Changes of procalcitonin level in multiple trauma patients

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Abstract

Background: Some aspects of the pathophysiology of complications in multiple-trauma patients still remain unclear. Mediators of inflammation have been postulated as playing a key role in being responsible for life threatening complications of multiple trauma patients. The objective of this study was to evaluate the prognostic value of procalcitonin (PCT) level in multiple trauma patients.

Methods: A prospective study took place including patients with multiple trauma hospitalised in several hospital units. PCT level was measured in blood from 45 patients, aged 18–70 years using enzyme-linked immunoassay. The patients were divided into three groups: group I — individuals with multiple trauma with central nervous system injury; group II — those with multiple trauma without CNS injury; and group III — patients with isolated central nervous system injury.

Results: Initial PCT levels were below 0.5 ng mL⁻¹ regardless of the cause of trauma. In the 24th hour of observation, a statistically significant increase of PCT concentration vs. initial levels was recorded in all groups of patients. Then PCT levels decreased significantly at the 3rd measurement point in all groups, and they remained unchanged until the last measurement. The highest levels of PCT were observed in multiple trauma patients without CNS injury (group II). In this group of patients, a significantly longer duration of surgery in the post-trauma period affected PCT levels. PCT concentrations in patients who died were significantly greater than in survivors.

Conclusions: A long lasting elevated concentration of procalcitonin in the post-traumatic period, or its repeated increase, is a good marker of developing complications observed earlier than clinical manifestations.

Key words: multiple trauma, inflammatory reaction; multiple trauma, procalcitonin; multiple trauma, prognosis

Physiological responses triggered by trauma are beneficial for the organism if not experienced to excess. They help to maintain circulating blood volume, remove necrotic tissue, heal wounds and boost immunity. However, some post-traumatic reactions are adverse for the organism and can lead to serious negative effects and even to death [1–3]. The reactions of the body to mechanical injury, surgical trauma or burns are complex and multistage. They include metabolic, neuroendocrine, and immune responses through activation of inflammatory mediators, and local and systemic reactions. Numerous studies have been performed in recent years aiming to clarify the reactions of organisms suffering from tissue damage, hypovolaemia, and infection. These have given important clues towards understanding the pathophysiology of post-traumatic response, and are crucial in distinguishing as early as possible beneficial processes from damaging ones [4–7]. Appropriate biochemical markers are inevitable in the diagnostic and therapeutic process in trauma. Procalcitonin is one of the most promising of these.
Procalcitonin (PCT) is a protein composed of 116 amino acids and originates from a precursor of preprocalcitonin produced in the thyroid gland, liver and neuroendocrine cells of the lungs and intestine. However, it is converted to calcitonin only in the thyroid C-cells. Procalcitonin synthesised in other tissues is now considered as a ‘hormokine’ but its exact role in health and disease has not yet been established [8].

Healthy individuals have a low concentration of PCT in their blood. The level of procalcitonin rises in response to proinflammatory stimuli, especially those of bacterial origin. In experiments, hepatic tissue stimulated by TNF-alpha or IL-6 produce PCT in significant amounts in the 24th hour after stimulation [9]. According to previous studies [10, 11], PCT is a very good marker of bacterial infections, although its prognostic value in multitrauma patients has not been made clear yet.

Multitrauma patients manifest an increase in PCT serum concentration, which depends on the severity of the injury. Peak values are observed in the first 24 hours and around the 3rd day following trauma. High levels of PCT during the first days after injury are believed to be a prognostic factor in severe systemic inflammatory response syndrome (SIRS), infection or multiple organ dysfunction syndrome (MODS) [12–16].

The purpose of this study was to evaluate procalcitonin (PCT) as a marker for inflammatory reactions in multitrauma patients.

METHODS

This study was approved by the Bioethical Commission in the Regional Medical Chamber in Rzeszow. 45 patients older than 18 and younger than 71 years were included into the study; all were hospitalised because of various types of injury.

Inclusion criteria were based on the results of physical examination and imaging examinations revealing physical injuries of different body parts. Patients underwent emergency CT examination within an hour of hospital admission. Individuals with diabetes and autoimmune diseases were excluded from the study.

Patients or their families were informed about the purpose and design of our study before they were registered as study participants. Written consents were obtained from all patients or their relatives. If the patient had been unconscious and there were no relatives, the consent would have been implied and taken later from a family member. No blood samples were collected from patients who didn’t agree to participate in the study or whose relatives refused to give their consent.

The patients were divided into three groups, each comprising 15 patients:

Group I — multiple trauma with central nervous system injury (MT + CNS).
Group II — multiple trauma without CNS injury (MT).
Group III — only central nervous system injury (CNS).

BLOOD SAMPLING

Two samples of 7.5 mL of blood were collected from patients in order to perform standard laboratory tests and PCT assay in serum. Blood was drawn from the vena basilica after small pressure was applied for a short period of time or from the femoral artery in serious injuries. No anticoagulants were added to blood samples. The samples were collected according to the following time pattern:

1. Within the first hour following hospital admission (A),
2. One day after hospital admission (B),
3. Three days after hospital admission (C),
4. Five days after hospital admission (D).

