



September 17th, 2021 15:00 - 17:00

PARALLEL SESSION 30

ID 76. NOSOCOMIAL INFECTIONS IN NEONATAL CARE: A SCOPING REVIEW OF THE SURVEILLANCE CASE DEFINITIONS THAT ARE USED FOR PNEUMONIA IN NEWBORNS ADMITTED IN THE HOSPITAL

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Background

Neonatal nosocomial infections (NNI) may lead to increased risk of morbidity, mortality and increased hospital stay. Therefore it is critical to monitor and prevent NNI. Surveillance of NNI is an indispensable tool in this process. The objective of this review is to provide an overview of surveillance case definitions, surveillance methods and outcome measures for NNI.

Methods

A scoping review was performed according to the guidelines of the Briggs institute. Only results for the subtypes hospital acquired pneumonia” (HAP) en “ventilator acquired pneumonia” (VAP) are presented here.

Results

Full text screening was performed on n=294 of 16.067 articles of which n=86 were included.

HAP:

Surveillance case definitions were provided in 17 studies: 5 were according to CDC, 3 according to NEO-KISS, 4 used other sources and 5 were formulated by researchers (table1). Manual surveillance was used in six; semi-automatic in two studies. Surveillance method was not reported in 53%. Outcome measures were: number of episodes (1x); number of neonates with HAP (11x); days with HAP/per 1000 in hospital days (3x).

VAP:

Surveillance case definitions were provided in 74 studies: 49 were according to CDC, 2 according to NEO-KISS, 18 used other sources and 5 were formulated by researchers.. Manual surveillance was used in 28; semi-automatic in 17 studies. Surveillance method was not reported in 39%. Outcome measures were: days with VAP/per 1000 ventilation days (33x); number of neonates with VAP (23x); % neonates with VAP (8x); number of episodes (2x); cases of VAP/per 100 mechanically ventilated neonates (1x).

Conclusion

There is a serious lack of reporting and an extensive variation in surveillance case definitions, surveillance methods and outcome measures for neonatal HAP and VAP. This makes it impossible to compare results from different studies. A possible solution for this is a core outcome and minimum reporting set developed through consensus. By using a consistent, pragmatic surveillance method for neonatal HAP and VAP, as well as other subtypes of NNI, we will be able to study the true burden in terms of neonatal outcome and costs, as well as the effects of preventive measures.

HAP	Article	Chest X-ray changes	Worsening gas exchange	Clinical criteria	Laboratory findings	Antibiotic therapy	At least 48h of hospitalization
	Abdel-Wahab, F. et al	x	x		x		



Asanathong, N. W. et al	x	x	x			x
Bartels, D. B. et al	x		x	x		
Gadallah, M. A. H. et al	x		x	x		
Geffers, C. et al	x		x	x		
Gulcan, H. et al	x		x	x		
Hibbard, J. U. et al	x		x			
Keene, S et al	x	x	x		x	
Kordek, A. et al	x	x		x		
Pessoa-Silva, C. L. et al	x		x	x		
Su, B. H. et al	x	x		x		
Tavora, A. C. V. C. F. et al	x	x	x	x		
Touati, A. et al	x		x			
van der Zwet, W. C. et al	x		x	x	x	
Walter, J. et al	x	x	x	x		
Wang, Y. et al	x	x	x			
Wojkowska-Mach, J. et al	x	x	x	x		

Table 1: Frequency of the elements used in the surveillance case definitions for HAP as an illustration of the variation

None declared



ID 285. BODY WEIGHT MEASUREMENTS SUPPORT MACHINE-LEARNING ALGORITHMS IN NEONATAL SEPSIS PREDICTION

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Background

The initially subtle clinical signs in combination with its high mortality makes neonatal sepsis a challenging diagnosis. Clinical decision support systems (CDSS), continuously evaluating the risk of sepsis from vital signs time series can assist in the diagnosis of neonatal sepsis. However, it is currently unknown how body weight affects development of vital signs, and its potential influence on the predictive ability of CDSS in neonates.

