ID: LB1
TITLE: NICU Telemedicine and Telesimulation for neonatal resuscitation
SENDER / PRESENTER: Kogoro Iwanaga,Japan

CONTENT:

In Japan, more than 10 years have passed since the initiation of the project to promote neonatal resuscitation (Japanese Neonatal Cardio-Pulmonary Resuscitation (NCPR) Project) and more than 3,000 healthworkers have been certified as NCPR instructors. Since about half of deliveries are carried out in local obstetric clinics in Japan, NCPR instructors are expected to hold NCPR course sessions in each local region and improve resuscitation skills of healthworkers engaged in delivery room in local clinics. The association for the promotion of NCPR proposed 'repetition of high-quality simulation-based education in each facility', but specific measures other than nurturing instructors have not yet been presented. In this study, we developed a educational simulation tool for the remote support of neonatal resuscitation applicable for clinical practice as a tool for the Perinatal Medical Center to educate healthworkers at community delivery facilities, and performed an operational experiment.

Seven simulation-based education tools were developed: 1) Stethoscope with a built-in speaker, 2) simulated pulse oximeter (iOS application operated using an iPad), 3) iPhone iOS application for wireless operation of 1) and 2), 4) compact camera for video recording of resuscitation training, and 5) iPad for debriefing of training. In addition, 6) a bag valve mask-equipped atmospheric pressure sensor and 7) Chest compression monitoring sensor were developed for remote evaluation of the reliability of resuscitation techniques of trainees. All these tools were wireless-linked through Wi-Fi and Bluetooth to prepare a remote support system.
To verify the efficacy and operation of this system, 64 trainees of an NCPR professional course held at Kyoto University Hospital participated in a remote scenario practice using the system described above after participating in scenario training of neonatal resuscitation in the curriculum of the NCPR course.

Scenario operation was performed 6 times and could be carried out without equipment failure. There was no two-way communication time lag and facilitation by an instructor from a remote location was mostly the same as in a normal session. The instructor could easily evaluate the skills of the trainees through a streaming video and monitoring index.

It was suggested that the system contributes to cooperation between a hospital and delivery facilities in the community. Since the real cost was low, about 300 US dollars excluding the cost of the mobile device, introduction of the system may serve as an important social foundation for regional cooperation in not only Japan but also other countries worldwide. And it can be applied to the educational system of each region. There are technical problems, such as the setup of equipment and the angle of view for video recording, but if 4)-7) of the system described above and communication environment can be prepared, remote support of neonatal resuscitation in human clinical practice may be possible.

This research and development work was supported by the MIC/SCOPE # 181607012.

ID: LB3
TITLE: Commercially Processed Donor Human Milk-Derived Products Retain a Full-Spectrum of Functionally Active Oligosaccharides
SENDER / PRESENTER: Victoria Niklas,United States

CONTENT:

Human milk (HM) contains many bioactive substances, including a family highly abundant and structurally unique glycans, called human milk oligosaccharides (HMOs). HMOs constitute the third most abundant component in HM, following lactose and fat, and are more abundant than protein. The best-characterized function of HMOs is their prebiotic activity, which supports the colonization of the gut by mutualist bacteria in the period after birth. Bifidobacterium spp. and other, commensal bacteria may reduce diseases like NEC and sepsis by supporting gut colonization by commensal bacteria over pathobionts. We sought to explore the impact of commercial vat pasteurization and ultrafiltration on the concentration, spectrum, and activity of HMO present in donor HM and a human milk-derived HM protein fortifier.

HPAEC-PAD with 11 oligosaccharide standards were used to annotate the spectrum and extrapolate the concentration of HMO extracted from native and pasteurized donor HM and a HM-derived, HM protein fortifier. I-screen assays (TNO, Zeist) were performed in triplicate using fecal matter prepared from infant, adult or aged donors. Serial dilution of a HM-extract were added from ~3.0 mg/ml to 0.03 mg HMO per well and incubated at 37C for 24 hours under anaerobic conditions. Bacterial DNA was isolated, 16S V4 rRNA amplicons prepared and sequenced using Illumina MiSeq with downstream analysis using a standardized pipeline. Assembled reads and taxonomic classification was performed using Ribosomal Database Project (University of Illinois, Urbana) with composition presented as OTU. The supernatant of individual wells was collected, and small chain fatty acids were enumerated using gas chromatography and mass spectroscopy.

We identified a similar spectrum of neutral and acidic HMO in a pasteurized donor HM, and human milk-derived HM protein fortifier similar to native donor HM tested before processing. There were no statistically significant differences in the concentration of total, neutral, or acidic HMO across the product pipeline. Statistically significant increases in OTU specific for Bifidobacterium spp. moreover, commensal Clostridial spp. were found in all fecal pools although infant fecal pools resulted in a more robust response in Bifidobacterium spp. than did fecal pools from adult or aged adults. When the composition of small chain fatty acids was analyzed, acetate and butyrate were identified in adult and aged fecal samples whereas only acetate was identified in infant fecal pools.

Commercial processing of HM, including vat pasteurization, freeze-thaw, and ultrafiltration preserves the content, spectrum, and activity of naturally occurring HMOs with ex vivo fidelity of prebiotic activity and SCFA production. Our data support that supplementation and fortification of mother's milk or donor HM complement the bioactivity of a smaller assortment of HMOs. Ongoing clinical studies to determine the impact on exclusive human milk feeding con the microbiome of preterm newborns are in progress.

