings in a hypoxia-ischaemia piglet model[2].


Infants were recruited to the ABAaNA study investigating risk factors for[1], and outcomes from NE at Mulago Hospital, Uganda.

Serum IL1α, IL6, IL8, IL10, TNFα and VEGF were measured at <36h in 159 NE and 157 non-NE infants. NE severity was graded (Sarnat score). Infants were assessed at 2 years using Griffiths Mental Developmental Scales II and Hammersmith Infant Neurological Examination(HINE). Adverse outcome included death, Griffiths developmental quotient <70, HINE<67 or cerebral palsy.

Cytokines for NE and non-NE infants were compared. The association between cytokines, NE severity and 2-year outcome were assessed using Kruskal Wallis and Mann Whitney U. Logistic regression assessed ability of cytokines to predict poor outcome, adjusting for neonatal bacteraemia, sex and sample time.

In NE infants, 91% had moderate-severe encephalopathy and 59% had adverse 2-year outcomes. NE was associated with higher maternal c-reactive protein(CRP) (>90thcentile OR 3.82 p97thcentile OR 4.19 p=0.03) and incidence of neonatal bacteraemia (OR 3.86, p=0.17) compared with controls.

Infants with NE had higher IL10 (median 6.7pg/ml (IQR 0.6-25) control 1.0 (IQR 0-3.2) p<0.001), lower TNF (median 5.2pg/ml (2.6-10) control 7.8 (2.6-10) p=0.001) and lower VEGF (median 92pg/ml (17-201) control 203 (82-367) p<0.001).

Higher IL10 was associated with increased NE severity (mild 0.1pg/ml (IQR 0-5.4) moderate 6.7 (IQR 1.1-24) severe 8.5 (IQR 1.3-30), p=0.01) and adverse 2-year outcomes (median difference +10.9pg/ml compared with good outcome group, p<0.01) (Figure). After adjusting for covariates, IL10 remained a significant predictor of poor outcome (aOR 2.4 p<0.01).

In Ugandan infants with NE, elevated serum IL10 on day 1 is associated with NE severity and is a significant predictor of adverse 2-year outcome. IL10 levels were elevated and TNF and VEGF were lower in NE compared to non-NE infants. These
findings concur with pre-clinical piglet studies where IL10 at 24-48h correlates with injury assessed using magnetic resonance spectroscopy, and adds weight to the use of serum cytokines to predict NE outcomes.

**IMAGE / TAB:**
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**IMAGE / TAB CAPTION:** Fig: Cytokine profile of infants with NE by severity of encephalopathy according to Sarnat Classification (A) and 2-year outcomes (B). Box and whisker plot showing median, 25th, 75th quartiles and range on log10 scale. Mann Whitney U or Kruskal Wallis *p<0.05 **p<0.01

**COI:** None declared
ID: 903  
**TITLE:** POSTNATAL DEXAMETHASONE ACTS BY LIMITING MACROPHAGE MEDIATED INFLAMMATION AND UPREGULATING SURFACTANT PROTEIN mRNA IN THE LUNG.  
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**CONTENT:**

The immunological and surfactant response of the ventilated preterm lung to postnatal glucocorticoids are described poorly. This study aimed to describe these aspects of early postnatal lung development in response to ventilation and early low-dose dexamethasone.

Ewes were delivered operatively at 129d after antenatal betamethasone (5.7mg, 48 and 24h prior). Lambs were intubated and received surfactant (poractant alpha; 100mg/kg), then volume-targeted ventilation (~6mL/kg) and graduated weaning of respiratory support as tolerated. Lambs were randomised to tapered IV saline (SAL, n=9) or dexamethasone (DEX, n=8; commencing 0.15 mg/kg) from ~2h age, and euthanised at 7d. Fetal controls (FC, n=5) were euthanised at 136d. Lung tissue was stained for macrophage (CD163), leucocyte (CD45) and smooth muscle (SMA). Cell number/field were averaged from 72 fields/lamb. Surfactant protein (SP) mRNA was measured using a Fluidigm assay. Cell counts and relative mRNA expression were compared using Mann-Whitney (SAL vs FC; DEX vs SAL) and reported as median (IQR).

Demographics are shown in Table 1. The number of CD163 and CD45 positive cells/field increased in SAL vs. FC (238 (115–411) vs. 2.3 (1.3–10.2); p=0.009 and 48(40–59) vs 0.3(0-0.6); p=0.06) respectively. Dexamethasone decreased the number of CD163 positive cells/field (44(34-115)) vs. SAL lambs (238 (145-411; p=0.0003)) but did not alter CD45 cell counts. SMA expression (positive cells/field) increased in SAL (933(815-1032) vs FC (577(461-813); p=0.04) but was unchanged by dexamethasone. Dexamethasone increased relative gene expression of SP-A (DEX vs. SAL, 164(72–526) vs 27.3(14.7–45.5); p<0.005) and SP-C (DEX vs. SAL, 13.1(7.8–34.9) vs7.7(5.2–9.4); p <0.05). Similar but non-significant increases in gene expression of SP B (p=0.09) and SP-D (p=0.05) were observed.

Preterm lambs receiving contemporary lung protective ventilation have evidence of pulmonary inflammation at 7-days compared to gestation and antenatal exposure matched fetal controls. A tapered low-dose course of dexamethasone from soon after birth decreased pulmonary inflammation and increased gene expression of surfactant proteins. The anti-inflammatory effect of dexamethasone was restricted to macrophage mediated inflammation.

**IMAGE / TAB:**

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IMAGE / TAB CAPTION: Table 1. Characteristics of the study population

COI: Unrestricted support: National Health and Medical Research Council (Australia) GNT1057759; 1057514, 1077691; Chiesi Farmaceutici S.p.A. (surfactant); F&P Healthcare (circuits), ICU Medical (monitoring lines).
ID: 906

TITLE: ASSOCIATION OF BRONCHOPULMONARY DYSPLASIA (BPD) WITH FEEDING INITIATION AND ADVANCEMENT

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CONTENT:

Breastfeeding and the use of human milk are the standards for the feeding of newborn infants. The use of donor milk (DM), when Mother’s Own Milk (MOM) is unavailable, is recommended for preterm infants (AAP and WHO). The Exclusive Human Milk Diet (EHMD) (MOM or DM, fortified with human milk based fortifiers) has been associated with decreases in mortality and morbidity in Very Low Birthweight Infants (VLBW) (Sullivan, 2010; Hair, 2015; Assad, 2015; O’Connor, 2018) as well as improvements in feeding tolerance. Specifically, decreased incidence of BPD has been associated with EHMD. We report a novel association of earlier, rapid EHMD feeding with a lower incidence of BPD.

Post hoc analysis of raw data from three recent publications (Sullivan, 2010; Hair, 2014; Assad, 2015). VLBW infants received very early BM feedings and also EHM, and so an was performed in an attempt to describe the possible association with BPD. Day of 1st feeding and age at full feeding (150ml/kg/d) were the primary variables of investigation. Data analysis consisted of Wilcoxon rank-sum tests for unadjusted comparisons between the BPD and non-BPD groups and multivariate logistic regression for adjusted comparisons.