Method

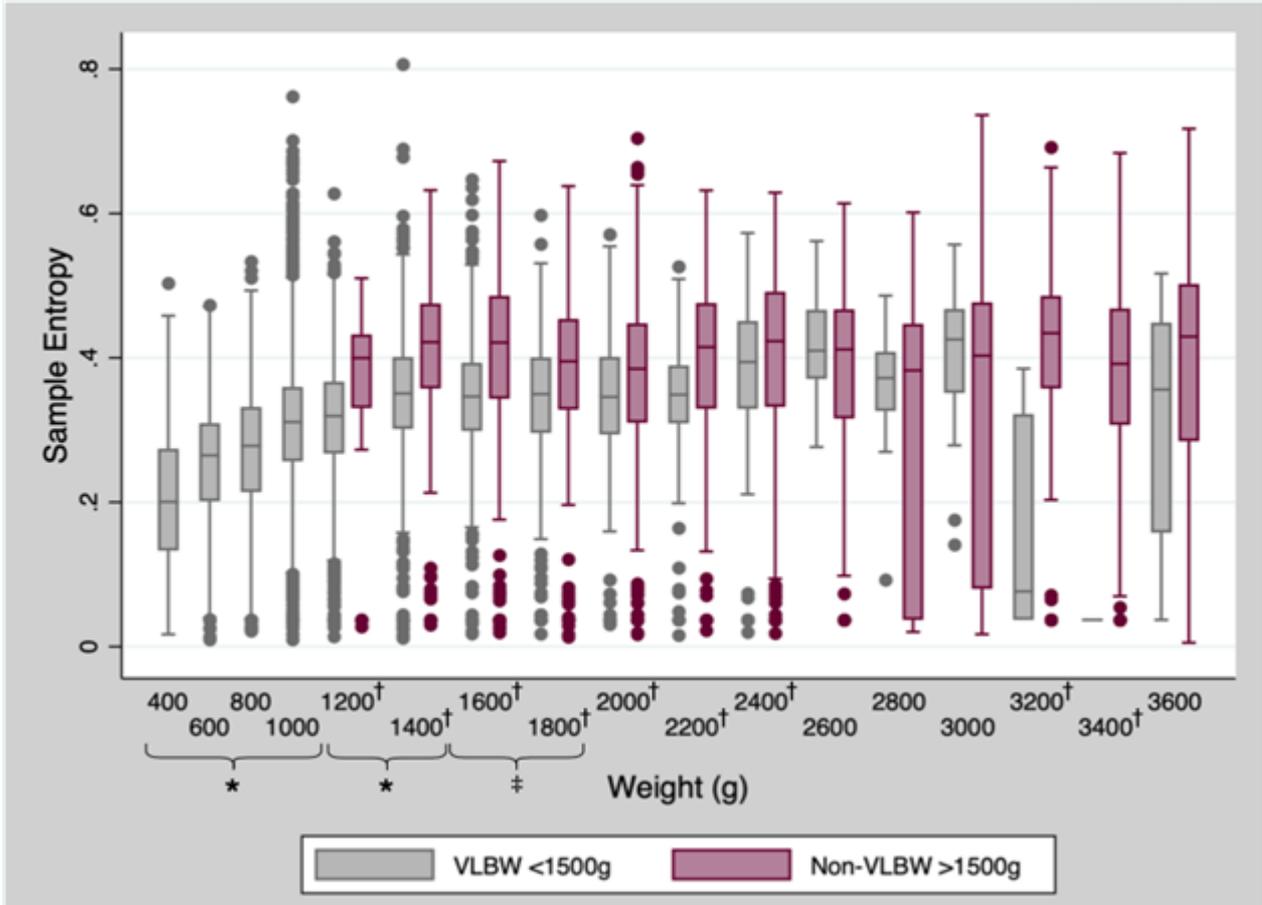
This was a longitudinal cohort study including 342 infants admitted to the neonatal intensive care unit at Karolinska University Hospital, Sweden. We prospectively collected high frequency monitor data with manually annotated event timelines. We then studied the influence of body weight on sample entropy measures of inter-beat interval time-series. Repetitive weight measurements were then added to a novel machine-learning-based algorithm, partly based on sample entropy measures of inter-beat intervals for sepsis prediction.

Results

Median birth weight for the study cohort was 2609g and median gestational age was 36 weeks. A total of 4262 weight measurements were used. Sample entropy increased with gain of body weight, suggesting augmented heart rate variability during postnatal development in the subgroup of very low birth weight (VLBW) infants (n=91) ($p < 0.05$, Figure 1). Further, the group of VLBW infants did not fully catch up in entropy, even when reaching a comparable weight to their non-VLBW peers ($p < 0.05$). Our CDSS algorithm achieved a predictive ability with an area under receiving operating characteristics (AUROC) of 0.8 up to 24h before clinical suspicion of sepsis, with a trend towards higher predictive ability when adding repetitive weight measures to the model.