ID: LB4
TITLE: Prophylactic ibuprofen in premature infants below 1250gm and 32 weeks may not protect against intraventricular hemorrhage or patent ductus arteriosus closure and may increase O2 requirement at 28 days of life.
SENDER / PRESENTER: Hadeel Atout,Israel

CONTENT:

Patent ductus arteriosus (PDA) is a common diagnosis among extreme premature infants and associated with significant neonatal morbidities. Administration of prophylaxis cyclo-oxygenase (COX) inhibitors (eg, indomethacin or ibuprofen) to promote closure of the ductus arteriosus may decrease such morbidities. Prophylaxis cyclo-oxygenase (COX) is still controversial as potential side effect of therapy and long term benefits are not clear.

To determine the effectiveness, safety and adverse effect of prophylactic ibuprofen in preterm (below 32 weeks) and/or very low birth weight infants (below 1250 gm).

This cross sectional trial at Al-Makassed Hospital NICU in Jerusalem city in which inborn preterm infants with gestational ages of < 32 weeks and birth weight below 1250 gm from January 2016 to December 2018, who received prophylactic ibuprofen within first 24 hours of life (10 mg/kg, followed by 5 mg/kg after 24 and 48 hours) compared with preterm infants of same characteristics who received nothing in that period, The decision to give ibuprofen was upon consultant opinion after discussion of the details of each case.
The primary outcome was Presence of patent ductus arteriosus (clinically symptomatic or diagnosed by echocardiography in response to clinical suspicion; secondary outcomes were mortality , bronchopulmonary dysplasia (defined as oxygen requirements at 36 corrected gestational age), severity of respiratory distress syndrome (defined as use of more than two doses of surfactant), Definitive sepsis (clinical symptoms and signs of sepsis and a positive bacterial blood culture in a specimen obtained by sterile technique), massive pulmonary hemorrhage, Intraventricular hemorrhage (IVH) (grade III or IV), oxygen requirements at 28 days' postnatal age and Necrotizing enterocolitis (NEC) (stage 2 or 3).

Forty four preterm infant were given prophylactic ibuprofen and 71 preterm with no intervention. PDA diagnosed in 14 patients (31.8%) of prophylactic ibuprofen group compared with 25 patients (35.2%) of no intervention group (control group) and P-value was 0.709. Analysis for secondary outcome showed No difference was identified for mortality (18 patient(40.9%) in prophylactic group compared with 22(31.0%) control group with P-value 0.278) , severe intraventricular hemorrhage (IVH) (5 patient(11.4%) in prophylactic group compared with 10(14.1%) of control group with P-value 0.674), definitive sepsis (18 patient(40.9%) in prophylactic group compared with 18(25.4%) of control group with P-value 0.080), or NEC (6 patient(13.9%) in prophylactic group compared with 15(21.2%) of control group with P-value 0.597). There is an increased risk of pulmonary hemorrhage (12 patients (27.3%) in prophylactic group compared with 9(12.7%) of control group with P-value 0.049), and O2 requirement at 28 days (19 patients (43.2%) in prophylactic group compared with 11(15.5%) of control group with P-value 0.001.

Prophylactic use of ibuprofen, compared to no intervention, did not result in decreasing the incidence of patent ductus arteriosus, mortality, and severe IVH with no significant increase of NEC or sepsis risks. There has been an increased risk of pulmonary hemorrhage, and O2 requirement at 28 days.

Current evidence does not support the use of Prophylactic ibuprofen for prevention of PDA in premature infants below 1250 gm and 32 weeks or prevention of morbidities associated with it.

ID: LB7
TITLE: HIGH PREVALENCE OF SUBCLINICAL VITAMIN K1 DEFICIENCY AMONG HUMAN MILK-FED PRETERM INFANTS IN EARLY INFANCY
SENDER / PRESENTER: Paul Clarke,United Kingdom

CONTENT:

Vitamin K (VK) status of preterm infants post-NICU discharge and in early infancy is unknown. Exclusive breast milk feeding is often the only factor identifiable in cases of idiopathic VK deficiency bleeding. Despite the low VK content of human milk, VK supplements are not routinely given to human milk-fed preterm infants after NICU discharge; in contrast, vitamins A, B, C, D, and E are widely given.
We examined the VK status of breast milk fed preterm infants nearing discharge and in early infancy. Our hypothesis was that, in the absence of VK supplementation, exclusively/predominantly human milk fed preterm infants have a high prevalence of subclinical VK deficiency in early infancy.

Prospective, multicentre, observational cohort study of preterm infants born <33 weeks' gestation who were exclusively or predominantly human milk fed approaching NICU discharge. We excluded infants with cholestasis. With ethics approval and parental consent, we determined VK status by assaying serum concentrations of vitamin K1 (VK1) and PIVKA-II (Protein Induced by Vitamin K Absence/antagonism of blood clotting factor II; undercarboxylated prothrombin) at two time-points: ~35 weeks postmenstrual age (PMA) for baseline VK status, and at ~2 months corrected age (CA) (primary outcome). Satisfactory VK status was taken as normal PIVKA-II (<50.9 mAU/mL); VK deficiency was taken as raised PIVKA-II (≥51.0 mAU/mL). VK status at ~2 months CA was evaluated in relation to feeding history.

