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Evaluation of Procalcitonin level in patients with Pneumonia

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KEYWORDS

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A B S T R A C T

Acute pneumonia is one of the most common and important diseases with high morbidity and mortality rates. Rapid diagnosis, determining the severity of the disease, and appropriate antibiotic therapy in these patients are of paramount importance. Procalcitonin rapidly increases in bacterial infection so that it is the primary marker in community acquired pneumonia (CAP) during infection. The aim of this study is to investigate the level of PCT in patients with CAP. In a cross-sectional study which I conducted in a private clinic in Tabriz, I examined Procalcitonin serum level in patients with community-acquired pneumonia. In this study, 20 patients with CAP enrolled into the study. 10 male patients and 10 female patients were selected. Mean age of patients was 63.40±20.42 year. Five patients had positive history of HTN and 4 patients had positive history of DM. Mean level of PCT was 0.6741±1.1465. Significant difference was not found between two genders of patients (P=0.334).

Introduction

Acute pneumonia is one of the most common and important diseases with high morbidity and mortality rates (1). Rapid diagnosis, determining the severity of the disease, and appropriate antibiotic therapy in these patients are of paramount importance (2).

Despite the development of many types of antibiotics in the society, the CAP is one of the important clinical problems with high morbidity and mortality rates and it has been regarded as the sixth leading cause of death in the United States.

Late diagnosis and appropriate treatment increase the mortality rate (3). Acute phase reactants, which are secreted as a physiological response in inflammatory cases, are increased in infections, malignancies, and physical trauma. Of the most acute phase reactants are CRP, fibrinogen, and ESR, and haptoglobin (4-5).

Overuse of antibiotics is common in all societies, particularly in our hospitals and this is leading to antibiotic resistance and nosocomial infections. In order to diagnose pneumonia, in addition to chest X-ray, other

diagnostic tests such as studies of sputum and other respiratory samples, blood cultures, serological studies, PCR, and urine studies are used(6).

Despite guidelines and imaging techniques and cultivation of different secretions samples of patients, biochemical markers have recently been proposed to detect the presence of infection due to some problems as well as direct detection and and cultivation being time consumed. Some of these tests are specific and some are non-specific. Among the available biochemical markers, CRP and Procalcitonin and recently Fibrinogen are more important than the rest and more research is devoted to them.

Procalcitonin is a 116 amino acid glycoprotein which is calcitonin pro-hormone and is normally secreted in response to hypercalcemia by the thyroid C cells. During viral infections and inflammatory diseases, it has a slight increase but barely reaches higher than 1 ml / ng. However, in severe bacterial infections, it increases up to the range of 200-20 ml /ng (7).

This major change in the concentration of Procalcitonin has made it a useful marker in the diagnosis and prognosis of bacterial factors. However, the mechanism of Procalcitonin after inflammation and its role are not yet well known. Some believe that the PCT is produced by liver and peripheral blood mononuclear cells and are adjusted by Lipopolysaccharides and sepsis-related cytokines. PCT is secreted within 4 hours after stimulation and reaches its peak after 8 hours and is cleaned up when the disease was under control (8).

Procalcitonin rapidly increases in bacterial infection so that it is the primary marker in CAP during infection and its increased level to 5/0-25/0 ng/ml is indicative of antibiotic treatment. In addition, reduction in its level is useful in decision-making for the duration of antibiotic treatment and helps predicting the mortality rate (9).

Several biomarkers are increased in bacterial infections. Such biomarkers include ESR, CRP, and Procalcitonin. Procalcitonin is the primary marker in CAP during infection and its increased level to 5/0-25/0 ng/ml is indicative of antibiotic treatment. In addition, reduction in its level is useful in decision-making for the duration of antibiotic treatment and helps predicting the mortality rate (10). The aim of this study is to investigate the level of PCT in patients with CAP.

Materials and Methods

In a cross-sectional study which I conducted in a private clinic in Tabriz, I examined Procalcitonin serum level in patients with community-acquired pneumonia.

After examining and recording their history, patients with suspicion of pneumonia received chest radiography and after verifying the diagnosis of CAP and before beginning antibiotic treatment, blood samples were taken to measure serum levels of CRP and PCT.

A written consent was obtained from all patients after providing necessary explanations to them and their families about aims of the study and the method. Chest radiography was performed and blood samples were obtained and were delivered to the laboratory. The measurement was performed using electro-chemiluminescence method which is a fast and high quality experiment. Finally, the values of CRP and PCT were extracted and analyzed.

