

Presepsin (soluble CD14 subtype) in term and preterm newborns: preliminary reference ranges and usefulness in the diagnosis of sepsis

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Background:

Sepsis is a major cause of morbidity and mortality in newborns, especially in preterm infants. Several biochemical markers (C-reactive protein, procalcitonin, interleukin-6, etc.) have been proposed over the past years to diagnose and manage neonatal sepsis. However, these markers have a low diagnostic accuracy in neonatal infections. Recently, presepsin (soluble CD14 subtype, sCD14-ST), a circulating molecule fragment derived from sCD14, has been shown to be beneficial as sepsis marker. Nevertheless, few data are available on the usefulness of presepsin in the diagnosis of neonatal sepsis.

Objectives:

- 1) To determine the reference ranges for presepsin in healthy term newborns
- 2) To determine the reference ranges for presepsin in preterm newborns without clinical signs of sepsis
- 3) To evaluate the diagnostic accuracy of presepsin as a marker of sepsis in the neonatal period

Design/Methods:

Observational prospective study. The study cohort includes all infants admitted to our Neonatal Unit during a 18-months period. Infants enrolled in the study are stratified into 3 groups: 1) healthy term newborns (sample size = 400), 2) preterm newborns without clinical signs of sepsis (sample size = 200), 3) term and preterm newborns with clinical signs of sepsis and need for antibiotic therapy (sample size = 100). Exclusion criteria are the presence of major congenital malformations and lack of parental consent. A blood sample (100 microliters of whole blood) is collected to measure presepsin on day 3 of life in newborns of group 1 and 2. Blood samples for measuring presepsin are collected from infants with suspected sepsis at the following times: at the onset of clinical signs of sepsis (T0), every 12 hours for the next 48 hours (T1, T2, T3, T4), and at the end of antibiotic therapy (T5). C-reactive protein (CRP) and procalcitonin (PCT) are also determined at T0, T2, T4 and at the end of antibiotic therapy. A blood culture is performed at T0. Blood presepsin levels are determined using Pathfast® Immunoanalyzer (Mitsubishi Chemical Medience Corporation; Gepa Diagnostics, Milan, Italy). Demographic data, clinical and laboratory data are collected for all newborns and statistical analysis is performed.

Preliminary results:

Until now, we enrolled 487 newborns in group 1 (mean GA 38.9 ± 1.2 , mean BW 3211 ± 417.6), 168 in group 2 (mean GA 33.9 ± 2.5 , mean BW 2052.2 ± 594.8) and 42 in group 3 (mean GA 32.4 ± 5.9 , mean BW 1811 ± 1204). In group 1, mean presepsin value was 650.17 pg/ml (SD 258.18; Median 603.5, Q1-Q3 468 – 794). No significant difference in presepsin levels was observed at the different gestational ages after the 37th week of gestation. Gender, ethnicity, mode of delivery, small for gestational age, twin, maternal fever/elevated CRP, and stained amniotic fluid did not affect presepsin levels. In group 2, mean presepsin value was 722.32 pg/ml (SD 339.39; Median 636, Q1-Q3 506 – 862). No significant difference in presepsin levels was observed at the different gestational ages also in preterm infants. In group 3, mean presepsin value was 1243.05 pg/ml (SD

653.64; range 307 – 3261) at the onset of suspected sepsis and gradually decreased over time up to 754.41 pg/ml (SD 386.37) at the end of antibiotic therapy. The only infant who died of sepsis had a persistent high blood presepsin level (1888 pg/ml before death).

Of the 42 neonates enrolled in group 3, 14 (33.3%) had a positive blood culture at the onset of clinical signs of sepsis, 26 (61.9%) had a negative blood culture; blood culture was not performed in 2 babies. Infants with proven sepsis had a lower GA (31.5 ± 5.7 vs. 33.3 ± 6.1 weeks) and a lower BW (1501.3 ± 1039 vs. 2064.2 ± 1262.4 g) than infants with only clinical signs of sepsis. Conversely, infants with negative blood culture showed signs of infection earlier than infants with proven sepsis (mean age 15.4 vs. 44.6 days); furthermore, they had less severe symptoms and were born more frequently of mother with fever/elevated CRP or stained amniotic fluid compared with infants with proven sepsis. Presepsin values were significantly higher in infants with proven sepsis than in the others at T0, 1, 2, and 3. CRP values were also higher in infants with proven sepsis; however, our data showed that while CRP reached the peak at T2, presepsin reached the peak at T0.

Conclusions:

This is the first study that has determined the reference ranges for presepsin in a large sample of healthy term newborns and preterm newborns. Reference ranges for presepsin we have found are slightly higher in preterm than in term neonates and higher than those previously reported for preterm babies (Mussap M, JMFNM 2012). Presepsin appears an accurate biomarker for the diagnosis of neonatal sepsis and it seems to be earlier and more specific than CRP, even though these preliminary results need to be confirmed at the end of the study with a more in-depth statistical analysis. The development of Pathfast® as a point-of-care assay system may improve the management of septic newborns.