45 infants recruited in four UK neonatal centres underwent VK status assessment prior to NICU discharge at median PMA 35+1 (IQR: 34+6 – 36+3) weeks, and 37 completed the study with later assessment at median CA 8 (IQR: 5-14) weeks. Prior to discharge only 1/45 (2%) was VK deficient, a baby of birth gestation 23+6 weeks aged 11 weeks postnatal with PIVKA-II 83.7 mAU/mL and undetectable (<0.1 ug/L) serum VK1. At the later follow up visit, only 12/37 (32%) remained exclusively breast milk (BM) fed, while 25/37 (68%) were formula milk (FM) or mixed BM-FM fed. Overall by 8 weeks CA, 9/37 (24%) infants had developed VK deficiency as shown by raised PIVKA-II: 8/12 (67%) BM-fed were VK deficient vs. only 1/25 (4%) FM/mixed feeding babies, p=0.0001. VK1 concentrations were significantly lower and PIVKA-II concentrations significantly higher in exclusive BM vs. FM/mixed fed babies, Table.

Table: Measures of vitamin K status of preterm infants in early infancy according to mode of feeding.

	Exclusive breast milk fed n=12	Formula/mixed fed n=25	P-value
Vitamin K_1 (µg/L)*	0.15 (<0.10–0.59) [IQR: 0.11–0.24]	1.91 (0.16–5.31) [IQR: 1.29–2.32]	<0.0001
PIVKA-II (mAU/mL)	80.8 (23.6–496.6) [IQR: 36.2–232.7]	21.2 (14.1–129.1) [IQR: 18.8–25.9]	<0.0001

Data are median (range) [IQR, interquartile range]

*VK_1 reference range: 0.15-1.55 µg/L

Preterm infants who remain exclusively human milk fed post NICU discharge are at high risk of developing VK deficiency. Routine post-discharge VK1 supplementation of preterm infants may prevent subclinical VK deficiency in early infancy.

ID: LB8
TITLE: Oral amoxicillin/clavulanic acid in near term and term newborns: do we reach target levels?
SENDER / PRESENTER: Fleur Keij,The Netherlands

CONTENT:

Background
Oral antibiotic use is scarce in neonates due to pharmacokinetic uncertainties in the first weeks of life. Amoxicillin/clavulanic acid covers most causative pathogens of early-onset neonatal sepsis, eg. group B streptococci (GBS) and E. coli. Efficacy of amoxicillin depends on time above MIC; for clavulanic acid, a target is currently lacking but its efficacy is thought to be dependent of the area under the curve (AUC). Amoxicillin/clavulanic acid has a good bio-availability in children and adults, but evidence in neonates is lacking. We evaluated the pharmacokinetics of oral amoxicillin/clavulanic acid in term newborns (0-28 days of age).

As part of a multicenter RCT evaluating neonatal intravenous-to-oral switch therapy in probable bacterial infection (1), we measured serum levels in patients allocated to the intervention group. They switched to amoxicillin/clavulanic acid suspension (25/6.25mg/kg tid), after 48 hours of intravenous penicillin/gentamicin. Two blood samples from different dosing intervals, were obtained and directly stored at -80°C. Initially, and to ensure that amoxicillin levels were attained as safety marker, levels in the second part of the timeframe (4-8h after administration) were collected. For the second batch, peak levels (1-2h after administration) were collected. Analysis was performed using Liquid Chromatography and Mass Spectrometry. For amoxicillin, an MIC of 8 mg/L for ≥50% of time was considered appropriate.

Samples of 30 patients have been analysed (mean GA 40+1 ± 1.0 weeks; mean birthweight 3641 429 grams). Patients switched to oral therapy on average after 2.5 days of intravenous therapy. Through levels (n=44) were collected 6.0±1.3h after antibiotic administration. Top levels (n=13) were collected on average 1.6±0.5h after administration (mean±S.D.). Amoxicillin levels were all above MIC of GBS (0.25 mg/L) and E. coli (8 mg/L); range: 5.4-72.9 mg/L for more than 50% of time. Clavulanic acid levels were also detected in all patients but a great variance was observed. Trough level: 1.4mg/L (0.20-4.82); top level: 1.9 mg/L (0.39-6.79); median (range). AUC's in individual patients were in range with reported AUC's in literature.

Oral amoxicillin is well absorbed in newborns leading to adequate serum levels. Oral clavulanic acid is absorbed in term newborns, but a great variance is seen. AUC's following oral administration are comparable to those of children and adults.

This trial has been registered in Clinicaltrials.gov Trial number NCT03247920
1. Keij FM, Kornelisse RF, Hartwig NG, Mauff K, Poley MJ, Allegaert K, et al. RAIN study: a protocol for a randomised controlled trial evaluating efficacy, safety and cost-effectiveness of intravenous-to-oral antibiotic switch therapy in neonates with a probable bacterial infection. BMJ

ID: LB9
TITLE: Two-year outcomes of therapeutic hypothermia in perinatal hypoxic-ischemic encephalopathy at Chiang Mai University Hospital
SENDER / PRESENTER: Varangthip Khuwuthyakorn,Thailand

CONTENT:

Therapeutic hypothermia (TH) is a standard treatment of moderate to severe hypoxic-ischemic encephalopathy, which is a consequence of perinatal asphyxia. The outcomes of TH in Thailand have never been reported.

