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LETTER

Serum pentraxin 3 concentrations in neonates

ANDERS LANNERGÅRD[1], FREDRIK ROSENSTRÖM[1], ERIK NORMANN[2] & ANDERS LARSSON[1]

[1]*Department of Medical Sciences, Uppsala University, Uppsala, Sweden, and*
[2]*Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden*

Dear Editor,

C-reactive protein (CRP) is one of the most commonly used diagnostic biomarkers in the clinical setting for diagnosing and monitoring of inflammatory and infectious diseases. However, in neonates several questions remain, regarding the interpretation of an increased serum CRP concentration during the first days of life in otherwise healthy newborns, especially in preterms (1). Pentraxins are endogenous substances that neutralize or eliminate a variety of pathogenic agents in concert with the complement system and macrophages. These complex biological responses to tissue injury, necrosis, infections, or immune-related diseases are part of the natural innate defence system (2). The pentraxin family consists of proteins with cyclic multimeric structures. The well-known acute-phase protein CRP belongs to the short members of the family, while pentraxin 3 (PTX3) belongs to the long counterparts. PTX3 is released from macrophages and endothelial cells among a great variety of other cell types in which the protein is synthesized and stored. On stimuli from primary inflammatory signal proteins, as interleukin-1 (IL-1), tumour necrosis factor-alpha (TNF-α), and microbial lipopolysaccharides (LPS) as well as toll-receptor-mediated signals, PTX3 will be synthesized, and the serum concentration will increase up to 100-fold in 6–8 hours. Interleukin-6 (IL-6) is a weak inducer for PTX3 (3,4). PTX3 synthesis is thus produced close to the site of inflammation and is not dependent on cytokine production or liver function.

All subjects in our study were recruited from the Department of Women's and Children's Health, Uppsala University Hospital, Uppsala, Sweden. Three groups were included: umbilical venous cord blood collected from term healthy newborns ($n = 36$), venous blood from term healthy newborns at 3–7 days of age at phenylketonuria (PKU) testing ($n = 11$), and venous blood from very preterm (VPT) newborns at the neonatal supportive care unit ($n = 40$). The median gestational age and postnatal age were 26 weeks (range 23–31, IQR 4) and 27 days (range 4–103, IQR 26), respectively. The median birth weight was 954 g (range 422–2244, IQR 400). The study was approved by the local Ethical Review Board of Uppsala University. Serum PTX3 was determined by a commercial sandwich ELISA kit (DY1826, R&D Systems, Minneapolis, MN, USA), as described elsewhere (5).

Serum concentrations of PTX3 in term healthy newborns were lower than in term healthy newborns at 3–7 days of age and VPT newborns at the supportive care unit ($P < 0.0001$) (Figure 1). VPT newborns showed a lower serum concentration of PTX3 than term healthy newborns at 3–7 days of age ($P < 0.0001$) (Figure 1). To our knowledge, no studies have presented such data before. Previous studies on serum amyloid A and high-sensitivity (hs) CRP reported gestational age-related differences, with higher concentrations in VPT compared with full-term healthy babies, during the neonatal period (6-8). A similar pattern seems to apply to PTX3. Because PTX3 may be a faster acute-phase protein that is not

Correspondence: Dr Anders Lannergård, MD, PhD, Department of Medical Sciences, Section of Infectious Diseases, Uppsala University, S-751 85 Uppsala, Sweden. E-mail: anders.lannergard@akademiska.se

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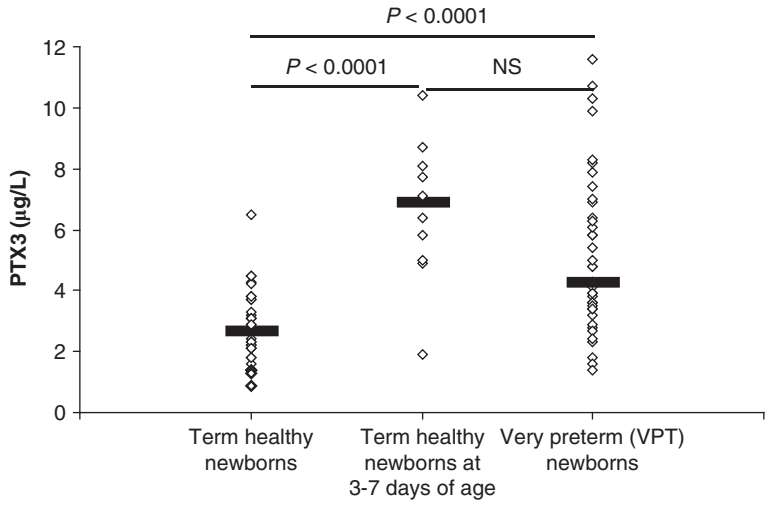

Figure 1. Serum concentrations in term healthy newborns (n = 36), term healthy newborns at 3-7 days of age (n = 11), and very preterm newborns (n = 40). A Kruskal–Wallis test was used for continuous three-group comparisons. Data were computed by Statistica 10 (StatSoft, Tulsa, OK, USA). A P value of <0.05 was considered statistically significant. Median values are shown with filled bars.

liver-dependent, it is probable that it is superior to traditional biomarkers for mirroring rapid inflammatory courses. Compelling indications are present that a high serum concentration of PTX3 predicts shock, poor outcome, and organ failure in meningococcal disease and severe sepsis, respectively, in children and adults (9,10).

The serum concentration of PTX3 in the cohort should be interpreted with care because a part of the sample was likely to have its origin from infants treated with antibiotics or with inflammatory reactions. It is important to remember that there is an extremely rapid foetal development up to the expected day of delivery. This means that there will be differences between a prematurely born child with a gestation age of 30 weeks from a child with a gestation age of 36 weeks. The cause of the prematurity may also involve inflammatory reactions which will further increase the variability in PTX3 values in samples from prematurely born babies. Nevertheless, the prematurely born cohort, despite the existence of possible factors that may influence the serum PTX3 concentration, could be representative for this group of newborn infants.

In summary, serum PTX3 may be a promising acute-phase protein for interpretation of affected newborns with symptoms and signs of sepsis. Serum PTX3 is measurable in both term and preterm babies in similarity with other acute-phase proteins. Considering the promising results from studies in adult patients with sepsis, PTX3 might represent a helpful tool in diagnosis of sepsis in the neonate as well. The predictive value of PTX3 may thus be higher compared with conventionally used acute-phase proteins. However, regarding serum PTX3 concentrations in infants with infection we propose a prospective study on neonatal sepsis with well-defined established criteria.

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