ID: 24

TITLE: EARLY DIAGNOSIS OF NEONATAL SEPSIS BY PROCALCITONIN COMBINED WITH 16S RRNA

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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.

COI: None declared
ID: 71

TITLE: ENDOCAN, A POTENTIAL NEW MARKER FOR NEONATAL INFECTION

AUTHORS: Gabriela I. Zonda1,2, Radu Zonda3, Andrei T. Cernomaz4, Andreea L. Avasiloaiei1,2, Bogdan D. Grigoriu4, Luminița Păduraru1,2

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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.

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: 79

TITLE: DIAGNOSTIC VALUE OF CYTOMEGALOVIRUS IGM ANTIBODY IN PCR-CONFIRMED CONGENITAL CYTOMEGALOVIRUS INFECTION

AUTHORS: Shohei Ohyama 1; Kazumichi Fujioka 1; Sachiyo Fukushima 1; Shinya Abe 1; Mariko Ashina 1; Toshihiko Ikuta 1; Kosuke Nishida 1; Hisayuki Matsumoto 2; Yuji Nakamachi 2; Kenji Tanimura 3; Hiteto Yamada 3; Kazumoto Iijima 1

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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.

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.

COI: None declared.
ID: 197
TITLE: IMPACT OF PRO-INFLAMMATORY CYTOKINES ON PREMATURE RUPTURE OF MEMBRANE
AUTHORS: JIN Ying-zi1; Moon-Sung Park2; XU Qing-yun1; LIU Meng-nan3; LIU Chun-yu3; WANG Yu-ying3; AN Ru-ru3; LI Jia3; JIN Zhen-ai3
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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 immunohistochemical 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.

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

AUTHORS: Jonathan Coutts 1; Richard Thwaites 2; John Fullarton 3; ElizaBeth Grubb 4; Carole Morris 5; Barry Rodgers-Gray 3; Xavier Carbonell-Estrany 6

AFFILIATIONS: 1 Royal Hospital for Children, Glasgow, UK; 2 Queen Alexandra Hospital, Portsmouth, UK; 3 Strategen Ltd, Basingstoke, UK; 4 AbbVie Inc, North Chicago, Illinois, USA; 5 Information Services Division Scotland, Edinburgh, UK; 6 Institut d’Investigacions Biomediques August Pi Suñer (IDIBAPS), Barcelona, Spain

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) 6-264] 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.

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.
ID: 299
TITLE: EFFECT OF ORAL CARE ON THE INCIDENCE OF EARLY-ONSET VENTILATOR-ASSOCIATED PNEUMONIA IN PRETERM INFANTS
 AUTHORS: Yoshinori Katayama ; Masahiro Enomoto ; Shin kikuchi
AFFILIATIONS: Department of Pediatrics, Takatsuki General Hospital, Osaka, Japan

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 reintubation 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 reintubation 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.

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.

IMAGES:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=5d1e8e7b322c6cf1d2350157581af9b92-MjAxOS0wNSM1Y2UyNjY2Yzi4ODZi

Figure 1: Outcomes in the two sequential cohorts

COI: None
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.

COI: None declared
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
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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.

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.

COI: None declared
ID: 549

TITLE: ORGAN DYSFUNCTION AS A PREDICTOR OF DEATH IN BLOOD CULTURE-PROVEN NEONATAL SEPSIS

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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.
COI: None declared
ID: 570

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.
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-

COI: None declared
ID: 739

TITLE: UNIVERSAL NEWBORN SCREENING FOR CONGENITAL CYTOMEGALOVIRUS INFECTION – RESULTS OF A PILOT TRIAL IN GERMANY

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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: 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.
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: 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 adaptative 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). Naive 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.

IMAGES:
https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=c712ab34034f171b513ec32730b0d5ce-MjAxAw0wNSM1Y2UyNjY2ZDMzYmU3

COI: None declared