5ICCN_008
Intrauterine inflammation and neonatal outcome: the role of funisitis

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Keywords: Chorioamnionitis; Funisitis; Prematurity; Neonatal outcome

Background: Intrauterine inflammation (chorioamnionitis, funisitis) is a leading cause of preterm delivery. Several studies have been performed to assess a gestation-independent effect of intrauterine inflammation on neonatal outcome with variable results.
Aims: To evaluate whether histological chorioamnionitis (HCA) and funisitis (FUN) make neonatal outcome worse.
Patients and Methods: All inborn infants with GA at birth <35 wks admitted to our NICU during a 18-months period were enrolled. HCA and FUN were diagnosed according to Redline's criteria. Infants were divided into 3 groups: exposed to HCA, exposed to both HCA and FUN, not exposed to intrauterine inflammation. We collected the following data: resuscitation and oxygen in the delivery room, Apgar score, ventilation, surfactant doses, sepsis, PDA, IVH, BPD, ROP and death before discharge. Univariable and multivariable random intercept linear and logistic models were used to evaluate the relationship between the extent of inflammation and outcomes, adjusting for GA, BW, preeclampsia and SGA.
Results: Of the 454 neonates enrolled, 58 (12.8%) were exposed to HCA (mean GA 31.7 wks, mean BW 1501.4 g), 34 (7.5%) were exposed to both HCA and FUN (mean GA 28.6 wks, mean BW 1337.7 g), 362 (79.7%) were not exposed to intrauterine inflammation (mean GA 32.1 wks, mean BW 1681 g). In univariable analysis, infants exposed to both HCA and FUN had lower Apgar score at 1 and 5 min, increased need for resuscitation and oxygen in the delivery room, increased need for surfactant therapy, and a higher incidence of all adverse outcomes than infants in the control group ($p < 0.05$ for all variables). No significant difference was found between the infants exposed only to HCA and the control group. In multivariable regression analysis, FUN was an independent risk factor for a lower Apgar score at 1 min (RC −1.3; 95% CI: −1.9, −0.7, $p < 0.001$) and 5 min (RC −0.6; 95% CI: −1.0, −0.2, $p = 0.004$), for an increased need for resuscitation (OR 10.7; 95% CI: 1.8, 65.0, $p = 0.01$) and oxygen in the delivery room (OR 5.8; 95% CI: 1.7, 20.6, $p = 0.006$).
Conclusions: Our data suggest that the involvement of umbilical cord vessels during intrauterine inflammation plays an important role in worsening the outcome of preterm infants since the first minutes of life.

5ICCN_009
Presepsin for the diagnosis of late-onset sepsis in preterm newborns

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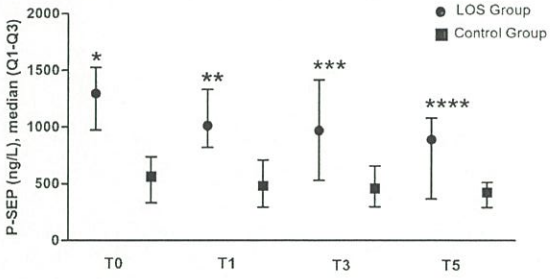
Keywords: Presepsin; Late-onset sepsis; Preterm newborn