To report clinical outcomes, including death, severe developmental delay, severe neurological impairment, severe hearing deficit and blindness at 2 years of age in perinatal hypoxic-ischemic encephalopathy (HIE) infants who underwent therapeutic hypothermia (TH) at Chiang Mai University (CMU) Hospital

At 2 years of age, the eligible infants who admitted at the CMU Hospital during February 2014 and December 2016 were recruited. Developmental assessment was performed by a developmental pediatrician, using Bayley Scales of Infant Development (BSID-III), gross motor function was classified by gross motor classification scale (GMFCS). Hearing was evaluated by auditory brainstem response (ABR) and blindness was evaluated by a pediatrician or ophthalmologist. Demographic data and clinical course during TH were drawn from electronic medical records.
Results: Of which 23 eligible patients, 4 (17.4%) died before discharge. At 2 years of age, overall death rate was 31.5% (6/19) and death or severe disability was 58.8% (10/17). Among the survivors, 11 patients were followed at median age (IQR) of 27 (19) mo. Weight<P3, Height<P3 and OFC<P3 were 18.1% (2/11), 45.5% (5/11) and 71.4% (5/7), respectively. Severe developmental delayed (<-2SD), severe motor disability (GMSCF3-5), blindness and profound hearing loss were 36.4% (4/11), 36.4% (4/11), 27.3% (3/11), and 0% (0/8), respectively. The patients who died and/or had severe disabilities at 2 years of age had significantly higher blood lactate on day 3 of life than those who survive without severe disability. (5.2 vs .2.4 mmol/L, p=0.03)

TH for perinatal HIE infants reduced death and combined death and/or severe disability at 2 years of age. To enhance these outcomes, improving supportive care and augmenting therapeutic hypothermia with neuroprotective agent should be considered.
Keywords: hypoxic ischemic encephalopathy, perinatal asphyxia, therapeutic hypothermia, low-to middle-income country, death and severe disability

ID: LB12
TITLE: Maternal LCPUFA profile and their Newborn Infants' MRI Brain Volumetrics
SENDER / PRESENTER: Enitan Ogundipe,United Kingdom

CONTENT:

Links between maternal nutrition and the developing brain's health is rapidly translating from bench to human clinical practice. This study is first showing a relationship between maternal prenatal blood essential fatty acid profile and their newborn infants' brain volumes measured using brain magnetic resonance imaging (MRI) scan. We previously showed for the first time that brain specific long chain polyunsaturated fatty acids (LCPUFA) supplementation of pregnant women increased newborn total and sub-regional MRI-measured brain volumes, (Ogundipe et al; PLEFA 2018). Large mammalian study found that various brain regions were rich in LCPUFAs essential for human brain development, primarily specific omega-3 and omega-6 LCPUFA derived from maternal stores.

Hypothesis was that maternal LCPUFA status in early pregnancy correlates to newborn infants' brain volumes measured on MRI scan. 300 pregnant women enrolled in triple blinded placebo RCT (FOSS trial) had maternal blood erythrocyte fatty acids taken at enrolment measured using FOLCH technique. Brain MRI scans performed at a neonatal MRI centre on 3-T Philips Achieva MRI system (Best, The Netherlands) used an eight-channel phased-array head coil on infants with parental consent. Pulse oximetry and full monitoring was undertaken throughout the MRI scan procedure with ear protection using mask and silicone-based putty earplugs. MRI scan images were analysed by a paediatric neuroradiologist. Maternal fatty acids levels were statistically correlated to the newborn brain MRI volumetrics. Statistical analyses utilised Pearson's correlation co-efficient (r) analyses using SPSS and significance level taken at $p < 0.05$.

Eighty nine scans were analysed; 49 (57%) male. Gestation ($r=0.82$; $p<0.0001$), birthweight ($r=0.67$; $p<0.0001$), birth length ($r=0.32$; $p=0.007$), head circumference($r=0.40$; $p=0.001$) and 5 minute Apgar scores ($r=0.50$; $p<0.0001$) all correlated positively with infant brain volumes on MRI. Higher essential brain fatty acids in maternal blood at booking correlated positively with their newborn infants' MRI measured brain volumes ($p < 0.0001$). Of note, maternal lipid markers of essential brain fatty acids deficiency correlated with the newborn infants brain MRI volumes with lower grey matter ($p<0.0001$) and also lower white matter volumes ($p < 0.0001$).

This is the first study to show that maternal levels of the essential brain LCPUFAs in early pregnancy is related to newborn infants' total and sub-regional brain volumes determined by MRI scan. Maternal LCPUFA status predicts anatomically measured brain size and better neonatal outcome measures.

ID: LB14
TITLE: A Clinical Comparison of Beractant and Poractant Alfa in Premature Neonates with Respiratory Distress Syndrome Utilizing Real-World Evidence Studies and Randomized Controlled Trials
SENDER / PRESENTER: MICHAEL BRUNE,United States

CONTENT:

Several clinical comparisons have been conducted to assess whether the animal-source of the surfactant (bovine: beractant; porcine: poractant alfa) has an impact on efficacy or safety outcomes in premature neonates with respiratory distress syndrome (RDS). However, such previous assessments did either consider randomized controlled trials (RCTs) for meta-analyses or were conducted in patient cohorts of real-world evidence (RWEs) studies, often with thousands of patients. To our knowledge, this investigation is the first approach combining both sources for a systematic review. Based on previous evaluations, we hypothesized that there won't be any significant differences between the two products.

