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ORIGINAL RESEARCH

Medicine Science 2017;6(3):424-6

Medicine Science International Medical Journal

The importance of procalcitonin in early diagnosis of sepsis

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Received 03 November 2016; Accepted 26 December 2016
Available online 29.12.2016 with doi: 10.5455/medscience.2016.05.8582

Abstract
Despite the advances and a wide range of studies conducted, sepsis is one of the most frequent causes of death in patients with critical health condition. Early diagnosis, rapid and effective treatment are extremely important. Use of procalcitonin (PCT) for this purpose has become widespread and notable recently. Procalcitonin is an important test as "point-of-care testing (POCT)" just like C-reactive protein (CRP). Procalcitonin is the prohormone of calcitonin. It is released from the parenchymal cells of the liver, kidneys and muscles, and in response to bacterial toxins, it is released from the adipocytes. As a response to bacterial infection, the serum procalcitonin level may increase by 5000-fold within 2-4 hours. C- reactive protein is synthesized in the liver as a result of interleukin-6 (IL-6) trigger due to tissue injury, inflammation and/or infections. The aim of our study was to emphasize the importance of PCT as an indicator in patients suspicious of sepsis in the early period. A total of 66 patients with critical situation were included in the study conducted at the İnönü University Medical Faculty Turgut Özal Medical Center Investigation Hospital between February 2007 and August 2008. These patients were appropriate for the diagnostic criteria of systemic inflammatory response syndrome (SIRS). Appropriate antibiotiotherapy was begun for the patients. The PCT and CRP levels were investigated on the first day after having been included in the study, and on the third and seventh days. The mean C-reactive protein levels were 132.41, 108.39 and 83.47 mg/l on the 1st, 3rd and 7th days, respectively. The minimum level of procalcitonin was 0.095 ng/ml on the first day, and the maximum level was 316.054 ng/ml. The minimum/maximum levels were 0.091 and 306.043 ng/ml on the 3rd day, and 0.081 and 12.15136 ng/ml on the 7th days, respectively. No statistically significant difference was observed betweern the serum procalcitonin levels on the 1st and the 3rd days ($p<0.229$), whereas a significant difference was observed between its levels between the 1st and the 7th days ($p<0.002$). Likewise, the difference between the 3rd and the 7th days was statistically significant ($p<0.005$). C-reactive protein levels revelaed a significant difference between the 1st and the 7th days ($p<0.013$) and between the 3rd and the 7th days ($p<0.010$). The Wilcoxon Signed test was used to investigate statistical significance. The diagnostic value of procalcitonin has been widely used in septic patients. Although conflicting results have been obtained in different studies, despite the fact that some studies have not found PCT supportive for the diagnosis of sepsis, we believe that PCT is an appropriate and important indicator in the early diagnosis and follow-up of sepsis as CRP.

Keywords: Procalcitonin, early diagnosis, sepsis

Introduction

Early diagnosis and treatment dramatically increase the survival rates in sepsis. Procalcitonin (PCT) is an acute phase reactant. It is an important indicator in the diagnosis and treatment of sepsis. It was first detected in the medullary thyroid carcinoma cells [1]. Procalcitonin is formed of 116 amino acids, and is the precursor protein of calcitonin [2]. Under normal circumstances, PCT is transformed into calcitonin, catacalcin and N-terminal residues in a healthy individual. Therefore, it is in undetectable levels in the blood. However, it becomes detectable in the blood in severe bacterial infections and sepsis. The serum PCT concentration may reach 1000 ng/ml. Early detection of the increased PCT level is extremely important in the diagnosis and follow-up of the patients, and it is also useful [3]. The procalcitonin level is increased, particulary in bacterial infections and other septic conditions. This increase helps the clinician make a quick decision. Procalcitonin induction is fairly rapid. Initial levels increase within 2-6 hours, and reach a plateau within 6-12 hours. Its concentration remains elevated for up to 48 hours, and begins regressing in the subsequent 2 days [4]. The CRP increase becomes notable 4-6 hours after the stimulation by inflammation or infection, and makes a peak in 36-50 hours [5].