In the Sullivan, 2007 trial, delay in first enteral feed and increased days to full feeds were both related to the development of BPD. This effect was not seen in the cow milk fed group. In the retrospective Assad study, infants were started on feeds earlier than in Sullivan. This post hoc analysis showed a significant association between feeding and BPD in both the EHMD and bovine groups with increased time to full feeds. In the Hair, 2014, all infants received EHMD, but there was a significant decrease in days on TPN in infants without BPD. This can arguably be a surrogate marker for days to full feeds. A logistic regression model relating BPD to day of 1st feeding or age at full feeding on data from Sullivan, 2007 revealed a 9.9% increase in the odds of developing BPD for every day longer to first feed and a 5% increase for every day longer to full feeds.

There is an association of early enteral feeding and fairly rapid advancement to full feeds and a decreased incidence of BPD. Exclusive human milk intake may enhance to that effect.
Derangement in vital signs are known antecedents of clinical deterioration. This underlies Early Warning Systems (EWS), which detect patient deterioration and trigger responses such as a Medical Emergency Team (MET) attendance. In Victoria, the Victorian Children’s Tool for Observation and Response (ViCTOR) Special Care Nursery (SCN) observation chart has been proposed as the standard of care for infants admitted to a SCN. Its predictive utility has however not been previously validated. The aim of this study was to therefore assess the ViCTOR SCN MET call criteria’s predictive utility.

A prospective study was designed and carried out over a two month period in 2018. Parameters (heart rate, oxygen saturation, respiratory rate) for admitted SCN infants with a length of stay > 24 hours were continuously recorded from every bedside monitor using the Draeger eData-grabber program. Temperature, blood pressure, infant skin color, level of activity and blood glucose measurements were also retrospectively collected from standardised nurse observation recordings. The ViCTOR parameter thresholds were then applied to the dataset, and analysed against outcomes, defined as any clinical deterioration event. The correlation of derangements in parameters with outcomes was then used to calculate predictive utility. Data analysis was performed using MATLAB, Stata and MS-Excel.

Over the data collection period, data was recorded for 214 infants. 60 patients recorded 93 episodes of clinical deterioration, the majority of which were respiratory decompensations. 80% of these events had >1 documented antecedent. The current ViCTOR MET call criteria mandate a MET response when three vital signs breach a predefined threshold. This criterion showed a sensitivity of 93.9% [84.99, 98.30] and a specificity of 66.7% [57.83 to 74.72].

The current ViCTOR SCN MET thresholds have a sensitivity of 93.9% and a specificity of 66.7%, making it an appropriate screening tool for patient deterioration.

**IMAGE / TAB:**
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**IMAGE / TAB CAPTION:** Table 1. Predictive utility of the selected ViCTOR SCN Chart MET Criteria

**COI:** None declared
ID: 921

TITLE: PREDICTION OF SIGNIFICANT HYPERBILIRUBINEMIA USING AN ARTIFICIAL INTELLIGENCE APPROACH

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CONTENT:

Prediction of significant neonatal hyperbilirubinemia is classically based on hour-specific nomograms of total serum or transcutaneous bilirubin (TcB). However, the clinical performance of such tools is limited, mainly due to their inability to adjust for the numerous confounding factors related to neonatal jaundice. Machine learning represents an ideal method for approaching tasks that involve multiple and interacting classifiers. The purpose of the present study was to explore whether artificial intelligence can be applied to predict significant hyperbilirubinemia during the first 120 hours of life in healthy term and late-preterm neonates.

A computer model was developed using a database of 6,869 healthy newborns (gestational age [GA] ≥35 weeks) with a total of 35,648 serial TcB measurements at 12 ± 2, 18 ± 2, 24 ± 4, 36 ± 4, 48 ± 4, 60 ± 4, 72 ± 4, 96 ± 4 and 120 ± 6 postnatal hours. The outcome of interest consisted of significant hyperbilirubinemia (i.e., need for phototherapy) according to the hour-specific nomograms of the American Academy of Pediatrics. Sex, birthweight, GA, mode of delivery, ABO and Rh incompatibility, feeding method and daily weight loss were included as confounders. A multi-class classification approach was applied; for each iteration, an initial pool of 6,180 randomly selected samples was used for training and the rest for a 10-fold validation. The model was developed in MatLab.

The overall predictive ability of the model (at least 2 serial TcB measurements) was excellent, with an AUC of 0.98 at 24 postnatal hours and > 0.99 after 36 postnatal hours. A single TcB measurement at 24 hours had an AUC of 0.97 for predicting significant hyperbilirubinemia up to 48 postnatal hours, and an AUC of 0.91 for predicting significant hyperbilirubinemia up to 72 postnatal hours (Figure 1). The addition of a second TcB measurement at 36 or 48 postnatal hours would increase the AUC of the latter to 0.950 and 0.98, respectively (Figure 1).

Artificial intelligence can be used for the accurate prediction of significant hyperbilirubinemia during the first 120 hours of life in healthy term and late-preterm neonates. Our results suggest that machine-learning models are able to reflect the dynamic characteristics of neonatal bilirubinemia and, thus, may assist health care professionals in implementing individualized follow-up strategies for jaundiced neonates.

IMAGE / TAB: https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=bc6aa547be229de9d2ac5608b872234c-MjAxOS0wNSM1Y2UyNjY2ZDI2Y2Vj

IMAGE / TAB CAPTION: Figure 1. Predictive ability of the artificial intelligence model

COI: None declared
ID: 924
TITLE: THE EFFECT OF RESPIRATORY MANAGEMENT VARIATIONS ON BRONCHOPULMONARY DYSPLASIA IN EXTREMELY PRETERM INFANTS
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CONTENT:

Recent comparisons between different national neonatal registries have shown variations in clinical outcomes such as survival and bronchopulmonary dysplasia (BPD). There is often greater inter-centre variability in terms of clinical practices and respiratory management strategies, which warrants further investigation of how these variations influence neonatal outcomes, in particular BPD. The aim of this study was to evaluate if different respiratory management styles exist between two neonatal units in differing healthcare systems and if variations in respiratory management strategies for extremely preterm infants have any effect on the risk of BPD outcome or mortality.

A retrospective cohort study was conducted for all extremely preterm infants admitted to Monash Newborn at the Monash Children’s Hospital (Melbourne, Australia) and the Oxford Newborn Care Unit at the John Radcliffe Hospital (Oxford, United Kingdom) over a period of three years, from 2015 to 2017 inclusive. Statistical analysis was performed using Stata/IC Version 14.0 for Mac (StataCorp LLC 2015: Texas, USA). To compare two independent population medians, the two-sample Wilcoxon rank-sum test was used and for categorical data, the chi-squared test was performed. Multiple logistic regression was performed to analyse the contribution of various determinants on the development of BPD. A total of 492 infants were included in the study – 310 from Oxford and 182 from Monash.

The overall incidence of BPD for extremely preterm infants was 62.20%. There was a significantly higher crude mortality rate at Oxford compared to Monash (6.59% at Monash vs. 16.45% at Oxford, p=0.002). There was no difference in terms of the combined outcome of BPD or mortality between study sites (70.88% at Monash vs. 76.45% at Oxford, p=0.172). Oxford had significantly higher rates of intubation at resuscitation, surfactant administration and use of nitric oxide. Monash used nasal CPAP and parental nutrition more frequently than Oxford. Independent risk predictors for the development of the combined outcome (BPD or mortality) included the use of nitric oxide (adjusted odds ratio 18.257, 95% CI 2.358-141.337, p=0.005), days on mechanical ventilation (adjusted OR 1.134, 95%CI 1.074-1.197, p=0.000) and days on high flow oxygen therapy (adjusted OR 1.017, 95% CI 1.002-1.034, p=0.029).