In order to generate a complete overview of full-text original articles which compare beractant and poractant alfa, a systematic literature search was conducted. Search terms, such as product names, RDS, and terms associated with comparative studies in premature infants/newborns were used to scan 7 common search engines with a last update on March 27, 2019. No limits were applied for publication dates or language. Data were extracted regarding study design, eligibility criteria, demographic characteristics, and key outcome parameters, such as death, bronchopulmonary dysplasia (BPD), pneumothorax (PT), and air leak syndrome (ALS). For RWE studies, the odds ratios (ORs), confidence intervals (CIs), and p-values are reported. For RCTs, a meta-analysis was conducted with all dosing regimens aggregated and treatment arms pooled.

Our literature search identified 119 articles/abstracts of which 4 RWE studies and 15 RCTs fulfilled our selection criteria and were used for our evaluation. All RWE studies with adjusted ORs found no statistical significant between-treatment differences in key outcome parameters. In our meta-analysis using the identified RCTs, also no statistically significant between-treatment differences were observed for death (OR [95% CI]: 1.35 [0.98-1.86]), BPD (1.25 [0.96-1.62]), PT (1.21 [0.72-2.05]), and ALS (2.28 [0.82-6.39]). One sensitivity analysis using only doses labeled in the USA revealed a borderline significance in BPD (beractant vs poractant alfa): 1.34 [1.00-1.79], however, when only 100mg/kg doses were compared, again no significant differences were noted (BDS: 0.99 [0.64-1.52].

It is critical to utilize all available information coming from both, RCTs and also from RWE studies for comparative analyses. This analysis showed that the efficacy and safety profiles of beractant and poractant alfa are very similar, confirming our hypothesis. Therefore, other criteria, such as the animal source, approved indications, and/or pharmacoeconomic parameters could become more important when selecting a surfactant for patients at need.

Disclosures
Manuel Sánchez Luna received travel and lectures grants from AbbVie Inc. and served as a consultant for Chiesi and AbbVie.
Cristina Ramos Navarro has no relevant conflicts of interest.
Peter Bacher, Kristina Unnebrink, and Marisol Martinez-Tristani are employees of AbbVie and may own AbbVie stock and/or stock options.
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ID: LB16
TITLE: Use of inhaled nitric oxide in preterm neonates - data from the European Inhaled Nitric Oxide Registry over 10 years
SENDER / PRESENTER: Jean Yong,United Kingdom

CONTENT:

There is an increasing worldwide trend of using inhaled nitric oxide (iNO) in preterm infants (gestational age ≤ 34 weeks) with hypoxic respiratory failure. Conflicting views surround the use of iNO in preterm infants and these are reflected in recent, opposing recommendations. Unlike in term and late preterm infants, published evidence has not supported the use of inhaled nitric oxide (iNO) in preterm infants with hypoxic respiratory failure. However, iNO has been shown to improve oxygenation in preterm neonates particularly in those with echo-confirmed pulmonary hypertension (PH) without negative impact on survival.

A retrospective analysis of multi-centre, anonymised data from the European Inhaled Nitric Oxide Registry from 2008 to 2017 was conducted. Term and preterm neonates without a cardiac diagnosis were eligible for inclusion. Any incomplete or unknown data was excluded. Early response to iNO (within 60 minutes) was defined as a reduction in oxygenation index (OI) by 15% or fraction of inhaled oxygen (FiO2) by 15% when OI data was not available. PH was defined by echocardiography-confirmed right-to-left shunting at ductal or atrial level. Related outcomes including survival to discharge from hospital, chronic lung disease (CLD) at 36 weeks and final cranial ultrasound findings were analysed.

A total of 1661 neonates were included (≤ 34 weeks' gestation n=802; >34 weeks' n=859). Preterm infants showed significantly increased early responsiveness to iNO compared to term infants (Preterm 476/782 (60.9%) vs. Term 439/821 (53.5%); p= 0.0029). Preterm infants who showed an early response to iNO had increased survival compared to those who were unresponsive (Responsive and survived 284/469(60.6%) vs. Unresponsive and survived 145/299 (48.5%); p = 0.0013). Preterm early response to iNO had no statistically significant association with CLD at 36 weeks or abnormal cranial ultrasound at discharge.
There was an improved early oxygenation response in preterm infants with echocardiography-confirmed PH (PH 167/248 (67.3%) vs. no PH 94/178 (52.8%); p=0.0026) but no difference in survival outcomes (PH survived 127/251 (50.6%) vs. no-PH survived 101/178 (56.7%); p=0.24).

Our data reflects extensive use of iNO in preterm infants in keeping with worldwide trends. Early oxygenation response to iNO is more frequent in preterm compared to term infants. Improved early oxygenation response in preterm infants was associated with improved survival without increasing long-term sequelae. Use of iNO in preterm patients with PH showed an improvement in early oxygenation response but no difference in survival outcomes.