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Materıals and Method

A total of 66 patients with a critical situation were included in the study conducted at the İnönü University Medical Faculty Turgut Özal Medical Center Investigation Hospital between February 2007 and August 2008. The patients comprised 33 (50%) females and 33 (50%) males. The age range was 18-86 years. These patients met the diagnostic criteria of systemic inflammatory response syndrome (SIRS). Blood, urine, wound or the related samples of the patients were collected on admission for bacterial culture investigation. Appropriate antibiotherapy was started for the patients. The PCT and CRP levels were measured on the first day after inclusion, and on the 3rd and the 7th days. All data were recorded into the "Statistical Package

for Social Science, version 17" (SPPS, Inc. Chicago, IL,USA). Among the non-parametric tests, the Wilcoxon Signed Test was used in order to evaluate the distribution of the dependent variables. The mean values were reported for the CRP level since the collected data showed a normal distribution for CRP level, and minimal and maximal values were reported for PCT due to the distibution range of PCT.

Results

The mean C-reactive protein levels were 132.41, 108.39 and 83.47 mg/l on the 1st, 3rd and 7th days, respectively. The minimal level of procalcitonin was 0.095 ng/ml on the first day, and the maximal level was 316.054 ng/ml. The minimum/maximum levels were 0.091 and 306.043 ng/ml on the 3rd day, and 0.081 and 12.15136 ng/ml on the 7th days, respectively. No statistically significant difference was observed between the serum procalcitonin levels on the 1st and 3rd days ($p<0.229$), whereas a significant difference was observed between it slevels between the 1st and the 7th days ($p<0.002$). Likewise, the difference between the 3rd and 7th days was statistically significant ($p<0.005$). C-reactive protein levels revelaed a significant difference between the 1st and the 7th days ($p<0.013$) and between the 3rd and the 7th days ($p<0.010$). The Wilcoxon Signed test was used to investigate statistical significance. C-reactive protein levels revelaed a significant difference between the 1st and the 7th days ($p<0.013$) and between the 3rd and the 7th days ($p<0.010$). The Wilcoxon Signed test was used to investigate statistical significance.

Discussion

Procalcitonin is indicated as an important early diagnostic and treatment marker due to easy sample collection, easy pre-analysis period, rapid measurement, and related patient satisfaction, whereas it has the disadvantages of high cost, uncertain standardization and calibration, and unsuitability for local laboratory methods [3]. However, assessment of PCT as a point-of-care testing is also important. The detection limit of procalcitonin has been reported as 0.1 ng/ml. It is generally below 0.1 ng/ml in healthy individuals [6]. Different limit levels of PCT have been defined by some authors as follows: <0.5 µg/L: severe bacterial infection does not seem possible, 0.5-2 µg/L: possible local bacterial or systemic viral infection, 2-10 µg/ml: possible systemic bacterial, fungal or plasmodial infection, >10 µg/ml: possible sepsis or septic shock [7].

The mortality rates have been reported as 28–50% in severe sepsis [8,9). In a recent meta-analysis comparing the survivors and losses due to sepsis, early period levels of procalcitonin have been found to be significant [10]. It has been emphasized in the study of Haung et al. that PCT is an important marker in the diagnosis and follow-up of bacterial sepsis as much as CRP, and the PCT level has been found to be even more sensitive and specific compared to the CRP level as well [11]. Likewise, the PCT levels were found to be significantly high in the early period (1st and 3rd days) in our study. Similarly, early period levels of CRP (1st and 3rd days) were found to be significantly higher compared to the late period levels. Furthermore, statistical significances obtained by PCT ($p<0.002$, $p<0.005$) were over the significance obtained by CRP ($p<0.013$, $p<0.01$). This difference was found to be significant with the Spearman's rho (Spearman's rank order correlation coefficient) as well. This suggested that PCT may be more sensitive than CRP in the early period. Likewise, there are many studies reporting PCT as a better marker compared to CRP among point-of-care tests in the early diagnosis of sepsis [3,12].

It has been reported in another meta-analysis that PCT avoids unnecessary antibiotics use without increasing the mortality rates in the decision for beginning and cessation of antibiotics [13]. An increased PCT concentration was found to be related to high mortality rates in septic patients. Furthermore, the absence of PCT clearance in septic patients has been shown as a prognostic factor [14].

The calcitonin concentration is an important parameter in the differential diagnosis of patients with malignancies with increased plasma CRP concentration. When the clinical condition and sympoms are considered, PCT provides important contribution for the exclusion of infection. It provides an important contribution in the differential diagnosis of infection, particularly in patients with delayed chemotherapy due to elevated CRP levels related to paraneoplastic reasons and/or induction of the drugs, and thus placed under risk.

In conclusion, despite different assessments in the studies conducted, PCT should be accepted as an important marker in the early diagnosis of sepsis. It was demonstrated as a valid marker in the early diagnosis of sepsis and a more significant point-of-care analysis marker compared to CRP in our study as well.

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