Bronchopulmonary dysplasia remains a significant cause of neonatal morbidity amongst extremely preterm infants. Despite significant differences in clinical practice, both units had similar rates of the composite outcome (BPD or mortality). Use of nitric oxide, days on mechanical ventilation and days on high flow oxygen were independent predictors of the primary outcome.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 927

TITLE: Hemodynamic effects of PDA closure in stable preterm infants in the first 72 hours of life: a longitudinal study using echocardiography and non-invasive cardiac output monitoring

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CONTENT:

The pathophysiological consequences of a PDA in preterm infants are well known. However, PDA management remains controversial. The natural history of PDA has been studied but on specific postnatal days. This study investigated the longitudinal effect of PDA over the first 72 hours of life.

A prospective observational study was performed in the neonatal service of Tygerberg Children’s Hospital, Cape Town, South Africa to determine the accuracy of bioreactance measured non-invasive cardiac output, as compared to transthoracic echocardiography. All infants underwent 6-hourly TTE and CUS with continuous bioreactance monitoring during the first 72 hours of life. LVO, RVO and SVC flow were measured according to standard methods. In this sub-study, infants with PDA’s were identified. Numerous hemodynamic and cerebral perfusion parameters were compared pre and post PDA closure. Hemodynamic and cerebral perfusion parameters in infants with open or closed PDA at 72 hours of life were also compared.

48 Infants with ductal closure and 7 infants with an open PDA at 72hrs of life were identified. Pre/post PDA comparison: PDA closed at a mode of 18 hrs (IQR 12-30 hours) with an average pre-closure PDA size of 0.17±0.06cm pre-closure. No statistically significant factors were found in cardiovascular parameters, respiratory parameters, TTE parameters, bioreactance parameters or cerebral perfusion parameters. CUS EDV difference between pre and post-PDA closure was the only significant factor (p=0.006) with PEEP level reaching borderline significance (p=0.068). Open/closed PDA at 72hours of life: No significant cardiovascular, respiratory, cerebral circulation or TTE or BR factors were identified. LVO had borderline significance (p=0.081) with higher cardiac output in infants with an open PDA (147.6ml/kg/min vs 124.1ml/kg/min, respectively).

In a stable preterm infants in the first 72 hours of life, the presence of an open or closed PDA did not affect respiratory, cardiovascular or cerebral perfusion parameters. Infants with an open PDA at 72hours of life had a higher LVO.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: Amayezu Medical, South Africa, loaned the NICOM Reliant machines and provided sensors for the study. No financial aid was provided in any form.
ID: 933  
TITLE: NEONATAL INTUBATION SUCCESS RATES AMONG PAEDIATRIC TRAINEES  
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CONTENT:  
Neonatal intubation is a mandatory competency for paediatric trainees. It is however a challenging skill to learn and maintain, and one with risk of serious complications. Advances in obstetric care, discontinuation of routine intubation for infants born through meconium stained liquor, increased use of non-invasive respiratory support, less invasive surfactant administration and increased numbers of trainees have all resulted in fewer opportunities to learn and practice intubation. Success rates have been reported to be falling and the likelihood of infants requiring multiple attempts at intubation rising. We sought to measure intubation success rates in three sites in the United Kingdom.  

Over a 12 month period, May 1st 2018 until April 30th 2019, information was collected prospectively about all intubations carried out in one level three and two level two neonatal units in the United Kingdom. The setting and indication for each intubation, the level of experience of the intubator, the equipment and premedication used, the weight, corrected gestation and physiological stability of the infant for each attempt were recorded. Data sheets were completed after each intubation by the intubator. Patient notes, x-rays and electronic notes were checked weekly by study investigators to ensure all intubations were included. Primary outcome was the first attempt intubation success rate.  

There were 140 intubations during the 12 month period across the three sites. First attempt success rate overall was 55% (77/140) and 48% (16/33), 54% (25/46) and 59% (36/61) in the three different sites. First attempt intubation success rate for intubations during stabilisation at delivery without premedication was 45% (20/44). First attempt intubation success rate for elective premedicated intubations in the neonatal intensive care unit was 59% (56/95). Success rates by level of intubator are displayed in Table 1; junior trainees have 1-3 years of paediatric experience and middle grade have 4-6 years experience. The median number of attempts before successful intubation was 1, with a range of 1 – 7 attempts. There were 34 occasions (24% of intubations) where 3 or more attempts were necessary before successful intubation.  

Rates of neonatal intubation on first attempt are low across junior and middle grade paediatric trainees especially for emergency non-premedicated intubations. This highlights a requirement for high quality teaching of this skill to all levels of trainee in the neonatal unit before progressing to more challenging emergency intubation. The middle grade group require plentiful opportunity to intubate as success rates are similar to junior trainees.  

IMAGE / TAB:  
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=fd03248c844061001f1ace42988599d2-MjAxOS0wNSM1Y2UyNjY2ZDZhMzIz  

IMAGE / TAB CAPTION: Table 1; Success rates by level of intubator  

COI: None declared.
ID: 936

TITLE: Reduction in antibiotic therapy and safety associated with early-onset neonatal sepsis calculator use - A systematic review and meta-analysis

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CONTENT:

Empiric antibiotic therapy of newborns at risk for or with suspected early-onset sepsis (EOS) is a main contributor to overuse of antibiotics early in life. The neonatal EOS calculator is a clinical risk stratification tool, which is being adopted to guide and reduce the use of these empirical antibiotics. However, evidence on the effectiveness and safety of the EOS calculator is essential in order to inform clinicians considering implementation. The objective of this study was to assess effectiveness in reduction of antibiotic therapy and safety of management guided by the EOS calculator compared to conventional management strategies.

We searched MEDLINE, EMBASE, Web of Science and Google Scholar from 2011 (EOS calculator model introduction), through January, 2019, and included original data studies comparing management guided by the EOS calculator to conventional management strategies for allocation of antibiotic therapy to newborns with suspected EOS. The main outcome was the relative reduction in newborns treated with empirical antibiotics for suspected or proven EOS between management guided by the EOS calculator and conventional management strategies. Outcomes regarding safety involved missed EOS cases, readmissions, treatment delay, morbidity and mortality. Meta-analysis was conducted for those studies with separate cohorts for EOS calculator and conventional management strategies, using a random effects model.

Thirteen studies were included, which analyzed a total of 175 752 newborns. All found a substantial relative risk reduction (RRR) in empirical antibiotic therapy (range, 39.8 to 97.5%), favoring the EOS calculator. Meta-analysis of 6 observational studies (including more than 170 000 newborns) comparing use of antibiotics before and after implementation of the EOS calculator yielded a RRR of 44% (95% CI; 41-47%), Figure 1. For the 2 studies restricted to chorioamnionitis-exposed newborns, the RRR in antibiotic use was larger (80%), but with a large 95% CI (9-96%). There was limited evidence on safety outcomes, but the proportions of EOS cases missed were similar between management guided by the EOS calculator (5 of 18, 28%) and conventional management strategies (8 of 28, 29%) (pooled odds ratio 0.96, 95% CI; 0.26-3.52; P=.95).
Management guided by EOS calculator is associated with a substantial reduction in empirical antibiotics for suspected EOS. There is limited evidence regarding safety of the EOS calculator, but the available evidence contains no indications of inferiority when compared to conventional management strategies.

