


**Usefulness of Procalcitonin in Neonates at Risk for Infection**

**To the Editor:**

We are very interested in the report by Sachse et al. (1) on procalcitonin (PCT) variations in the neonatal period. This report confirms and extends previous work on the daily variations of PCT during the first days of life in noninfected newborn infants (2, 3). We agree that PCT could be a useful marker for the presence, course, and prognosis of bacterial infection, particularly in newborns hospitalized with a risk factor for infection (such as an increase in the mother’s body temperature during delivery, premature rupture of membranes, vaginal colonization by group B streptococcus, and other factors). In this context, prophylactic antibiotic therapy is started during labor and if clinical signs of infection are present at delivery, antibiotics are continued. Thus, the diagnosis of infection cannot be confirmed by culture because this preventive therapy is responsible for the negativity of bacteriological tests (blood and cerebrospinal fluid cultures).

We present additional data on PCT values obtained in 52 neonates hospitalized with a risk factor for infection. All mothers received a prophylactic antibiotic (Ampicillin®), and all samples were negative by bacteriological tests. Two groups were defined on the basis of health status. The first group (n = 44) comprised newborn infants with a risk factor for infection without clinical signs of infection. The second group (n = 8) comprised newborn infants with a risk factor for infection and clinical signs of infection at birth (bradycardia, hypotension, microcirculation impairment, changes of skin coloration, or an increase of the neonate’s body temperature).

The blood samples were obtained at 24 and 72 h of life. PCT was determined using an immunoluminometric assay (Brahms Diagnostica). The PCT concentrations (3.5 ± 0.5 μg/L) in the group of newborn infants without clinical signs of infection (Table 1) were similar to those published elsewhere (1–3). In contrast, in the second group a significant increase of PCT was observed on the first day of life (58.2 ± 7.1 μg/L). Nevertheless, these values were lower than our previous values described in materno-fetal infection, e.g., 162 ± 32 μg/L (2), but higher than the physiological peak reported by Sachse et al. (1) and by our group (2). In the second group, PCT concentrations decreased on the third day of life. Thus, increased PCT represents a biological marker of materno-fetal infection, the negativity of bacteriological samples being a reflection of the efficacy of the early antibiotic prophylaxis.

In conclusion, even with the existence of a physiological peak, PCT is useful in the diagnosis and monitoring of neonates at risk of infection, particularly when the bacteriological samples are negative. Additional data are needed to document the value of PCT measurements for reducing the need for invasive collection of samples for bacteriological testing and for reducing the use/abuse of antibiotics.

**Table 1. Serum PCT concentrations (μg/L) during the first days of life obtained in 52 neonates hospitalized for a risk factor for infection with or without clinical signs of infection.**

<table>
<thead>
<tr>
<th>Patients</th>
<th>24 h of life</th>
<th>72 h of life</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group 1 (n = 44): without clinical signs of infection</strong></td>
<td>Mean ± SE</td>
<td>3.5 ± 0.5</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>1.7</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>0.4–16</td>
</tr>
<tr>
<td><strong>Group 2 (n = 8): with clinical signs of infection</strong></td>
<td>Mean ± SE</td>
<td>58.2 ± 7.1a</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>23–111</td>
</tr>
</tbody>
</table>

a Significance of results between group 1 and group 2; P < 0.001, Mann–Whitney test.
PCT (1), transplacental passage of this substance must be considered, although we are not aware of any study dealing with this issue. Parallel measurements of maternal and neonatal serum PCT concentrations at delivery could give insight into the possible sources of increased PCT in the first hours of life.

Regarding the serum PCT concentrations in newborn infants without infection, the data presented by Dr. Martin-Denavit and co-workers combine with those presented by another group (2) and our group to give a clearer picture of a physiological peak in serum PCT occurring between 12 and 36 h after birth. Physiological peak PCT concentrations generally are <20 μg/L; therefore, values exceeding that limit can be regarded as a sign of infection even in this time period.

References


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The authors of the report cited above respond:

To the Editor:

We appreciate the comments of Dr. Martin-Denavit and co-workers on our report and the information they presented, which throws additional light on the use of serum procalcitonin (PCT) for the diagnosis of neonatal infection. They regard markedly increased serum PCT as a marker of maternal-fetal infection, although fetal involvement is difficult to confirm. In the absence of microbiological evidence, the diagnosis of infection relies on clinical signs, which can be found in a variety of conditions. Alternatively, the high serum PCT concentrations measured in eight neonates could represent maternal PCT, increased by an infection not involving the fetus, after passage through the placenta. Given the low molecular mass (≈12 kDa) of PCT (1), transplacental passage of this substance must be considered, although we are not aware of any study dealing with this issue. Parallel measurements of maternal and neonatal serum PCT concentrations at delivery could give insight into the possible sources of increased PCT in the first hours of life.

Regarding the serum PCT concentrations in newborn infants without infection, the data presented by Dr. Martin-Denavit and co-workers combine with those presented by another group (2) and our group to give a clearer picture of a physiological peak in serum PCT occurring between 12 and 36 h after birth. Physiological peak PCT concentrations generally are <20 μg/L; therefore, values exceeding that limit can be regarded as a sign of infection even in this time period.

References


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Influence of Age and Sex and Day-to-Day and Within-Day Biological Variation on Plasma Concentrations of Fatty Acid-binding Protein and Myoglobin in Healthy Subjects

To the Editor:

Fatty acid-binding protein (FABP), like myoglobin (Mb), increases significantly within ~3 h after onset of symptoms of acute myocardial infarction (AMI) and returns to health-related values within 12 to 24 h (1). For the early assessment or exclusion of AMI, FABP performs better than Mb (2, 3). Although FABP, like Mb, is also found in skeletal muscle, the distinct ratio of the contents of Mb over FABP in heart (ratio, 4–5) and skeletal muscle (ratio, 20–70) allows the discrimination between myocardial and skeletal muscle injury (4).

For the assessment of clinical reference values, it is important to know the possible influence of biological variations such as age, sex, and day-to-day and within-day fluctuations (5); however, for FABP such data are lacking. The aim of the present study was to establish these parameters for FABP first in a large group of volunteers of different ages. Mb was also measured to delineate possible effects of age and sex on the ratio of the plasma concentrations of Mb over FABP. We also studied day-to-day and within-day biological variation (within-person) for both FABP and Mb concentrations in another group of volunteers.

For the first substudy, plasma samples were taken from 312 donors (110 women and 202 men; ages, 21–70 years) visiting the blood bank of Liège, Belgium. EDTA was added to samples to prevent clotting. For the study of within-person biologic variation, blood samples were obtained from young and apparently healthy volunteers (six men and six women; ages, 19–27 years) recruited from the student population of Maastricht University. Samples were obtained at the following time points: on day 1, at 0930, 1100, 1400, 1700, 2000, and 2300; on days 2, 1700, 2000, and 2300; on day 2, at 0930, 0700, 0930; and on days 8, 15, 22, 29, and 57 at 0930. Citrate was added to prevent clotting, and samples were immediately aliquoted and stored at −80 °C until use. The study was approved by the medical ethics committee of the Academic Hospital Maastricht, and all subjects gave informed consent. FABP was measured with a sensitive noncompetitive sandwich-type ELISA (6), using recombinant human (heart-type) FABP as the calibrator (7). Mb was measured with a turbidimetric im-