ID: LB26
TITLE: Near-Infrared Spectroscopy assessment of cognitive cortex hemodynamics in premature late-onset IUGR neonates compared to AGA peers during the early postnatal period
SENDER / PRESENTER: GkiougkiEvangelia,Greece

CONTENT:

Intrauterine growth restriction (IUGR) affects 5–10% of newborns and is associated with neurodevelopmental and cognitive dysfunctions. Despite hemodynamic brain sparing, complex microstructural changes occur in the IUGR brain, total brain blood flow is reduced and structural integrity of the neurovascular unit is altered. A pathologic perfusion of the cognitive cortex during the 1st postnatal week is associated with cognitive morbidity in the long term.
In late-onset IUGR that concerns 70–80% of cases, the umbilical artery Doppler may be normal, but in cases of brain sparing there is evidence of abnormal neurobehaviour.

To investigate NIRS as a potential prognostic indicator of cognitive dysfunction in late-onset IUGR neonates.
Subjects/Methods: We studied prospectively 15 late-onset IUGR preterms with normal umbilical artery Dopplers (Group B) in comparison with 27 AGA control peers (Group A). All subjects had normal brain ultrasound. Exclusion criteria were the normal SGA status, perinatal asphyxia and major congenital anomalies.
Neonates were recorded on the 1st, 3rd and 5th postnatal day using the NIRO-200 system to evaluate the Tissue Oxygenation Index (TOI) and the normalized Tissue Hemoglobin Index (nTHI). Brain ultrasound, mean arterial pressure, hematocrit, blood glucose, oxygenation and aeration indexes were verified within normal levels before each record. Statistical analysis was performed with SPSS 17.0 using Mann-Wittney and Oneway ANOVA test.

Median gestational age (±SD) was 31,9±1.05weeks for Group A and 31,8±2,9weeks for Group B, while median BW was 1737±285gr and 1185±380gr respectively. TOI was significantly reduced on the 1st and 5th day of life in the IUGR group while THI presented no statistically significant difference (Table 1).

NIRS data reveals a decreased cortical oxygenation in late-onset IUGR neonates during the early postnatal period. Larger subject groups are required in order to propose NIRS as a prognostic tool of potential cognitive impairments.

ID: LB32
TITLE: Downregulation of large conductance Ca2+-activated K+ (BKCa) channels in human umbilical arterial smooth muscle during gestational diabetes mellitus conditions
SENDER / PRESENTER: Jin Ryeol An, South Korea

CONTENT:

Large conductance Ca2+-activated K+ (BKCa) channels are main determinants of vascular smooth muscle cell excitability and vascular tone. Nevertheless, BKCa channels roles and expressions have not been investigated in human umbilical arterial smooth muscle cells. Interestingly, we discovered the changes of BKCa channel function and expression in umbilical arterial smooth muscle cells from gestational diabetes mellitus (GDM) patients.

Human umbilical arteries were obtained from patients with control and GDM subjects during cesarean section procedure. We enzymatically isolated single smooth muscle cells from human umbilical arteries and recorded changes of BKCa channels by using patch clamp technique. In addition, the alterations of vascular contractility and vascular function-related gene/protein expression were measured using umbilical arteries isolated from control and GDM subjects.

The amplitude of the BKCa current was reduced in the umbilical arterial smooth muscle cells isolated from GDM group. The application of NS-1619 (BKCa channel activator) showed dose-dependent vasodilation in normal umbilical artery. However, NS1619-induced vasodilation was decreased in the GDM group than the normal group. Real Time RT-PCR and Western blot analysis revealed that the gene and protein expression of BKCa channel subtypes were decreased in the GDM group. The treatment of YC-1, which activate guanylyl cyclase (sGC) and thereby BKCa channels, evoked BKCa current amplitude in both groups. However, the channel current amplitudes were not different between the control and GDM groups.

These findings suggest that the downregulation of BKCa current and the channel-induced vasodilation are due to the reduction of BKCa channels expression, not to the impairment of BKCa channels-related intracellular signaling pathways.

Keywords: large conductance Ca2+-activated K+ channels, human umbilical artery, gestational diabetes mellitus

ID: LB35
TITLE: Cost-comparison analysis of withdrawing immunoprophylaxis for respiratory syncytial virus (RSV) in infants born at 33-35 weeks gestational age in Quebec (2013-2017)
SENDER / PRESENTER: Mahwesh Saleem,Canada

CONTENT:

In Canada, palivizumab has been provided for RSV prevention in premature infants (≤ 35 weeks gestational age [wGA]) since 2002. However, in 2015, the Quebec Ministry of Health revised their eligibility criteria to limit the use of palivizumab to infants <33 weeks wGA, unless other indications were present. A cost analysis was performed to assess the impact of withdrawing RSV immunoprophylaxis in otherwise healthy infants born at 33-35 wGA.

A cost-comparison model from the societal perspective was constructed using clinical inputs from a 2013-2017 retrospective cohort study of 25 Quebec hospitals. Based on chart review and parent interview, direct (immunoprophylaxis, hospital stay, procedures, specialist consultations and discharge) and indirect (resource utilization and productivity losses) costs were estimated. Costs were derived from the Ontario Case Costing Initiative, Régie de l'assurance maladie du Québec, the Ontario Health Insurance Plan, CHU-Sainte-Justine, Statistics Canada and the Fédération interprofessionnelle de la santé du Québec and converted to 2018 Canadian dollars. Costs were modeled for infants hospitalized for RSV lower respiratory tract infection (LRTI) pre- and post-revision of guidelines.