**IMAGE / TAB:**
https://www.eiseverywhere.com/eeselectv3/v3/events/351149/submission/files/download?fileID=df1c1e0cf7efc392bde9514d197b5c37-MjAxOS0wNSM1Y2UyNyY2ZDjIMtg5

**IMAGE / TAB CAPTION:** Forest plot presenting relative risk reduction in use of empirical antibiotics. Data presented for before-after studies included in the meta-analysis. Data were pooled under the assumption of a random effects model.

**COI:** None declared
ID: 938

TITLE: INFLUENCE OF TIME AND MATERNAL CHARACTERISTICS IN THE COMPOSITION OF VERY PRETERM HUMAN MILK

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CONTENT:

Very Premature Infants (VPI) frequently experience growth failure in early neonatal life, partially due to inadequate nutrient supply, which, after an initial period of parenteral nutrition, mostly depends on human milk. Variations in macronutrient content in breast milk related to maternal characteristics has been described in mothers of term infants and might play a role, helping to identify babies at higher risk. The aim of this study was to analyze milk macronutrient composition from mothers of Very Premature Infants during the first weeks of life and identify relationships between macronutrient concentration and maternal characteristics.

Mothers and Very Premature Infants were recruited if milk production was in excess of their baby feeding volumes. The present report represents a section of a broader study looking for influence of milk components on growth of Very Premature babies, and because of this major malformations, chromosomal diseases, congenital metabolic disorders or poor chance of survival were exclusion criteria. Aliquots from 24-hour milk pools were used to measure composition with the mid-infrared technique (MIRIS Human Milk Analyzer®, Uppsala, Sweden). Demographic, anthropometric, clinical, general health and obstetric data were collected from clinical charts or through maternal interview. The generated data were analysed with SPSS (Social Package for Social Sciences) v25.

103 mothers participated in the study. Of them, 31.9% were overweight or obese. Twenty one (20.4%) delivered twins and 20 (19.4%) had a diagnosis of IUGR. Mean gestational age (GA) was 28.5±2.5 weeks. A total of 590 milk samples were analyzed. Between weeks 1 and 6 carbohydrate concentration increased (7.1±0.6g/100mL vs 7.4±0.5, p<0.0001) and protein decreased (1.9±0.4g/100mL vs 1.3±0.2, p<0.0001). Milk from mothers with a BMI ≥25 had a higher protein content on week 4 (1.5±0.3g/100mL vs 1.3±0.2, p=0.008) but not on week 1. Fat (3.4±1.1 vs 4.2±1.3g/100mL) and energy were lower on week 1 in mothers of IUGR babies and protein was slightly lower (weeks 1 and 4) in mothers of multiples (1.7±0.2 vs 1.9±0.4g/100mL, p=0.026 and 1.3±0.1 vs 1.4±0.3g/100mL, p= 0.003). We found no differences in relation to other maternal or obstetric characteristics (GA, breast surgery, previous breastfeeding).

Very preterm milk changes composition along the first few weeks postpartum. Although our results are in line with previously reported average figures, individual variation in very preterm milk macronutrients is high and maternal health/anthropometric and obstetric characteristics can have an impact in the macronutrient composition of their milk. Awareness of these facts may help improve nutrient supply in premature nutrition.

COI: None declared
ID: 944

**TITLE:** INTENSITY OF PERINATAL CARE FOR EXTREME PRETERM BABIES AND OUTCOMES AT A HIGHER GESTATIONAL AGE

**AUTHORS:** Andrei S. Morgan (1,2,3); Babak Khoshnood (1); Caroline Diguisito (1,4,5); Laurence Foix-L’Helias (1,6,7); Laetitia Marchand-Martin (1); Monique Kaminski (1); Jennifer Zeitlin (1); Gérard Bréart (1); François Goffinet (1,8); Pierre-Yves Ancel (1,9)

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**CONTENT:**

Perinatal decision-making affects outcomes for extremely preterm (EP) babies (22-26 weeks gestational age (GA)): units with more active care have improved survival without increased morbidity. Such units may gain skills and expertise that mean babies at a higher GA also have better outcomes than if they were born elsewhere. We examine whether there are differences in survival and sensorimotor (blindness, deafness or cerebral palsy) disability at age 2 for babies born at 27-28 weeks GA in relation to the intensity of perinatal care (IoPC) provided to EP babies. We hypothesised there would be higher survival without increased morbidity for babies born in units with a higher IoPC for EP babies.

Fetuses from the 2011 French national prospective EPIPAGE-2 cohort, alive at maternal admission to a level 3 hospital and delivered at 27-28 weeks GA, were included. Sensorimotor disability and Ages & Stages Questionnaire (ASQ) result below threshold among survivors were primary and secondary outcomes. Survival and morbidity-free survival were also examined. IoPC level was based on birth hospital (3 groups using the ratio of 24–25 weeks GA babies admitted to neonatal intensive care to foetuses of the same GA alive at maternal admission). Multiple imputation was used for missing data; hierarchical logistic regression was used to account for births nested within centres. Sensitivity analyses used ratios based upon antenatal steroid usage, Caesarean section, and newborn resuscitation rates.

At 27-28 weeks, 633 of 747 fetuses (84.7%) survived to age 2 (179/214 in low, 210/249 in medium and 244/284 in high IoPC hospitals). There were no differences in sensorimotor disability (adjusted odds ratio (aOR) 2.02 (95% CI 0.66-6.13) and 1.68 (0.53-5.28) in medium and high compared to low IoPC hospitals) or ASQ below threshold (aOR 1.09 (0.59-2.01) in medium, 1.16 (0.62-2.16) in high IoPC hospitals). Units with different IoPC levels had unchanged survival (medium: aOR 0.96 (0.54-1.71); high: 1.12 (0.63-2.00)) and morbidity-free survival (medium: 1.09 (0.59-2.01); high: 1.16 (0.62-2.16)). Sensitivity analyses were consistent: aORs for sensorimotor disability in medium and high IoPC hospitals for antenatal steroids were 1.10 (0.35-3.42) and 1.16 (0.44-3.01), for Caesarean section 0.98 (0.40-2.40) and 0.49 (0.14-1.71), and for neonatal resuscitation 1.76 (0.59-5.25) and 1.46 (0.50-4.33).

