September 22nd, 2023 15:00 - 17:00

PARALLEL SESSION 29

ID 403. The interplay between glucogenic amino acids and carbohydrate metabolisms in regulating the clinical fate of infected preterm newborns

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Background:

Neonatal sepsis remains one of the most common morbidities in newborn preterm infants and may be related to extensive use of parenteral nutrition (PN) with high glucose levels. Using a preterm piglet model of neonatal sepsis, we have demonstrated that hyperglycemia, induced by high glucose supply, predisposed infected animals to sepsis; whereas glucose restriction prevented sepsis but led to severe hypoglycemia. Based on this, we hypothesized that supplementing glucogenic amino acids (GAA) in a glucose–restricted PN regime would both reduce the risk of sepsis and help maintain normoglycemia via enhanced hepatic gluconeogenesis.

Methods:

Two experiments with similar setups were performed in cesarean–delivered preterm pigs (90% gestation). Newborn animals were inoculated with either Staphylococcus epidermidis (SE) or saline control (CON) and nourished with different compositions of PN until euthanasia at 15 h. Clinical signs, physiological, metabolic, and immunological responses to infection were evaluated during the study. In experiment 1, animals were allocated to PN with either restricted glucose (2 g/kg/d, rGLU)

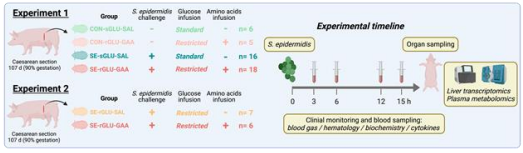
supplemented with four GAA (glutamine/valine/aspartate/asparagine, 1 g/kg/d each) or standard glucose (14.4 g/kg/d, sGLU) with saline (SAL). In experiment 2, GAA animals were compared with those only receiving restricted glucose PN (rGLU–SAL group, Figure).

Results:

Experiment 1: relative to standard glucose supply, restricted glucose with GAA in PN led to reduced sepsis incidence (11.1 vs. 63%) and sepsis severity outcomes (higher blood pH, lower blood bacterial density, pCO2, lactate, and inflammatory response) while maintained normoglycemia. Experiment 2: Under restricted glucose provision, GAA supply provided better clinical benefits (higher blood pH, lower blood bacterial density, pCO2, and inflammatory response), together with elevated blood glucose levels. Relative to both standard and restricted glucose animals, GAA animals showed activated hepatic pathways related to gluconeogenesis, TCA cycle, oxidative phosphorylation, fatty acid metabolism, and suppressed Th1, Th2, and Th17 inflammatory pathways.

Conclusion:

We demonstrated a clinically relevant nutritional regime with enriched GAA in low parenteral glucose setting to prevent sepsis and maintain glucose homeostasis in infected preterm newborns. This sepsis preventive approach should therefore be considered in future clinical trials in infection–sensitive preterm infants.



Overview of the experimental design and animal procedures

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None declared

ID 898. Neonates < 3 months with late-onset sepsis display specific signatures of the immune-microbiome interaction

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Background: Infants < 3 months with fever are at high risk of invasive bacterial infection (IBI), resulting in frequent exposure to empiric antibiotic therapy. A possible sepsis–predisposing profile of the immune–microbiome interaction has not yet been explored in this specific cohort as well as the long–term consequences of early sepsis and antimicrobial exposure on the microbiome.

Methods: Previously healthy infants < 3 months with fever/suspected infection were included, clinically characterized and divided into subgroups of bacterial and viral infections and "symptoms of unknown cause" due to detailed diagnostics that were performed (sepsis workup, multiplex PCR, enterovirus diagnostics). Immunophenotyping (B– and T cell subsets, regulatory T cells) and sequencing of the gastrointestinal microbiome were used to investigate sepsis–predisposing profiles in comparison to healthy children without infection. Follow–up included clinical examinations and microbiome profiling at one year of age.

Results: N= 51 infants with fever and sepsis work–up were enrolled. Invasive bacterial infection was diagnosed in 25 (49%) patients. Infants with suspected LOS displayed a decreased abundance of regulatory CD4+ FoxP3+ T cells as compared to healthy controls, which was most pronounced in the subgroup of infants with IBI. Further, we observed distinct microbiome characteristics, that were associated with sepsis, such as a reduced microbial diversity (Shannon diversity index: p=0.007) and a reduced

abundance of bifidobacteria, especially Bifidobacterium longum (canonical correspondence analysis: p=0.03). Significant relations between microbiome signatures and immune cells, such as the association between the abundance of Bifidobacterium longum and regulatory T cell–frequencies, were observed in healthy babies but not in infants with sepsis (p=0.001). In children with early sepsis and consecutive antibiotic therapy, we demonstrate long–term changes in the gastrointestinal microbiome at one year of age, such a reduced abundance of Bifidobacterium breve as compared to healthy controls.

