

Assessment of soluble protein biomarkers for early diagnose and monitoring of late-onset neonatal sepsis

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Aim: The availability of a panel of protein biomarkers that can differentiate sepsis from Systemic Inflammatory Response Syndrome (SIRS) earlier may cause a significant impact on the morbidity and mortality of neonatal sepsis. The purpose is to describe the protein expression of selected biomarkers in newborns (NBs) with clinical late-onset sepsis (SIRS) and/or culture-positive caused by Gram-positive bacteria, Gram-negative bacteria and fungi at the day of diagnosis (day 0), in the intermediate stage (3rd day) and in the convalescence phase (7th and 10th post-diagnosis days).

Methods: To date, blood samples were collected from 12 Gram-positive, 8 Gram-negative, 5 fungi cases and 19 NBs with SIRS compared to 26 controls. Cytokines IL-1 β , IL-6, IL-8, IL-10, TNF- α , IL-12 were analyzed by flow cytometry. Soluble proteins IL-18, IL-27, CX3CL1, MBL, TREM-1, ESM1 and hepcidin were evaluated by ELISA; Lipoproteins were determined by gel filtration chromatography and enzymatic-colorimetric method using Labtest kits. **Results:** Hematological and laboratorial data on day 0 from culture-proven sepsis and SIRS groups were characterized by higher immature neutrophil count, immature/total neutrophil ratios and CRP than control group. IL-6, IL-8, IL-10, IL-27 and CX3CL1 concentrations were higher on day 0 of Gram-negative group compared to the other groups. On day 3, Gram-negative group still presented higher levels of IL-6, IL-8, IL-10 and IL-18, and on day 7, IL-6, IL-18 and CX3CL1 remained higher compared with the control group. IL-1 β , IL-10 and TNF- α analysis revealed higher levels on day 7 in SIRS group compared with the other groups. No differences were found in hepcidin and MBL levels. TREM-1 and ESM1 levels were higher on day 0 of Gram-negative group compared to controls. Of the lipoproteins tested, only HDL was lower in all culture-proven sepsis and SIRS groups when compared to control group. **Conclusion:** The results, so far, indicate that several biomarkers, such as IL-6, IL-8, IL-10, IL-18, CX3CL1, sTREM-1 and ESM1 could be useful in the diagnosis of Gram-

negative sepsis, and HDL levels indicate that this lipoprotein could be used as a general early biomarker of late neonatal sepsis.