We found no difference at 2 years of age in sensorimotor disability or presence of an ASQ below threshold for survivors born at 27-28 weeks GA in hospitals with differing IoPC for EP births. We also found no difference in overall survival or morbidity-free survival among fetuses alive at maternal admission to hospital. We conclude there is no evidence for an impact of the IoPC for EP babies on births at a higher gestational age.
COI: None declared.
ID: 947  
TITLE: PROTECTION OF THE FETAL GUT AGAINST UREAPLASMA-INDUCED CHORIOAMNIONITIS: A POTENTIAL ROLE FOR PLANT STEROLS  
AUTHORS: Charlotte van Gorp 1,†, Ilse H. de Lange 1,2,†, Owen B. Spiller 3, Frédéric Dewez 4, Berta Cillero Pastor 4, Ron M. A. Heeren 4, Lilian Kessels 1, Nico Kloosterboer 1, Wim G. van Gemert 2, Michael L. Beeton 5, Sarah J. Stock 6, Alan H. Jobe 7, Matthew S. P  
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CONTENT:  
Chorioamnionitis, clinically most frequently associated with Ureaplasma, is linked to intestinal inflammation and subsequent gut injury. No treatment is available to prevent chorioamnionitis-driven adverse intestinal outcomes. Evidence is increasing that plant sterols possess immune-modulatory properties. Therefore, we investigated the potential therapeutic effects of plant sterols in lambs intra-amniotically (IA) exposed to Ureaplasma.  
Fetal lambs were IA exposed to Ureaplasma parvum (UP) for six days from 127 d–133 d of gestational age (GA). The plant sterols β-sitosterol and campesterol, dissolved with β-cyclodextrin (carrier), were given IA every two days from 122 d–131 d GA. Fetal circulatory cytokine levels, gut inflammation, intestinal injury, enterocyte maturation, and mucosal phospholipid and bile acid profiles were measured at 133 d GA (term 150 d).  
IA plant sterol administration blocked a fetal inflammatory response syndrome. Plant sterols reduced intestinal accumulation of proinflammatory phospholipids and tended to prevent mucosal myeloperoxidase-positive (MPO)+ cell influx, indicating an inhibition of gut inflammation. IA administration of plant sterols and carrier diminished intestinal mucosal damage, stimulated maturation of the immature epithelium, and partially prevented U. parvum-driven reduction of mucosal bile acids.  
In conclusion, we show that β-sitosterol and campesterol administration protected the fetus against adverse gut outcomes following UP-driven chorioamnionitis by preventing intestinal and systemic inflammation.
COI: None declared
ID: 948
TITLE: Palliative Care Services for the Perinatal Population in Switzerland
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CONTENT:
Despite major diagnostic and medical advances in perinatal medicine, nearly 40% of all childhood deaths in Switzerland occur in the first four weeks of life, making neonates the largest subgroup. While there is a body of knowledge about key elements of perinatal palliative care (PC), evidence shows the inconsistency and fragmentation in the application of PC principles for this patient group. Although many recommendations advise what health care professionals (HCPs) should do, there is little data on how HCPs actually proceed in perinatal PC.

It is, therefore, the goal of this study (1) to explore existing local guidelines with a documentation analysis and (2) to assess the structure of perinatal PC services through a questionnaire across Swiss perinatal centres. In a first step, we performed a quantitative content analysis on protocols, concepts and hospital guidelines concerning perinatal PC in the nine perinatal centres. In a second step, we sent out a questionnaire to neonatal HCPs in each centre. The survey was distributed randomly to allow for participant anonymity. Analyses were carried out using Stata 15.1 (StataCorp LP, College Station, TX).

Documentation of internal hospital guidelines, protocols and concepts illustrated concepts and topics such as symptom management, advance care planning, end-of-life care, loss and grief, and social and spiritual support. Whereas the survey collected data about personal views on perinatal PC, the hospitals approach on implementation of perinatal PC and each HCPs satisfaction with the execution of perinatal PC in its centre.

In this study, we have taken a first step in gathering national data on how HCPs actually proceed in the practice of perinatal PC. Showing gaps in the implementation of perinatal PC, the gathered knowledge can undergird national clinical guidelines, so that families could benefit from consistent care as well as strengthen perinatal PC nation-wide.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 953  
TITLE: THE IMPACT OF FEEDING REGIMES ON ENDOGENOUS LEVELS OF IGF-1 IN THE PRETERM RABBIT PUP  
AUTHORS: William Hellström 1; Kristbjorg Sveinsdottir 2; Suvi Vallius 2; Susanne Grönlund 2; Helena Karlsson 2; Matteo Bruschettini 2; David Ley 2  
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CONTENT:

Serum levels of insulin growth factor 1 (IGF-1) are low in the preterm infant compared to term. IGF-1 is linked to metabolic and neuro-developing pathways and brain growth, and the role of IGF-1 on organ development has been widely investigated. Due to lagomorphs comparably late cerebral development and early lung development in fetal life, the preterm rabbit model serves as an excellent platform for research addressing preterm brain development and injury. The aim of this investigation was to evaluate serum levels of IGF-1 in two different feeding regimes of potentially central importance during early postnatal development.

In total 70 preterm rabbit pups were included, 38 in the wet nurse (W) regimen and 32 in the formula fed (F) regimen. 46 term pups were included. Preterm pups were delivered by C-section at E29 (three days prior to term age). Blood samples were collected at E29, P0 (=3 days after C-section), P2, P5, P9 and P10 and serum concentration of IGF-1 was determined with ELISA. In W, pups were given 0.5 ml of bovine colostrum once and then placed with a foster doe in a litter size ranging from 7-8 pups in total. In F, pups were hand-fed with kitten-milk replacement formula, using a 3.5 Fr feeding tube; the first feeding at 2 h of age at a volume of 1 mL and then every 12 h achieving an incremental increase from 70 to 250 ml/kg/d. The term pups were housed with and received milk from their mothers.

Serum levels of IGF-1 at day E29, P0, P2, P5, P9 and P10 are illustrated in Figure 1. Serum levels were significantly lower in the formula fed group compared to preterm pups in the wet nurse nutritional regime at P0 (p=0.001) and lower compared to term pups at P0, P2, P9 respectively (p=0.021, p=0.001, p=0.004). Preterm pups fed by wet nurse exhibited levels of IGF-1 corresponding to those of healthy term pups when adjusting for gestational age. Serum levels of IGF-1 correlated with weight development irrespective of nutritional regime; formula fed preterm pups (p=0.006, rSpearman=0.487), pups fed by wet nurse (p=<0.001, rSpearman=0.950) and term pups (p=<0.001, rSpearman=0.843).

Serum levels of IGF-1 were clearly affected by feeding regime in preterm rabbits showing that clinically relevant modifications of feeding and nutrition have a strong potential to modify alterations in the central IGF-1 pathway normally associated with preterm birth. Continued study will address several potentially influencing components of maternal care beyond those of nutritional content.

IMAGE/TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=228d4aaf8986490f3c4289c739a478d0-MjAxOS0wNSM1Y2UyNjY2ZDMwNjNj

IMAGE/TAB CAPTION: Serum levels of IGF1 in the wet nurse nutritional regimen were low and comparable with endogenous levels of IGF-1 in term pups adjusting for age. Rabbit pups in the formula fed nutritional regimen had significantly lower levels of serum IGF-1. Error bars represent 95% CI. IGF-1 = Insulin like growth factor 1, CI = confidence interval

COI: None declared
ID: 956

TITLE: OBJECTIVE PHARMACODYNAMIC EVALUATION OF DOXAPRAM THERAPY IN PRETERM INFANTS

AUTHORS: Jarinda Poppe 1; Willem van Weteringen 2; Swantje Völker 3; Sten Willemsen 1,5; Tom Goos 1,4; Irwin Reiss 1; Sinno Simons 1

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CONTENT:

Pharmacodynamic evaluation is very challenging in newborn infants. It is often based on subjective, intermittent human interpretation of clinical and physiological parameters. Continuously available physiological monitor data provide the exciting opportunity of continuous and objective drug evaluation. This concept is potentially very relevant for the evaluation of doxapram therapy, a respiratory stimulant to avoid mechanical ventilation and adverse outcomes of hypoxemia in preterm infants. The aim of the study was to evaluate the pharmacodynamics of doxapram therapy using continuously available physiological and ventilatory parameters.