Blood samples were cooled to +4°C. Then blood was centrifuged (3,000 revolutions per minute for 10 minutes) and the sera were stored at −20°C.

Procalcitonin (PCT) levels were determined using enzyme-linked fluorescent immunoassay (ELFA) (BIO-TEK Instruments Inc.) using an EIT-System ELX 800 device. This is a one step immunoassay sandwich method with a final fluorescent detection. PCT concentration in the serum of healthy individuals is below 0.5 ng mL\(^{-1}\).

STATISTICAL ANALYSIS

Data was analysed statistically using software SPSS 16.0, SPSS Inc, USA. Assessed parameters were described as follows: mean ± SD or minimum, maximum and median. Quantitative features were compared using the Mann-Whitney U test for independent variables or the Wilcoxon test for comparing related samples. A significance level of \( P < 0.05 \) was applied.

RESULTS

The demographics of the studied patients (age, height, body mass, body mass index (BMI), duration of surgery) are presented in Table 1.

The median of initial PCT concentration in group I was 0 ng mL\(^{-1}\). A significant increase of PCT levels up to 1.87 ng mL\(^{-1}\) \((P = 0.039)\) was observed on the 1\(^{st}\) day after the trauma followed by a decline towards 0.595 ng mL\(^{-1}\) \((P = 0.017\) against the 24 hour results) i.e. to values not different from the initial PCT level in terms of statistical significance.

Similar patterns of PCT concentrations were observed in group II but the values on day 1 were even higher than in group I (median 2.50 ng mL\(^{-1}\)) After three and five days the PCT levels declined also in this group but did not reach the initial low levels. In group III, PCT plasma concentrations
Table 1. Patient characteristics, duration of surgical interventions, and the need for blood transfusions

<table>
<thead>
<tr>
<th>Group</th>
<th>Data</th>
<th>Age (years)</th>
<th>Body mass (kg)</th>
<th>Height (cm)</th>
<th>BMI (kg m$^{-2}$)</th>
<th>Duration of surgery (min)</th>
<th>PRBC transfusions (units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I MT + CNS</td>
<td>Median</td>
<td>27</td>
<td>82</td>
<td>174</td>
<td>25.1</td>
<td>150</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Min–Max</td>
<td>18–70</td>
<td>63–86</td>
<td>157</td>
<td>21.0</td>
<td>40</td>
<td>0–8</td>
</tr>
<tr>
<td>II MT</td>
<td>Median</td>
<td>29</td>
<td>74</td>
<td>175</td>
<td>24.4</td>
<td>240</td>
<td>4</td>
</tr>
<tr>
<td>III CNS</td>
<td>Median</td>
<td>58</td>
<td>80</td>
<td>174</td>
<td>26.4</td>
<td>104</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Min–Max</td>
<td>30–71</td>
<td>68–88</td>
<td>155–180</td>
<td>24.7–29.6</td>
<td>60–165</td>
<td>0–3</td>
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<tr>
<td>Group I</td>
<td>vs. II</td>
<td>$P$ value</td>
<td>0.348</td>
<td>0.318</td>
<td>0.907</td>
<td>0.411</td>
<td>0.267</td>
</tr>
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<td></td>
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<tr>
<td>Group I</td>
<td>vs. III</td>
<td>$P$ value</td>
<td>0.693</td>
<td>0.796</td>
<td>0.546</td>
<td>0.222</td>
<td>0.299</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group II</td>
<td>vs. II</td>
<td>$P$ value</td>
<td>0.327</td>
<td>0.123</td>
<td>0.558</td>
<td>0.055</td>
<td>0.035</td>
</tr>
</tbody>
</table>