The overall societal costs related to hospitalization due to RSV/LRTI for 33-35 wGA infants post- immunoprophylaxis guidelines revision (2015-2017; n=130) was higher at $3,659,785 compared to $1,701,496 for infants pre-revision (2013-2015; n=105). The societal costs were lower in the pre-revision years despite the added estimated costs of palivizumab and administration of prophylaxis ($93,184). Possible cost drivers in infants post-revision included more time spent in the pediatric intensive care unit (7.0 versus 5.9 days) and more days on mechanical ventilation (6.1 versus 4.8 days) and supplemental oxygen (4.4 versus 4 days), compared to infants pre-revision.

Immunoprophylaxis for RSV may be cost-saving in infants born at 33-35 wGA.

ID: LB36
TITLE: Randomised Controlled Trial: Very Low Microdrop Doses of Phenylephrine and Cyclopentolate Eye Drops for Retinopathy of Prematurity Eye Examinations
SENDER / PRESENTER: Lisa Kremer,New Zealand

CONTENT:

Premature infants are being exposed to doses of mydriatic eye drops that are equivalent to, or more than, what an adult would be administered. These mydriatic eye drops are used to dilate the pupil to prepare the eye for a retinopathy of prematurity eye examination (ROPEE).
Mydriatics have been associated with unwanted side effects, such as; bradycardia, apnoea, and necrotising enterocolitis. In some cases the use of these eye drops has been associated with fatalities.
To address these findings, this pilot study has evaluated the efficacy of low dose, microdrop administration of phenylephrine and cyclopentolate eye drops in premature infants.

Sixteen premature infants were randomised to receive microdrop administration of treatment A; phenylephrine 1% and cyclopentolate 0.2%, or treatment B; phenylephrine 0.5% and cyclopentolate 0.1%.
Efficacy of the two regimens was ascertained from, 1) pupil measurements at baseline, time of ROPEE (approximately 45 min), 90 min and 120 min, 2) successful ROPEE performed by the Ophthalmologist. Additionally the Ophthalmologist gave a score on the ease of the ROPEE as being easy or difficult.

All participants had sufficient pupil dilation for a successful ROPEE. Ophthalmologists rated the ROPEE as easy in 90% of the time. Pupil dilation measurements at the time of examination, mean ± SD, 4.8 mm ± 0.2 mm (95% CI 4.5-5.2) for treatment A, and 5 mm ± 0.2 mm (95%CI 4.6-5.4) for treatment B, with a non-statistically significant p-value of 0.61. Conclusions: Very low microdrop doses of phenylephrine and cyclopentolate eye drops provide sufficient pupil dilation for the ophthalmologist to successfully screen for ROP. To date, this is the first randomised controlled trial evaluating the efficacy of very low microdrop doses of phenylephrine and cyclopentolate. This pilot study has provided valuable information to design a sufficiently powered non-inferiority randomised controlled trial.

ID: LB38
TITLE: Positive Reporting Outcomes and Excellence (PROE) Tool: a positive feedback tool in the Neonatal Intensive Care Unit
SENDER / PRESENTER: Allan Jenkinson,Ireland

CONTENT:

Incident reporting is an integral component of quality improvement in healthcare. Our current practice of incident reporting is to place emphasis on identifying and examining failure of systems. Psychological research has revealed that people can learn effectively both from reflecting on failure and success (positive reinforcement).

We created an online (electronic) positive feedback tool, the Positive Reporting Outcomes and Excellence (PROE) Tool: PROEtool.com. Staff at our Neonatal Intensive Care Unit (NICU) were asked to reflect on individual co-workers behaviours, interactions, processes and outcomes in their work and to feedback positive observations and learning points. The aim was to recognise excellent work practices, identify learning opportunities from excellence and influence a positive cultural change.

The PROEtool.com was successfully piloted amongst the staff at the NICU at the National Maternity Hospital, Dublin for the month of June 2019. Sixty-two members of staff voluntarily registered to participate including doctors, nurses, and allied health professionals, administrative and ancillary staff.
Over the four week period a total of one-hundred and ten nominations were made. The data was then analysed with five key themes identified: communication, team work, employee wellbeing, patient advocacy and leadership. Feedback was in the form of a departmental feedback session highlighting the key learning points across the 5 domains and formally acknowledging individual staff members for their contribution to excellence in the Department. Individual feedback was also provided to all members of staff who received a nomination.

The PROEtool.com provides a platform for reflection, recognition and reward. It allows for interdisciplinary communication, collaboration and collegiality. Most importantly, the PROEtool.com creates a platform from which we can identify the best behaviours, processes and outcomes and use it to educate others. On-going study is required to examine the scope of the tool outside the department and to optimise the feedback process.

ID: LB42
TITLE: Early parenteral nutrition use and outcomes in preterm neonates
SENDER / PRESENTER: James Webbe,United Kingdom

CONTENT:

Preterm babies are among the highest users of parenteral nutrition (PN). The evidence underpinning PN use is low quality and neonatal trials, powered for clinically meaningful end-points, have not evaluated impact on key outcomes. There is therefore wide variation in commencement, duration, and composition. Recent studies in critically ill adults and children show that harms, particularly increased rates of nosocomial infection, outweigh the benefits of early PN administration. We aimed to evaluate whether in a population of very preterm neonates, PN use in the first seven postnatal days, compared with no PN use, in the rate of survival (and other important morbidities) is higher.