Preterm infants admitted to a level III NICU centre who received doxapram therapy were eligible for inclusion. Stored physiological and ventilatory parameters were analysed. Additionally, the oxygen saturation (SpO2)/fraction of inspired oxygen (FiO2)-ratio and the area under the 89% SpO2 curve (duration x depth of SpO2 dips) were calculated. Trends (mean ± SD) of all parameters were visualized to evaluate the therapy effects. Logistic regression analyses were performed to predict therapy failure (intubation or death) or success per hour in the 2 days around therapy start.

The first episode of doxapram therapy was analysed in a total of 61 preterm infants with a median postmenstrual age at therapy start (PMA) of 28.7 weeks (Q1-Q3: 27.6-30.0). The success rate of doxapram therapy was 57%. In 11% of the patients therapy failed within 24 hours. The effects of doxapram were clearly present in the trends of the SpO2/FiO2-ratio and the Area under the SpO2 curve (Figure 1). Out of all parameters, the SpO2/FiO2-ratio showed to be the most indicative of therapy outcome. The predictive models in the 2 days around therapy start included therefore the SpO2/FiO2-ratio, corrected for the PMA. According to the relative quality of the models, therapy outcome can be predicted best at 10 hours after therapy start (AUC of 0.83). The SpO2/FiO2-ratio was inversely associated with therapy outcome (OR 0.30, CI 95% 0.13-0.64; p < 0.01).

The effects of doxapram can be clearly observed in the trends of the SpO2/FiO2-ratio and the Area under the SpO2 curve. The SpO2/FiO2-ratio at 10 hours after doxapram start is the most predictive of therapy failure or success. The use of continuous physiological data provides a new method for objective evaluation of neonatal therapy.

IMAGE / TAB:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=31ee06c61322bfc7b5bcbcd5b9a49d-MjAxOS0wNSM1Y2UyNjY2ZDMxY2Qx

IMAGE / TAB CAPTION: Figure 1. The trend in the SpO2/FiO2-ratio and the Area under the SpO2 curve from 7 days before until 14 days after therapy start.
COI: None declared
ID: 958

TITLE: CYTOKERATIN FRAGMENT 21-1 IS ASSOCIATED WITH MORTALITY AND LONG-TERM OXYGEN THERAPY IN NEONATES WITH CONGENITAL DIAPHRAGMATIC HERNIA.

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CONTENT:

Lung hypoplasia is a major contributor to morbidity and mortality in neonates with congenital diaphragmatic hernia (CDH). Therefore, CDH newborns are at high risk for ventilator-induced lung injury. The cytokeratin fragment 21-1 (C21-1) is part of the pulmonary cytoskeleton, providing cell stability and cell-to-cell communication. An increased detection of circulating C21-1 might be associated with poor outcome in CDH neonates. Aim of this study was to investigate the prognostic role of C21-1 in CDH neonates.

CDH neonates treated in our department 2014-2018 were eligible for prospective enrollment. C21-1 was measured from arterial blood using electroluminescence immunoassay at the age of 6, 12, 24, and 48 hours. The primary clinical endpoint was death or oxygen dependency at day 28 (BPD). C21-1 concentration was compared in CDH neonates with and without the clinical endpoint using Mann-Whitney-Test.

90 CDH neonates were prospectively enrolled, 40 met the primary endpoint death/BPD (death n=19; BPD n=21). Patients in the death/BPD group had significantly lower lung volumes and higher proportion of intrathoracic liver herniation. C21-1 was significantly higher in the death/BPD group at 6 hours (p<0.001), 12 hours (p=0.005), 24 hours (p<0.001), and 48 hours (p90. percentile at least at one time met the clinical endpoint in 94.4% while this occurred in 31.9% of patients with C21-1 always 90. percentile) versus 13.9% (<90. percentile), respectively. A significant correlation of C21-1 with the highest oxygenation index and highest peak inspiratory pressure in the first 24 hours of life was observed.

High C21-1 levels were associated with increased incidence of death and BPD in CDH newborns and correlated well with the severity of respiratory failure. C21-1 could serve as a prognostic biomarker in high-risk neonates.

IMAGE / TAB:
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IMAGE / TAB CAPTION: Table: Baseline and outcome data

COI: None declared
ID: 960

TITLE: ANALYSIS OF LYMPHOCYTE SUBPOPULATIONS, CRP, IL-6, WBC IN PRETERM INFANTS AND MOTHERS AFTER PREGNANCIES COMPLICATED BY PREMATURE PROLONGED RUPTURE OF MEMBRANES (PPROM)

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CONTENT:

The immune system, despite an adequate number of cells, lacks of function at birth and post-natal maturation proceeds over the first months of life. In preterms their innate and adaptive immunity may be compromised by factors associated with preterm births, such as pPROM, which is responsible for approximately one third of all preterm deliveries and may present with chorioamnionitis in half cases. Prenatal exposure to environmental microorganisms can result in a systemic fetal inflammatory response and has been associated with neonatal sepsis, IVH, NEC, RDS and BPD. The aim of this study is to evaluate if changes in the neonatal immune system are comparable to those of their mothers.

The study enrolled 6 women with diagnosed pPROM and 7 preterm babies born between 23rd and 36+6th weeks of gestational age vs. controls at the NICU of the Department of Women's and Children's Health of Padua University Hospital. We obtained maternal and neonatal blood samples on a routine assessment by the first 3 days of life, testing lymphocyte subpopulations (by flow cytometry), WBC count, IL-6 and CRP levels (ELISA). The laboratory analysis of the EDTA blood and the serum samples were carried out within 24 h of sampling. Data were expressed as median. A normal p value <0.05 was considered statistically significant.

The median value of gestational age was 30+4/7 and the median of neonatal weight was 1075 gr. Preliminary data analysis showed that non-MHC-restricted cytotoxic cells and Mature CD4+ T Lymphocytes were lower in the preterm infants compared with their mothers (p<0.0001). Naïve CD4+ and CD8+ T Lymphocytes were higher in the newborn group (p<0.0001). There were no differences in the absolute count of WBC, mature T lymphocytes, Helper and cytotoxic T lymphocytes, B lymphocytes, NK cells, CD4/CD8 ratio, CRP and IL-6 between mother and babies.

Seen these differences between mother and offspring exposed to the same immunogenic stimulation, we can hypothesize that gestational age seems to be more important than immunogenic stimulation in determining the lymphocyte profile of preterm babies. We are trying to demonstrate that intrauterine inflammation could affect the immune system of the newborn, but we are still waiting for the results from the control group to confirm our hypothesis.