BMI — body mass index; PRBC — packed red blood cells

Table 2. Changes of PCT concentrations (ng mL$^{-1}$) in examined groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Data</th>
<th>0–1 h (A)</th>
<th>24 h (B)</th>
<th>72 h (C)</th>
<th>120 h (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td>0.05</td>
<td>1.87</td>
<td>0.595</td>
<td>0.515</td>
</tr>
<tr>
<td>I MT + CNS</td>
<td>Min–Max</td>
<td>0–5.18</td>
<td>0–37.02</td>
<td>0–17.65</td>
<td>0.12–13.51</td>
</tr>
<tr>
<td></td>
<td>$P$ value</td>
<td>vs. 0 hour</td>
<td>0.039</td>
<td>0.128</td>
<td>0.123</td>
</tr>
<tr>
<td></td>
<td></td>
<td>vs. previous measurement</td>
<td>0.039</td>
<td>0.017</td>
<td>0.093</td>
</tr>
<tr>
<td>Group II</td>
<td>Median</td>
<td>0.05</td>
<td>2.50</td>
<td>0.78</td>
<td>0.39</td>
</tr>
<tr>
<td></td>
<td>Min–Max</td>
<td>0–5.62</td>
<td>0–8.48</td>
<td>0–47.33</td>
<td>0–13.19</td>
</tr>
<tr>
<td></td>
<td>$P$ value</td>
<td>vs. 0 hour</td>
<td>0.004</td>
<td>0.152</td>
<td>0.533</td>
</tr>
<tr>
<td></td>
<td></td>
<td>vs. previous measurement</td>
<td>0.13</td>
<td>0.152</td>
<td>0.533</td>
</tr>
<tr>
<td>Group III</td>
<td>Median</td>
<td>0</td>
<td>0.34</td>
<td>0.13</td>
<td>0</td>
</tr>
<tr>
<td>CNS</td>
<td>Min–Max</td>
<td>0–1.14</td>
<td>0–47.88</td>
<td>0–6.32</td>
<td>0–1.98</td>
</tr>
<tr>
<td></td>
<td>$P$ value</td>
<td>vs. 0 hour</td>
<td>0.018</td>
<td>0.043</td>
<td>0.893</td>
</tr>
<tr>
<td></td>
<td></td>
<td>vs. previous measurement</td>
<td>0.018</td>
<td>0.018</td>
<td>0.027</td>
</tr>
<tr>
<td>Group I</td>
<td>$P$ value</td>
<td>vs. II</td>
<td>0.975</td>
<td>0.676</td>
<td>0.872</td>
</tr>
<tr>
<td></td>
<td></td>
<td>vs. III</td>
<td>0.356</td>
<td>0.102</td>
<td>0.090</td>
</tr>
<tr>
<td>Group II</td>
<td>$P$ value</td>
<td>vs. III</td>
<td>0.312</td>
<td>0.170</td>
<td>0.072</td>
</tr>
</tbody>
</table>

DISCUSSION

Procalcitonin is a protein synthesised in different tissues originating from a precursor of preprocalcitonin, and in this form it is secreted into body fluids. Healthy people have low concentrations of PCT in their blood. Multiple trauma patients manifest an increase of PCT serum concentration, depending on the severity of the injury [17].

In our study, an increase in PCT serum levels was observed in multiple trauma patients depending on the kind of injury. The highest values were measured on the 2\textsuperscript{nd} day following trauma. PCT concentration remained unchanged during the 1\textsuperscript{st} day after injury.

PCT seems to be a good marker for monitoring the status of inflammatory reaction in patients suffering from multiple trauma [12], although significant gender differences between men and women have been found [13]. Experiments have shown that hepatic tissue stimulated by TNF-alpha or

Figure 1. Mean PCT levels measured in the studied groups. MT+CNS (Group I) — multi organ trauma with CNS injury; MT (Group II) — muli organ trauma; CNS (Group III) — isolated CNS injury

were outside the measurable values both at the beginning and at the end of the studied period, and also the levels on day 1 were lower compared to groups I and II. The obtained results are presented in Table 2 and Figure 1.
IL-6 produced PCT in significant amounts on the 1st day after stimulation [9]. A prospective study in a group of 175 patients admitted to the ICU revealed correlations between various mediators (IL-6, PCT, TNF-alpha) and the intensity of inflammatory response for multiple injury. The authors concluded that PCT was the best marker of inflammatory reaction to trauma [14]. If a second increase in PCT concentration is observed (unlike C-reactive protein), it should be treated as a sign of severe infection complicating trauma [15]. However, not all studies have confirmed that PCT has a greater prognostic value in the diagnosis of infection than CRP. A study including 205 surgical patients showed greater sensitivity of CRP compared to PCT (71.8% vs. 67.6%) and greater specificity (66.6% vs. 61.3%) when confirming the presence of infections. The cut-off levels for PCT and CRP in this study were 0.6 ng mL\(^{-1}\) and 7.9 mg dL\(^{-1}\), respectively. In another study including 60 patients, higher PCT levels were found in individuals with infections, although the results confirmed a better correlation for CRP [18].

A postoperative increase of PCT levels in patients without any signs of infection depends on the localisation of the injury and the type of surgery. After major operations, higher PCT levels have been measured compared to more minor interventions [19].

Our results are in concordance with the results of other published studies. In all three groups, and almost in all patients, the initial concentration of PCT was low i.e. below 0.05 ng mL\(^{-1}\). On the 1st day in all groups a statistically significant PCT increase was recorded, followed by a decline on the third and fifth days.

We found also that peak PCT concentrations in isolated CNS injury were significantly lower than in the two other groups of patients.

When analysing PCT levels in Group I (MT + CNS), we observed that patients who died had significantly higher levels of procalcitonin compared to trauma survivors (see Fig. 2).

**CONCLUSIONS**

1. Initial PCT concentrations were low regardless of the cause of injury and were below 0.05 ng mL\(^{-1}\).
2. After 24 hours, a statistically significant increase of PCT level was recorded, followed by a gradual decline in all groups.
3. The highest increase of PCT concentration was observed in multitrauma patients without CNS injury. There is no doubt that lengthier surgery had a significantly greater effect in the post-traumatic period in this group of patients.
4. PCT concentrations 24 hours after the trauma were significantly higher in patients who died compared to survivors.

In summary, our results confirm that PCT is a reliable marker of post-traumatic inflammatory response and the prognosis of multitrauma patients.

**References:**


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