Ethical considerations

Given that we did not interfere in the treatment process of patients, thus there is no moral problem in our study. Moreover, after providing the patients with sufficient, comprehensible information, their consent was obtained for participating in the study. Furthermore, with regard to measuring the PCT level, no cost was imposed to the patients and all expenses related to checking the PCT level were paid by the researcher. Patients were also free not to cooperate any more at any stage of the study.

Statistical Analysis

The collected data were analyzed by SPSS-17 statistical software. The collected data were expressed as percentage and mean ± SD. Continuous (quantitative) variables were compared by Independent samples and Paired t test. Categorical (qualitative) variables were compared by contingency tables and Chi-square test or Fisher's exact test. P-value ≤0.05 was considered statistically significant.

Results and Discussion

In this study, 20 patients with CAP enrolled into the study. 10 male patients and 10 female patients were selected. Mean age of patients was 63.40±20.42 year and demographics and clinical findings of patients between two genders were shown in table 1.

Five patients had positive history of HTN and 4 patients had positive history of DM. Mean level of PCT was 0.6741±1.1465. Distribution of PCT level of patients based on gender was shown in chart 1 and others laboratory findings were shown in table 2. Significant difference was not found between two genders of patients (P=0.334).

In pathologic terms, pneumonia refers to the infection of alveoli, distal airways, and the interstitial lung tissue. It is characterized by an increase in the weight of lungs, replacement of the spongiform state of lungs with concentration, and concentration blood cells and fibrins in alveoli (11).

In clinical terms, pneumonia refers to a series of signs and symptoms such as fever, shiver, coughing, pleuritic chest pain, sputum production, hyperthermia or hypothermia, increased respiratory rate, dullness in percussion, bronchial lung sounds, egophony, crackles, vizzing sound, and pleural friction rub, which are accompanied by a darkness in CXR.

Moreover, CAP (community-acquired pneumonia) is the type of pneumonia that occurs in outpatients. PCT is the precursor of the calcitonin hormone and is secreted by thyroid glands through the C cells. PCT is the most reliable parameter used for the diagnosis and separation of bacterial infections from viral infections in patients admitted in the early hours in the emergency centers and hospitals due to acute conditions such as burning, inflammation, and neonatal infections (12).

In other words, it is the prohormone for calcitonin, but PCT and calcitonin are two different proteins. Calcitonin is generated by the C cells of thyroid glands specifically in response to a hormonal stimulation. However, different cells can generate PCT in different organs in response to the proinflammatory stimulants especially bacterial stimulants (12).

If the level of PCT in serum or plasma of the patient is over 0.5 ng/ml in the early hours, it reflects a bacterial infection, but if the serum or plasma PCT level increases after 6 hours, it will be a suitable and reliable

indicator of septic shock in such patients. In the latter case, antibiotic treatment is necessary (13).

In healthy individuals, concentration of plasma PCT is lower than 0.5 ng/ml, while in patients with sepsis, severe sepsis or infectious shock this can increase to 1000 ng/ml (14).

With the release of PCT in blood, the INF Beta receptor is activated, which inhibits the IL-1 beta receptor. This characteristic distinguishes the bacterial infections leading to sepsis from viral infections. Undoubtedly, PCT has a higher level of sensitivity and specificity as compared to CRP (15).

Table.1 Demographics and clinical finding of patients between two genders

	Sex		P
	Male	Female	
Age	55.40±18.63	71.40±19.78	0.079
Weight	78.00±9.73	69.60±10.59	0.081
Height	1.73±.06	1.65±.05	0.010
BMI	26.30±3.97	25.59±3.69	0.637
Respiratory Rate	20.20±3.19	23.60±5.89	0.126
Systolic Blood Pressure	120.00±16.16	129.50±23.86	0.311
Diastolic Blood Pressure	71.50±5.80	77.00±9.78	0.143

Table.2 Laboratory and clinical finding of patients between two genders

	Sex		P
	Male	Female	
WBC	9190.00±4686.02	9820.00±7149.64	0.818
Hb	14.76±1.64	12.51±2.11	0.016
Hct	46.88±6.64	39.06±7.34	0.022
PLT	246.20±58.01	194.10±51.38	0.048
Blood Sugar	164.90±83.16	179.60±101.60	0.727
$Na^{\pm}$	137.70±2.63	137.20±1.99	0.637
$K^{\pm}$	4.57±0.48	4.45±0.51	0.593