Conclusion

We provide insight into how weight development correlates with heart rate variability, described as sample entropy from inter-beat interval time-domain analysis. Entropy increase could be explained by the maturation of the autonomic nerve system. Premature infants have a lower heart rate variability, likely explaining the lower entropy in the VLBW subgroup. Repetitive weight measurements might have an additive predictive value in CDSS for sepsis detection in neonates. Thus, there might be possibilities to calibrate CDSS with weight measurements, increasing their predictive ability and enabling earlier therapeutic interventions to save lives.



*=p<0.05 change of median SampEn for VLBW infants. †=p<0.05 difference between VLBW/Non-VLBW median SampEn. ‡=p<0.05 change of median SampEn for Non-VLBW. Abbreviations: VLBW: very low birth weight. SampEn: Sample entropy

None declared



ID 539. Addition of pentoxifylline to gentamicin enhances anti-inflammatory and pro-resolution cytokines in brain tissue of one week old mice with Escherichia coli sepsis

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Background

Neonatal sepsis triggers an inflammatory response that contributes to high mortality and brain injury. Pentoxifylline (PTX), a phosphodiesterase inhibitor that suppresses pro-inflammatory cytokine production, is a candidate adjunctive therapy for newborn sepsis that has shown improved survival in small clinical studies. The effects of adjunctive PTX on sepsis-induced cerebral inflammation in the newborn remain poorly understood. We hypothesized that the addition of PTX to gentamicin (GENT) compared to GENT alone inhibits the concentrations of pro-inflammatory and/or augments anti-inflammatory and pro-resolution cytokines and chemokines in cerebral tissue of one week old mice with Escherichia coli sepsis.

Methods

E. coli K1 (ATCC #700973) 10^5 colony forming units (CFU)/g weight or no bacteria control (CTL) were injected intraperitoneally into 7 days old C57BL/6J pups, corresponding immunologically to term human newborns. After 1.5 hours, E. coli-septic pups were treated with GENT, PTX, (GENT+PTX) or saline (SAL), and euthanized after an additional 4 hours. CFUs, cytokines and chemokines were measured in homogenized brain tissue, and comparisons employed 1-way ANOVA or Kruskal-Wallis tests.

Results

Cerebral tissue CFUs from untreated E. coli-septic pups were significantly lower (median 14 CFUs/mg tissue, IQR 8-34) compared to other organs (e.g., liver: median 11923 CFUs/mg tissue) or blood (median 1970 CFUs/ μ l), and were mostly undetectable in pups treated with GENT, whereby the addition of PTX did not augment bacterial growth. Cerebral concentrations of pro-inflammatory cytokines significantly increased in untreated septic compared to CTL mice (mean TNF: 697 vs 396 pg/g tissue, $p < 0.05$). GENT and (GENT+PTX) significantly decreased the cerebral chemokines CXCL-1 (keratinocyte-derived chemokine) and CCL2. GENT alone suppressed cerebral CCL3, while (GENT+PTX) showed a non-significant trend towards reduced CCL3 concentration. CCL4 and TNF in cerebral tissue were not changed by GENT or (GENT+PTX). (GENT+PTX) and PTX alone enhanced cerebral concentrations of the anti-inflammatory and pro-resolution cytokines IL-10, IL-6 (Jones, J Immunol 2005) and G-CSF (Kitabayashi, Blood 1995), whereas GENT alone did not change IL-10 and significantly decreased IL-6 and G-CSF.

Conclusion

Addition of PTX to GENT in one week old mice with E. coli sepsis enhances cerebral concentrations of anti-inflammatory and pro-resolution cytokines without augmenting bacterial growth, suggesting potential protection from sepsis-induced cerebral injury.

None declared



ID 506. EARLY POSTNATAL ANTIBIOTICS INDUCE LATER BLOOD TRANSCRIPTIONAL CHANGES IN PRETERM PIGS

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BACKGROUND:

Antibiotics (AB) are commonly used for preterm infants. Prolonged treatment is associated with later immune-related dysfunctions and morbidities (NEC, LOS). We hypothesized that 4 days of early postnatal AB treatment affects later immune status, potentially via gut microbiota changes, as reflected by blood cell transcriptional responses.