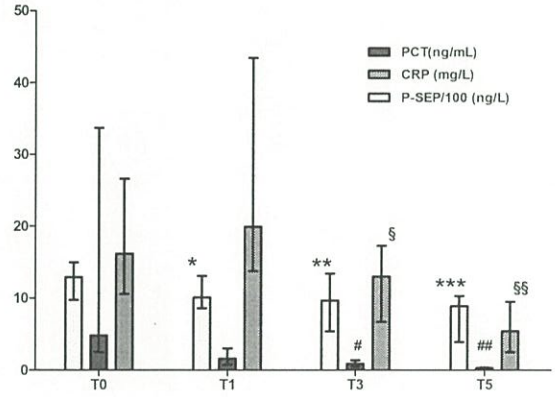
Late onset sepsis (LOS) is one of the leading causes of morbidity and mortality in preterm newborns. However, available diagnostic tools present inadequate performance. Despite blood culture is the golden standard for the diagnosis of sepsis, it is well known to possess poor and variable sensitivity in this population. The objective of this study was to evaluate the usefulness of presepsin (P-SEP), a novel biomarker of bacterial infection, for the diagnosis of LOS in preterm newborns.
We performed an observational prospective study which enrolled newborns ≤32 weeks of gestational age with LOS (LOS Group) and non-infected controls (Control Group), at 4–60 days of postnatal age over a 12 month-period. Exclusion criteria were the presence of major congenital malformations, fetal hydrops, or lack of parental consent. Infants who developed possible LOS (LOS Group) were consecutively enrolled during the study period. Blood was sampled at enrollment (T0) for culture and count, and for measuring P-SEP, procalcitonin (PCT), and C-reactive protein (CRP). P-SEP, PCT, and CRP were measured one (T1), three (T3), and five (T5) days after the first sample. For each patient enrolled in the LOS Group, the next infant born who did not develop signs and symptoms of infection and who fulfilled the inclusion criteria was enrolled in the control group, and his/her P-SEP was measured at T0, T1, T3, and T5 from waste blood samples.
Sample size was calculated assuming a difference in P-SEP concentration of at least 300 ng/L between the LOS and Control group, and a standard deviation for P-SEP of 300 ng/L. The estimated sample size was 14 patients in each group, with 80% power at $p = 0.05$ level. Statistical analysis was performed using Student's t test for parametric continuous variables, Fisher's exact test for categorical variables, Mann-Whitney U test for continuous nonparametric variables, and Wilcoxon signed rank test for non-independent data of continuous non-parametric variables. The receiver operating characteristics (ROC) curve for P-SEP values at T0 was analyzed in order to calculate the area under the curve (AUC) and the most accurate cut-off value for P-SEP.
We studied 40 newborns, 19 in the LOS Group and 21 in the Control Group. Infants in the LOS Group presented lower gestational age (25.6±2.0 versus 28.8±2.0 weeks, $p = 0.00001$) and birthweight (684±215 versus 1021±233 g, $p = 0.00003$), higher need of mechanical ventilation (79 versus 33%, $p = 0.005$) and surfactant administration (89 versus 57%, $p = 0.03$), higher occurrence of patent ductus arteriosus (89 verus 57%, $p = 0.03$) and longer NICU stay (54±28 versus 35±18 days, $p = 0.02$). The other main clinical characteristics and outcomes, as well as age at enrollment, did not differ between the two groups.
P-SEP at enrollment was higher in LOS than in Control Group (median 1295 vs. 562 ng/L, $p = 0.00001$) and remained higher throughout the study period (Figure 1). In the LOS Group P-SEP demonstrated a borderline reduction at day 1 vs. values at enrollment (median 1011 vs. 1295 ng/dL, $p = 0.05$), while CRP and PCT at day 1 did not differ from baseline values (Figure 2). The ROC curve of P-SEP at enrollment shows an AUC of 0.972 (95% CI 0.92–1.00). The best calculated cut-off value is 885 ng/L, with sensitivity of 94% (95% CI 74–100%) and specificity of 100% (95% CI 84–100%).

We demonstrated for the first time in a cohort of preterm newborns that P-SEP is an accurate biomarker for the diagnosis of LOS and may also provide useful information to monitor the response to therapeutic interventions. Further studies are needed to confirm the usefullness and accuracy of P-SEP as a screening tool for LOS in preterm newborns.



*p=0.00001 LOS vs. Control Group; **p=0.00006 LOS vs. Control Group; ***p=0.004 LOS vs. Control Group; ****p=0.01 LOS vs. Control Group.

Figure 1. Comparison of P-SEP levels in the LOS and Control groups.



*p=0.05 T1 P-SEP vs. T0 P-SEP; **p=0.03 T3 P-SEP vs. T0 P-SEP; ***p=0.02 T5 P-SEP vs. T0 P-SEP
#p=0.001 T3 PCT vs. T0 PCT; ##p=0.0001 T5 PCT vs. T0 PCT
§p=0.04 T3 CRP vs. T0 CRP; §§p=0.001 T5 CRP vs. T0 CRP

Figure 2. Changes of P-SEP, PCT and CRP in the LOS group. Median IQR1–3.