Conclusion: Our exploratory data indicate specific immune–microbiome profiles that are associated with neonatal late–onset sepsis as well as consequences of early sepsis with antibiotic therapy for the gastrointestinal microbiome at one year of age. The authors do not have any conflict of interest.

ID 868. THE RISK OF RETINOPATHY OF PREMATURITY IN EXTREMELY LOW GESTATIONAL AGE NEONATES INCREASES WITH EACH EPISODE OF CULTURE-PROVEN SEPSIS

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Background: Retinopathy of prematurity (ROP) is a major morbidity mainly in very premature preterm infants causing visual impairment including blindness. Timely diagnosis, treatment and prevention are critical. There is growing evidence of a contributing role of infection and inflammation in the pathogenesis of ROP. We herein hypothesized that extremely low gestational age newborns (ELGANs) having survived one or more episodes of sepsis are more likely to develop any ROP and/or progression to higher-stage disease.

Methods: We analyzed the impact of culture-proven sepsis on ROP risk in ELGANs enrolled in the German Neonatal Network multicenter study. Stepwise multivariable logistic regression analyses controlled for confounding.

Results: n = 12,563 infants were included (median gestational age 26 6/7 weeks, birth weight 840 g). 6,177/12,563 infants (49.2 %) were diagnosed with any ROP, comprising 2,700 infants (21.5 %) with stage 1 disease, 2,163 (17.2 %) with stage 2 ROP, 1,282 (10.2 %) with stage 3 and 32 (0.3 %) with stage 4 disease. 829/12,563 infants (6.6 %) required treatment for higher-stage ROP. Stepwise multivariable logistic regression identified neonatal sepsis as an independent risk factor. The number of sepsis episodes was directly related to the risk increase — with a 1.4-fold increase at one (95% CI 1.2–1.6, $p < 0.001$), and a 1.8-fold and 4.7-fold increase at two (95% CI 1.3–2.3, $p < 0.001$) and three episodes (95% CI 2.3–9.7, $p < 0.001$). Moreover, neonatal sepsis was associated with progression to higher-stage disease — with a 1.4-fold risk at one (95% CI 1.2–1.7, $p < 0.001$), a 1.9-fold risk at two (95% CI 1.4–2.5, $p < 0.001$), and a 2.3-fold risk at three sepsis episodes (95% CI 1.4–3.8, $p = 0.001$).

Conclusion: The risk of ROP and higher-stage ROP in ELGANs increases with each episode of neonatal sepsis. Future studies ought to investigate underlying mechanisms and may help to direct future ROP screening.

CH: grants (BMBF, Chiesi, DFG). EH: grants/travel/honoraria (Chiesi, Pfizer, Merck Sharp&Dohme, Sanofi, AstraZeneca). AS: consultancy/honoraria (Apellis, Allergan, Bayer, Novartis, Roche). WG: grants (BMBF); honoraria (Chiesi, Abbott).

No other disclosures.

ID 342. The magnitude of risk for early onset sepsis in neonates born after rupture of membrane ≥ 18 hours in Ibadan Nigeria.

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Background: Prolonged rupture of membranes (PROM) is a recognised risk factor for early onset sepsis, which often necessitates institution of empiric antibiotics in many babies born following PROM especially in resource constrained settings where laboratory support is limited. However, only a proportion of babies born after PROM actually develop sepsis. This study was carried out to determine the magnitude of risk for early onset sepsis in neonates born after rupture of membrane of 18 hours or more.

Methods: This was a cross sectional study of 164 consecutive neonates born to mothers with PROM of 18 hours or more. The neonates were screened for sepsis and monitored for clinical features of neonatal sepsis for 72 hours while placenta histology was carried out for evidence of chorioamnionitis.

Results: Nine (5.5%) mothers had features of clinical chorioamnionitis while 88(53.7%) had histologic chorioamnionitis. Thirty–seven (22.6%) neonates had clinical features of sepsis, mainly respiratory symptoms. Only 8 (4.9%) neonates had culture proven sepsis. The majority of the symptoms were observed within 24 hours of life. There was a minimal increase in the odds of having culture proven sepsis with

PROM ⩾ 18 hours by a factor of 1.04 (p=0.020, OR 1.04 C.I 1.01, 1.08). In addition, mothers with rupture of the membranes more than 3 days were 11.8 times more likely to have culture proven sepsis compared with mothers with rupture of the membranes less than 3 days (p=0.010, OR=11.8, CI=1.799 – 77.839).

Conclusion: The incidence of culture proven sepsis was low among neonates delivered following > 18 hours of PROM only as a risk factor. Most of the babies exposed to histologic chorioamnionitis were neither symptomatic nor had culture proven sepsis. It is recommended that PROM > 18 hours alone should not be an absolute indication for empiric antibiotic therapy in otherwise well neonates in order to stem the tide of emergence of antibiotic resistance.

Keywords: PROM, EOS, Chorioamnionitis

None declared