DETERMINING THE REFERENCE RANGE OF BLOOD PRESEPSIN IN TERM AND PRETERM NEONATES

Vener Claudia[1], Pugni Lorenza[2], Pietrasanta Carlo[2], Cortinovis Ivan[1], Casartelli Marina[2], Ronchi Andrea[2], Ghirardi Beatrice[2], Mosca Fabio[2], Milani Silvano[1]

[1]*Laboratorio G. Maccacaro - Dipartimento di Scienze Cliniche e di Comunità - Università degli Studi di Milano*

[2]*UOC di Neonatologia e Terapia Intensiva Neonatale - Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano - Dipartimento di Scienze Cliniche e di Comunità - Università degli Studi di Milano*

Introduction

Sepsis is still a major cause of morbidity and mortality in neonates, especially in preterm infants. Mortality can reach 60-70% in very low birth weight infants (birthweight <1500 g). Since this condition can rapidly progress to severe sepsis, septic shock and multiple organ dysfunction syndrome, early diagnosis is crucial to improve survival. Unfortunately, diagnosis may be difficult in the neonate: the earliest signs of the disease are often subtle and aspecific. Blood culture is the gold standard for the diagnosis of sepsis, but at least 48-72 hours are needed for the results and the number of false negative is not negligible. In 2005, Endo & al. identified a new biomarker, named presepsin (soluble CD14 subtype), that has proven to be a promising diagnostic and prognostic marker of sepsis in adult [1].

Objective

Data on presepsin in large cohorts of neonates have never been reported, neither for healthy nor for septic babies. Thus we planned a study to determine the reference range for presepsin in healthy term and preterm neonates.

Methods

This was a cohort study, carried out at the Neonatal Unit of Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico of Milan, Italy, between February 2014 and August 2014. Healthy 484 term (37 to 42 weeks' gestation) and 200 preterm (<37 weeks) neonates without clinical infection, according to CDC criteria [2], were enrolled in the study. Presepsin levels were determined on 100-200 μL of whole blood obtained via heel puncture or venipuncture from term neonates on day 3 of life, and from preterm neonates between 49 and 120 hours of life. Presepsin concentrations were measured using a compact fully automated immunoassay analyzer, PATHFAST® System (Mitsubishi Chemical Medience Corporation; Gepa Diagnostic, Milan, Italy).

Results

Term neonates. Among all the factors possibly affecting presepsin levels, the univariable analysis showed that those associated to the largest differences were Apgar at 1 min (≥8: 645 pg/ml ± 11.9 vs <8: 767 pg/ml ± 55.9), and multiple birth (twins: 538 pg/ml ± 62.2 vs singletons: 653 pg/ml ± 11.9). Anyhow, when simultaneously introduced into a multivariable linear model, all factors accounted only for 5.0% of the total sum of squares. A more parsimonious multivariable linear model was fitted after removing the factors that showed the lowest effect on presepsin level (those associated with a p-value >0.20). This reduced model explains 3.8% of the total sum of squares. After adjustment for all the factors in the model, presepsin levels appear to be significantly lower in twins (496 pg/ml ± 65.5 vs 655 pg/ml ± 11.8) and in neonates with Apgar at 1 min ≥8 (644 pg/ml ± 11.8 vs 774

pg/ml ± 56.2). So none of the above factors seems worth to be taken into account in determining the reference limits for presepsin blood levels in healthy term neonates.

Preterm neonates. The largest differences in presepsin level are observed between small for gestational age (SGA) (903 pg/ml ± 57.1) and adequate for gestational age (AGA) neonates (703 pg/ml ± 26.7), between neonates with and without mechanical ventilation at blood sampling (1090 pg/ml ± 86.9 vs 711 pg/ml ± 24.7) and at delivery (855 pg/ml ± 87.3 vs 729 pg/ml ± 25.8), between neonates with and without venous catether (801 pg/ml ± 47.5 vs 716 pg/ml ± 28.9), between neonates who underwent blood sampling after the 4^{th} day or before (797 pg/ml ± 46.2 vs 716 pg/ml ± 29.2), between males and females (778 pg/ml ± 35.1 vs 701 pg/ml ± 34.7). All these factors, when simultaneously introduced into a multivariable linear model, explain only 18.8% of the total sum of squares. A second multivariable linear model was fitted after removing the factors that showed the lowest effect on presepsin level (those associated with a p-value >0.50). This reduced model explains 13.4% of the total sum of squares. A third and more parsimonious multivariable linear model was fitted after removing the factors that showed the lowest effect on presepsin level (those associated with a p-value >0.20). This reduced model explains 12.3% of the total sum of squares. After adjustment for all the factors in the model, presepsin levels result to be significantly lower in AGA neonates (706 pg/ml ± 25.7 vs 890 pg/ml ± 55.0) and between neonates with and without mechanical ventilation at blood sampling (1074 pg/ml ± 85.3 vs 712 pg/ml ± 24.2). Even in this case, none of the above factors is expected to substantially affect the reference limits for presepsin blood levels in preterm neonates.

Conclusion

Presepsin blood levels seem to be quite independent of most of maternal and neonatal conditions examined in this study both in preterm and term neonates. The factors exerting significant effects (multiple birth and Apgar at 1 min, in term neonates, weight by gestational age and mechanical ventilation in preterm neonates) are expected to affect presepsin reference limits only to minor extent.

References

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AUTORE DI RIFERIMENTO: Claudia Vener (età superiore a 35 anni)

Claudia Vener, MD, PhD, MS,
Dipartimento di Scienze Cliniche e di Comunità,
Università degli Studi di Milano,
Unità di Statistica Medica e Biometria "Giulio A. Maccacaro",
Campus Cascina Rosa

Scuola di Specializzazione in Statistica Sanitaria e Biometria
Via Augusto Vanzetti, 5 - 20133 Milano
tel. 02.503.20855-20868-20854 (fax 02.502.20866)
Recapito Postale, Via G. Venezian, 1 - 20133 Milano