5ICCN_010
Umbilical NGAL level as predictior of acute kidney injury in infants with hypoplastic left heart syndrome

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Keywords: LCN2 protein; Newborn HLHS; Acute kidney injury

Acute kidney injury (AKI) is a primarily described complication after unbalanced systemic perfusion during fetal and neonatal periods in children with congenital heart defects. Among term-born children, hypoplastic left heart syndrome (HLHS) may be an important predisposing factor for this condition. The study focused on evaluation of umbilical neutrophil gelatinase-associated lipocalin (NGAL) levels, as an early biomarker predicting AKI in neonates with HLHS.

Among 1,271 neonates born from January 2013 to January 2014 in Department of Neonatology in Katowice, we enrolled 21 neonates with HLHS as the study group, and 60 healthy newborns as controls. Umbilical cord blood morphology with total counts of white blood cells and neutrophils, acid-base balance, NGAL, lactate, creatinine concentrations were performed in all study and control neonates. We also investigated the risk of AKI, diagnosed before cardiac surgery based on creatinine and umbilical NGAL concentrations in neonates born with HLHS.

Among neonates with HLHS, 8 children were diagnosed with AKI on average on the 3rd day of life. We observed higher umbilical NGAL concentrations in neonates with HLHS compared with controls. NGAL concentration was significantly higher in the group of neonates with HLHS and AKI, compared to those without AKI. ROC curve analysis demonstrated a critical level of NGAL in the umbilical cord blood >66.6 ng/mL, and this allows with 80% sensitivity and 94% specificity to predict AKI in newborns with HLHS.

We suggest that the umbilical blood NGAL concentration may be an early marker to predict AKI in neonates with HLHS.

5ICCN_011
Effect of *Bifidobacterium lactis* on total oxidant and antioxidant status in experimental NEC model

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Keywords: NEC; *Bifidobacterium lactis*; Total oxidant status; Total antioxidant capacity

Probiotics have been shown to be beneficial in preventing severe NEC development in VLBW infants. However these studies did not investigate mechanisms for the protective effect of the probiotics used and did not describe a rationale for the specific probiotic organisms selected. Little is known about how these organisms affect the intestine. Recently, clinical trials have also shown that the consumption of probiotics can decrease oxidative stress. In this study, we aimed to investigate the effect of *Bifidobacterium lactis* on total oxidant status (TOS) and total antioxidant capacity (TAC), in experimental NEC model.

Wistar-Albino rat pups were randomized into 3 groups on the 1st day of their lives. Pups in Groups 1 and 2 were taken away from their mothers and kept in an incubator for adjusted environment in means of temperature and humidity, throughout the study period. Each of these pups were fed with 4 × 0.2–0.3 ml of preterm formula prepared according to the study protocol. Group 1 (n = 8) received preterm formula + *Bifidobacterium lactis*, Group 2 (n = 8) received preterm formula. The control group (Group 3) (n = 6) were kept with their mother. Hypoxia-ischemia + cold injury was performed to create experimental NEC model, to all pups twice a day. All were sacrificed on the 4th day of the study. Tissues obtained were evaluated by pathological and biochemical tests.

Tissue examples were examined with TUNNEL method for examining apoptotic cell count in 1000 consecutive cells. Apoptotic cell count was 7.6±2.3 in Group 1, which was lower than 8.8±3.5 of Group 2 ($p > 0.05$). As expected, it was significantly lower in the control group, 2.5±1.3 ($p = 0.001$). Levels of total oxidant status (TOS) of all groups did not differ ($p > 0.05$). There was significant difference between Total Antioxidant Capacity (TAC) of groups ($p = 0.036$). TAC level of Group 1 was significantly higher than Group 2 ($p = 0.042$). TAC level of the Control group was significantly higher than the other two groups.

Our study demonstrated the potential mechanism of *Bifidobacterium lactis* in preventing NEC, which can be due to an increase in antioxidant mechanisms of the intestinal system.