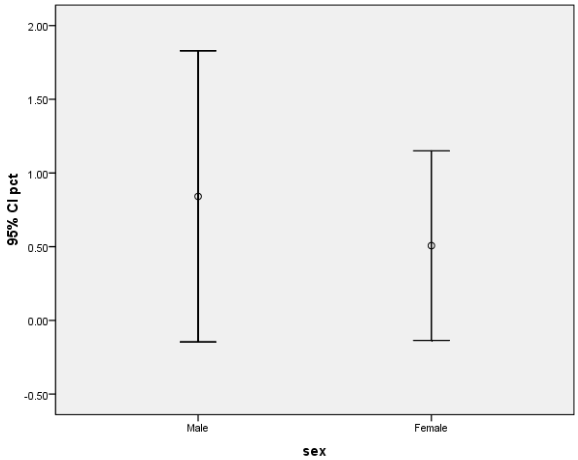

Chart.1 Distribution of PCT level of patients between two genders

The main biological role of PCT is mainly unknown, but recent research has revealed the possible pathologic role of PCT in sepsis. The PCT protein is a leukocyte absorbent and regulates the production of nitric acid by endothelial cells.

PCT is a stable protein in plasma and blood samples. At room temperature, more than 80% of PCT becomes stabilized after 24 hours, but if the sample is stored in refrigerator of 4 degrees this percentage grows to more than 90%(16).

PCT is a 116-amino acid protein with a molecular weight of 12793 Da. It is also a precursor of the calcitonin hormone. Most of the precursors of calcitonin, including PCT, are found in the serum of normal people with a plasma level lower than 0.1 ng/ml (17). In bacterial infections, PCT increases depending on the severity of infection. An example of these infections is bacterial meningitis (18).

The post-inflammation mechanism for production of PCT and its role are still not known precisely. Some researchers believe that PCT is produced by the liver and the mononuclear cells of peripheral blood and is regulated by lipopolysaccharides (LPS) and sepsis-dependent cytokines. PCT is secreted within four hours after the stimulation and reaches its peak level after 8 hours. It is also removed when the disease is controlled (8).
The increase in PCT is related to the presence and effects of sepsis in humans. PCT is not a perfect marker, but it is adequately reliable for monitoring purposes and reduces the use of antibiotics in lower respiratory infections. Level of PCT escalates rapidly in bacterial infections to the extent that it is initial infection marker in CAP cases. Moreover, an increase in the level of PCT to 0.25-0.5 ng/ml is an indication of the beginning of the antibiotic treatment. In addition, a reduction in the level of PCT is useful for deciding on the duration of antibiotic treatment and for predicting the rate of mortality (9).

In view of the significance of the topic and the challenges in the diagnosis and treatment of CAP, we studied the serum PCT levels in patients with CAP (community-acquired pneumonia) and patients with intensified chronic obstructive pulmonary disease (COPD).

PCT increases rapidly in bacterial infections to the point that it is the initial infection marker in CAP. An increase in the PCT level to 0.25-0.5 ng/ml is an indication of the beginning of antibiotic treatment. In addition, a reduction in PCT levels is useful for deciding on the duration of antibiotic treatment and predicting the mortality rate (6).

Stolz et al. indicated that a PCT of over 0.1 ng/ml is useful for starting antibiotic treatment in patients suspected of pneumonia (19). Masia et al. stated that the PCT serum level is useful for CAP assessment, and PCT is mainly a prognostic marker (20).

Miiller et al. showed that PCT is valuable for the diagnosis of CAP along with other signs and symptoms of pneumonia such as radiography findings and clinical signs (8).

Mirjam et al. reported that PCT is useful as a diagnostic and therapeutic marker of CAP (21). Polzin et al. stated that the level of PCT increased significantly in CAP patients as compared to the control group (22). Berg et al. stated that the level of PCT grows in CAP patients (23). Falsey et al. found that the average PCT level was significantly higher in CAP patients (24). Badadhel et al. reported an increase in the PCT levels of

CAP patients (3). Lacoma et al. concluded that the levels of PCT and CRP were significantly higher in patients suffering from pneumonia (25). Daniels et al. examined the levels of PCT and CRP in patients with intensified asthma and stated that there was a direct significant relationship between PCT and CRP levels in patients under study (5). Walsh et al. introduced PCT as a useful biomarker for diagnosis of pneumonia (26). Polzin et al. stated that Procalcitonin is a useful marker for assessment of infections and a suitable guide for the start of antibiotic treatments in such patients (22). Holm et al. indicated that a Procalcitonin level of over 0.06 ng/ml reflects the existence of infection in patients suspected of CAP (27).

Albrich et al. found that the Procalcitonin level is useful as guidance on the method and time of administration of antibiotics in CAP and UTI (28). Fazili et al. introduced Procalcitonin as a bacterial infection biomarker (29). Greulicn et al. stated that it is possible to use Procalcitonin as a biomarker for diagnosis of infections (30). In our study, the mean level of PCT was 0.6741±1.1465. Significant difference was not found between two genders of patients, that shown the mean of Procalcitonin of our patients was more than 0.6.

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