We prospectively registered this study (NCT03767634) and published the protocol. We used data from the UK National Neonatal Research Database to compare outcomes in neonates born between 30+0 and 32+6 weeks gestation, from January 2012 to December 2017, and admitted to a neonatal unit in England and Wales. The intervention was any administration of PN in the first seven postnatal days. The primary outcome was survival to discharge home. Secondary outcomes comprised the neonatal core outcome set; outcomes considered vital by over 400 former patients, parents, clinicians and researchers.
To minimise bias and confounding, we used propensity matching including 35 maternal, infant and organisational factors in the model. We calculated absolute risk differences for the outcomes.

Over the study period, there were 37,302 babies born between 30+0 and 32+6 gestation in England and Wales of which 36,644 were admitted to a neonatal unit. After propensity matching 8,207 pairs were formed. The pairs were well matched on principal background variables (Table 1), with a standardised mean difference of 0.013. Survival was higher in the group that received PN (survival: 'PN' 98.8% ; 'No PN' 97.3%; ; absolute risk reduction 1.54, 95% confidence interval 1.30, 1.76). However, the group that received PN also showed increased morbidity (bronchopulmonary dysplasia: 'PN' 9.9% ; 'No PN' 4.4%; absolute risk increase 5.5%; 95% confidence interval 4.9, 6.1; late-onset sepsis: 'PN' 2.5% ; 'No PN' 1.1%; absolute risk increase 1.4%; 95% confidence interval 1.0, 1.6).

We found that babies that received PN in the first postnatal week had improved survival, but an increase in major morbidities. The extensive background variables used in matching reduced the risk of confounding, but as this was an observational study, we cannot exclude the risk of residual and unmeasured confounding. We suggest that our data add to growing justification for a well-powered randomised clinical trial evaluating long-term outcomes.

Table 1 Principal background variables used in the propensity score matching

	Entire cohort				**Matched cohort**			
	No PN group (N=19,168)		**PN group (N=16,076)**		**No PN group (N=8,207)**		**PN group (N=8,207)**	
		Missing data		**Missing data**		**Missing data**		**Missing data**
Gestational age (weeks), mean (SD)	32.0 (4.4)	0	31.3 (0.9)	0	31.1 (0.8)	0	31.1 (0.8)	0
Birthweight (kg), mean (SD)	1.74 (0.28)	6	1.47 (0.32)	5	1.67 (0.27)	0	1.58 (0.29)	0

Proportion small for gestational age, n (%)	839 (4.4)	6	3762 (23.4)	5	1354 (16.5)	0	1354 (16.5)	0
Infant sex, n (%)								
Male	10326 (53.9)	0	8754 (54.5)	0	4481 (54.6)	0	4465 (54.4)	0
Female	8842 (46.1)	0	7322 (45.5)	0	3726 (45.4)	0	3742 (45.6)	0
Antenatal steroids, n (%)								
Yes, complete course	3175 (17.4)	920	2377 (15.4)	643	1249 (15.9)	468	1261 (16.0)	413
Yes, incomplete course	12354 (67.7)	920	11081 (71.8)	643	5553 (70.7)	468	5586 (70.9)	413
No	2719 (14.9)	920	1960 (12.7)	643	1052 (13.4)	468	1032 (13.1)	413
Umbilical arterial pH, mean (SD)	7.3 (0.1)	11346	7.3 (0.1)	9431	7.3 (0.1)	6018	7.3 (0.1)	5968
Apgar score at 5 minutes, mean (SD)	8.8 (1.3)	1616	8.4 (1.6)	1448	8.7 (1.4)	868	8.4 (1.6)	934
Intubation during resuscitation, n (%)	1668 (8.7)	0	3247 (20.2)	0	1518 (18.5)	0	1494 (18.2)	0
Admission temperature, mean (SD)	36.9 (3.3)	107	36.9 (8.2)	85	36.8 (1.9)	54	36.9 (3.0)	61
Admission heart rate, mean (SD)	157 (19)	1199	156 (22)	1145	157 (21)	627	157 (25)	719
Admission blood sugar, mean (SD)	3.1 (1.9)	3835	2.8 (4.4)	2879	3.0 (3.4)	1964	2.9 (2.3)	1806
Ventilated on first day, n (%)	699 (7.5)	9852	1500 (17.6)	7556	669 (15.9)	3997	678 (16.0)	3972
Treated for sepsis on first day, n (%)	911 (21.8)	14989	973 (24.6)	12121	457 (23.6)	6270	473 (24.0)	6237
Level of neonatal unit, n(%)								
Level 1 (LNU)	2588 (13.5)	0	1190 (7.4)	0	673 (8.2)	0	624 (7.6)	0
Level 2 (SCBU)	8319 (43.4)	0	7556 (47.0)	0	4005 (48.8)	0	3948 (48.1)	0
Level 3 (NICU)	8031 (41.9)	0	7170 (44.6)	0	3431 (41.8)	0	3537 (43.1)	0
Transferred on first day, n (%)	1093 (5.7)	0	1334 (8.3)	0	624 (7.6)	0	648 (7.9)	0