IMAGE / TAB:
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IMAGE / TAB CAPTION:

COI: None declared
ID: 964

TITLE: CURRENT PRACTICE IN UK: USE OF ECG DURING RESUSCITATION AND STABILISATION OF THE NEWBORN ON LABOUR WARD

AUTHORS: Avineet Kaur 1; Marika Lasokova 2; Thomas Hixson 3; Jean Egyepong 4

AFFILIATIONS: 1-4: Neonatal department, Luton and Dunstable University Hospital, United Kingdom

CONTENT:

- Heart Rate is the most important clinical parameter used in evaluation of physiological status of newborns during stabilisation/resuscitation (S/R)
- All interventions depend on it
- Use of continuous ECG (C-ECG) monitoring is: quicker to apply, detects HR quicker, more accurate, reliable and objective, solves the problem of poor perfusion and delayed pick up by pulse-oximeters (Phillipos et al, 2016)
- Therefore the current drive towards its use: International Neonatal Guidelines (Perlman et al, 2015; Wyckoff et al, 2015)- suggesting to ‘consider’ its use as part of the S/R as this has clinical, safety and risk implications (Katheria et al 2012; van Vonderen et al 2015; Mizumoto et al 2012)

To evaluate practice in UK:
- Current standard method used to assess heart rate in delivery suite
- The use of C-ECG monitoring during S/R of newborns on labour ward after delivery
- The type/make of ECG machines currently in use for this purpose

Design:
- Survey of practice in all UK Neonatal Units that provide neonatal S/R after birth
- Date: April 2019
- Telephone survey
- Sister-in-charge or Advanced Neonatal Nurse Practitioner (nursing team member involved in providing the above)/ ST1-3 or ST>4 on-call doctor on shift or consultant on the day (member of the medical team)

Questions:
1. Current standard practice used to assess heart rate at delivery (including use of pulse oximetry (Pox))
2. Use of C-ECG monitoring
3. The make of the ECG machine

- Total number of units surveyed/ contacted: 196
- All 196 gave responses
- Level 1 = 45 (23%): L2 = 95 (48.5%): L3 = 56 (28.6%)
- 95.9% use Pox and auscultation
- 27 (13.8%) units have access to ECG monitoring if required at delivery: L1 14.8%, L2 44.4% & L3 40.7%
- 10/27 of above have it on their Transport Incubator
- Number currently using C-ECG monitoring = 17 (8.6%)
- Out of the 17, 7 (41.2%) unit unsure since when using ECG, 2 (11.8%) for 5yrs
- 4 use ECG as standard practice; 10 use if prolonged resuscitation, 1 if antenatal cardiac concerns and rest have available but rarely used
- 2 units are in process of getting them
- Portable ECG monitors in use – 8x Phillips model, 2x Mindray monitor (detachable from full cardiac monitor), 1x GE healthcare medical system and rest unknown.

- Majority of UK NICUs currently use Pox for continuous HR monitoring
- C-ECG monitoring used as standard practice for S/R in only 8.6%
• Although several studies, systematic/meta-analysis cites the need for its use in S/R in delivery room, yet to be used as part of standard practice
• Would be useful to monitor future trend in line with risk and safety governance strategies and if this will change from a recommendation to a requirement

IMAGE / TAB:
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IMAGE / TAB CAPTION: Distribution of ECG monitor use on labour ward for neonatal stabilisation/resuscitation based of neonatal unit level (27Units)

COI: None declared
ID: 965

**TITLE:** CURRENT PRACTICE IN UK: USE OF END TIDAL CO2 DETECTOR OR RESPIRATORY MONITORING DURING RESUSCITATION AND STABILISATION ON LABOUR WARD

**AUTHORS:** Avineet Kaur 1; Marika Lasokova 2; Thomas Hixson 3; Jean Egyepong 4

**AFFILIATIONS:** 1-4: Neonatal department, Luton and Dunstable University Hospital, United Kingdom

**CONTENT:**

- Adequate airway management and commencing ventilation is crucial for newborn stabilisation/resuscitation (Wyllie and Carlo, 2006)
- Clinical methods to verify ETT position (i.e. air entry auscultation and vital signs improvement) may be fallible at times.
- Non-clinical methods through use of End tidal CO2 (ETCO2) and Respiratory Function Monitoring has proven to be safe, reliable and associated with faster detection of ETT position compared to clinical evaluation, effective tool for assessing accidental extubations and airway obstruction.
- There has never been any UK-wide survey of practice on its use, neither is this a recommendation in the nationally taught Newborn Life Support course.

- Telephone survey consisting of questions on standard and current practice of respiratory monitoring during neonatal resuscitation in the UK.
- Date: April 2019
- All Neonatal units in United Kingdom (UK) that provide neonatal resuscitation/stabilisation after birth were identified and contacted via telephone
  - Survey was targeted at Sister-in-charge/Senior nurse, ST1-3/ST>4 on-call doctor or consultant on the day
  - Questions were asked to assess current practice in UK Neonatal Units regarding:
    1. Use of ETCO2 monitoring during resuscitation/stabilisation in neonates on labour ward at delivery
    2. Type of ETCO2 used
    3. Use of respiratory monitoring to assess adequacy of mask ventilation and to confirm endotracheal intubation in clinical practice and for training

- Total number of units surveyed: 196 units
  - L1=45 (23%): L2=95 (48%): L3=56 (23%)

Respiratory Function Monitoring:
- 1 unit (0.51%) in UK is currently using respiratory monitoring of mask ventilation during resuscitation, however this was not for clinical indication but as part of a double blinded clinical trial
- 2 units (1.2%) had access to use of respiratory monitoring for training and education purposes.

ETCO2 monitoring:
- 189 units (96.4%) are using ETCO2 monitoring
- Equal numbers at all Levels: L1=95.5%, L2=96.8%, L3=96.4%)
- 186 (95.2%) use Calorimeters (pedi-cap); 8 (3.8%) capnometry & 2 (1.06%) other
- Of these main indication for use in 98.9% was to assess correct ETT placement.
- Other indications for ETCO2 use included assessing effectiveness of resuscitation, monitoring CO2 in babies who are intubated, ventilated and being transferred to the neonatal unit

- Respiratory Function monitoring to assess seal during mask ventilation is not widely used in UK NICUs
- Few units are looking into it for training purposes.
- 189 Neonatal Units (96.4%) currently use ETCO2 as a resuscitation tools for accurate assessment of correct ETT placement
Although use of ETCO2 monitoring does not form part of the NLS recommendations, almost all UK NICUs currently use this to ascertain correct ETT placement.

**IMAGE / TAB:**
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**IMAGE / TAB CAPTION:** Use of ETCO2 monitoring in UK in stabilisation and resuscitation of newborn

**COI:** None declared
ID: 966

**TITLE:** EFFECTS OF GLOBAL HYPOXIA-ISCHEMIA AND MESENCHYMAL STEM CELL TREATMENT ON PRETERM OVINE LUNGS

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**CONTENT:**

Perinatal asphyxia (PA) is a condition of impaired gas exchange during birth, leading to fetal hypoxia-ischemia (HI) and is associated with postnatal adverse outcomes such as hypoxic-ischemic encephalopathy (HIE) and necrotizing enterocolitis (NEC). Intravenous mesenchymal stem cells (MSC) administration showed therapeutic effects for HIE, but not in gut injury after HI in animal models. Few data are available about the effects of global HI on fetal lungs and the potential role of MSC cells. The aim of this study was to assess inflammatory and lung maturation effects after global HI and the potential role of intravenously delivered MSCs in an ovine model of global HI.