METHODS:

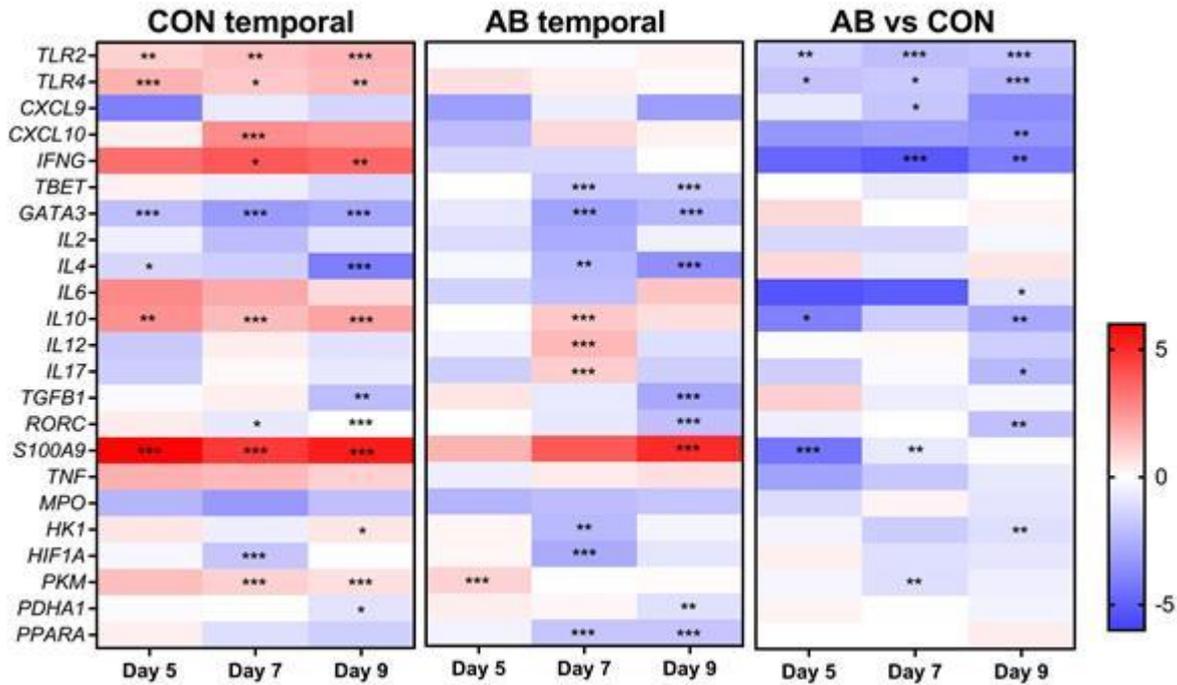
Using preterm pigs as a model for infants, newborn caesarean-delivered animals were treated with broad spectrum AB (amoxicillin/clavulanic acid 50/25ml/kg/d; neomycin 50ml/kg/d, oral administration) on day 1-4, and blood was collected at intervals until day 9. Temporal gene expression was analyzed by qPCR for selected genes related to immunity and cellular energy metabolism. Immune gene expressions (day 5-9) and whole blood transcriptome (RNAseq) and gut microbiota (day 9) were analyzed.

RESULTS:

Expression of genes related to immunity and energy metabolism (TLR2, TLR4, CXCL10, IFNG, IL10, S100A9, PKM, HK1) increased at day 5-9 in controls (vs day 1, Figure 1). AB-treated pigs showed less gene responses over time, with persistently low expression of TLR2 and TLR4 at day 5-9. Targets related to Th1 polarization showed lower levels in AB-treated vs. control animals (CXCL9, CXCL10, IFNG, IFNG/IL4, TBET/GATA3). Th17 related targets showed decreasing expression on day 9 (TGFB1, RORC) and lower levels of IL17A in AB-treated pigs. Temporary lower expression of S100A9 was seen in the AB-treated on days 5-7 (all $p < 0.05$). Transcriptomics showed 1487 differentially expressed genes (DEGs, 273 up, 1214 down) in AB-treated pigs. IL17A, IL17F, IFNG, and IL22 expression were among top 20 DEGs and AB affected pathways related to adaptive immunity, JAK-STAT-signaling, glycolysis, GPCR signaling, and ribosome function. The gut microbiota was minimally affected on day 9.

CONCLUSION:

Early postnatal AB treatment reduces expression of multiple immune-related genes, even after cessation of treatment and without notable effects to gut microbiota in preterm pigs. In a translational perspective, AB treatment of newborn preterm infants may be associated with immune suppression, potentially affecting later response to infection. Understanding how and when AB treatment affects immune maturation will help to improve ways to combat neonatal infections without inducing negative effects on the developing immune system and gut microbiota, thereby improving antibiotic stewardship.



Temporal gene expression (vs day 1) in preterm pigs without and with antibiotic treatment on day 1-4 (CON and AB, respectively) and group comparison (AB vs CON, log₂-fold-change, *p<0.05, **p<0.01, ***p<0.001) Funding from the Novo Nordisk Foundation for the BRIDGE translational Excellence Programme postdoctoral fellowship grant