In a preclinical ovine model, 28 fetuses at gestational age of 106d were randomized in 4 arms in which either umbilical cord occlusion (UCO) or sham was performed for 25 min followed by intravenous administration of either MSC cells (2x106/kg) or saline. The fetuses were euthanized 7d after UCO or sham. Lungs were stained for CD3 and MPO as inflammatory markers for T lymphocytes and neutrophils/macrophages, respectively. Additionally, the mRNA levels of the following cytokines were assessed IL-1, IL-6, IL-8, IL-10. To assess lung maturation, we measured surfactant protein (SP)-A, -B, -C, -D mRNA levels and SP-B concentrations.

Total number of MPO+ and CD3+ cells in lungs did not differ between HI and control group. IL-1, 6, 8 mRNA levels were not statistically different between the groups. IL-10 mRNA was 4 fold higher in HI-MSC group than in control (p<0.05). The
surfactant protein mRNA levels (SP-B) were increased in UCO group with MSC treatment. SP-B protein concentrations were increased after UCO. The intravenous administration of MSC did not change the increase of SP-B protein after UCO.

Global HI in combination with intravenous MSC cells administration induced increases in surfactant protein B concentrations and mRNA levels in the absence of inflammatory changes. Additional experiments are needed to understand the effects of systemic MSC in HI on the fetal lung.

IMAGE / TAB:

IMAGE / TAB CAPTION:

COI: None declared
ID: 973

**TITLE:** THE IMPACT OF MAGNESIUM SULFATE-ENHANCED THERAPEUTIC HYPOTHERMIA ON SELECTED BIOCHEMICAL MARKERS OF ASPHYXIA IN NEONATES WITH HYPOXIC-ISCHEMIC ENCEPHALOPATHY.

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**CONTENT:**

In recent years therapeutic hypothermia has become a standard method of neonatal hypoxic-ischemic encephalopathy treatment. At present, research focuses on finding ways to increase the therapeutic effect of hypothermia. Magnesium sulfate is promising as a potentially neuroprotective drug. It is possible that magnesium sulfate, used together with therapeutic hypothermia, may enhance its beneficial effect. Magnesium sulfate is a very interesting option as a neuroprotective drug also because of its easy availability. The drug can be administered to the patient in the birth hospital while the neonate is being prepared for the transport to the center with therapeutic hypothermia.

Prospective RCT was conducted at three perinatal centers. Neonates born at ≥36 GA, with perinatal asphyxia and confirmed moderate or severe HIE were included to the study. All neonates were treated with therapeutic hypothermia (for 72 hours). Neonates in study group (TH+MG) received three doses of MgSO4 (250 mg/kg) as iv infusion in addition to therapeutic hypothermia. Serum Mg level was analyzed in the 1st, 2nd, 4th day of life, whereas S100B protein, ceruloplasmin, MDA and iron serum concentration were assessed in the 1st, 2nd, 6th day of life. All measurements in the blood samples (except the Mg and iron concentrations) were assessed in the central laboratory. For this purpose blood serum frozen at -70°C was sent by a special transport dedicated for bioassays under cooling conditions.

There were 37 study subjects in the control and 38 in the study group. No statistically significant differences according to demographic data and clinical characteristic between the groups were observed. The body weight (mean, ± SD) was 3173.8 ±590.5g and 3321.9±524.0g in the control and study group respectively. The GA amounted to 38.6; ±1.9, and 38.7 ±1.7 (control vs study group). In this study, 2-fold lower S100B concentrations were observed in subsequent days of treatment in group (TH+MG) Statistically significant difference was confirmed in S100B protein concentration in the 1 day of life; 9.38±11.98 vs 3.93±7.07ug/L (p-value 0.017), as well as at all the measured points considered together (S100B protein p-values 0.014). No significant differences in iron, ceruloplasmin and malondialdehyde concentrations were observed.

Magnesium sulfate is promising potentially neuroprotective drug. It is also possible that magnesium used together with therapeutic hypothermia may enhance its beneficial effect. Herein reported twofold reduction of protein S100B serum concentration, although with only tendency for statistical significance, may encourage further research on neuroprotective properties of magnesium in newborns with hypoxic ischemic encephalopathy.

**IMAGE / TAB:**
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=9609e1a0f2f2ddfbad145c56bccc8e2ac-MjAxOS0wNSM1Y2UyNjY2ZDM4Yjkr

**IMAGE / TAB CAPTION:** Comparison of biochemical markers between neonates treated with hypothermia or hypothermia combined with magnesium sulfate.
COI: None declared
ID: 981

TITLE: NEONATAL INTUBATION - UK TRAINEES' EXPERIENCE

AUTHORS: Khadija Belkhatir 1; Alexandra Scrivens 1, 2; Joyce E O'Shea 3; Charles C Roehr 1, 2.

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CONTENT:

Neonatal intubation is a delicate but often lifesaving procedure, which must be mastered during paediatric and neonatal training. However, with a practice trend towards less invasive treatment options, trainees are presented with ever fewer opportunities to practice this critical skill. Trainees' neonatal intubation success rates are reported as low as 25%. Failed intubation attempts, resulting in multiple attempts increases the likelihood of adverse events during intubation and adverse long term outcomes. Senior trainees are frequently expected to teach junior trainees how to intubate, often with little experience of the procedure themselves.

Aim: To gauge the experience level of trainee paediatric doctors (below consultant level) in the UK in performing and teaching neonatal intubation.

An online survey was sent to trainee paediatricians in the UK via deanery tutors and trainee representatives. The survey asked doctors to recall their training in neonatal intubation, experience of intubation and success rates (for term and preterm infants (<37 weeks’ gestation)) and experience in teaching others to intubate. Names and contact details of respondents were not collected. Doctors working on a tier 1 (senior house officer) rota were deemed to be 'junior trainees' and doctors working on a tier 2 (middle grade/registrar) rota deemed to be 'senior trainees'.

The survey received 728 responses. Of these, 198 were junior trainees, 73 advanced nurse practitioners, 452 were senior trainees below consultant level and 5 were consultants. 44 (6%) respondents had no experience at all of neonatal intubation. 301(42%) had performed <5 term intubations and 242 (34%) 20 term and preterm intubations were 153(21%) and 167(22%). Self-reported success rates are shown in figure 1. 66% (470) of trainees had no formal intubation training. Half (50%) of respondents regularly supervised others performing intubation. Of these, only 16% had received training on how to teach intubation. 19% of respondents reported that they felt completely confident intubating neonates. Reasons for lack of confidence included lack of opportunity to practice(63%), short neonatal rotations(15%), lack of training(24%) and competition between junior staff for limited opportunities.

Many paediatric trainees have had no formal teaching on intubation skills. With limited opportunities to practice, many report a lack of confidence in neonatal intubation and are often asked to teach a skill to others, having not fully mastered it themselves. The results will be used to develop an intubation teaching programme for paediatricians, aiming to maximise learning from limited training opportunities and improve intubation success rates.

IMAGE / TAB:

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IMAGE / TAB CAPTION: Figure 1: Respondents’ self-reported intubation success rates within 2 attempts

COI: none declared