The Correlation between Serum Procalcitonin and Sequential Organ Failure Assessment Score in Severe Sepsis patients

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K E Y W O R D S: Sepsis, Septic Shock, Procalcitonin, Sequential Organ Failure Assessment Score (SOFA score)

ABSTRACT: Introduction: Sepsis is known as an ancient problem in medicine. As sepsis and its complications are responsible for lots of death in Intensive Care Unit (ICU), deferment in diagnosis and treatment can lead to increase the mortality rate. Studies on procalcitonin (PCT) as an acute phase reactant protein have been done broadly for prediction of severity and mortality in last years. Sequential Organ Failure Assessment (SOFA) score which evaluated the severity of disease is used as a factor in crucial state. AIM: This study was designed in order to assign the correlation between PCT and SOFA score as a severity determinant among patients with severe sepsis and septic shock. Methods: This cross sectional study was performed on 60 adult patients admitted in Intensive Care Unit (ICU) in Imam Reza hospital, AJA University of Medical Sciences, Tehran, Iran between August 2014 and August 2015. Assessment of severity of disease was performed by SOFA scores on day 1, 3 and 7 and the PCT level was measured on the same days. The statistical correlations were analyzed between PCT levels and SOFA score on days 1, 3, and 7. Results: There were no significant correlations found between sex, age, and weight with neither of SOFA score and PCT levels in days 1, 3, and 7. We found a positive correlation between PCT measured on days 1, 3, and 7 with SOFA Score. Conclusion: Our findings suggest that PCT could be introduced as an ideal biomarker for assessing the severity of sepsis and also higher amounts of PCT was associated with higher SOFA scores.

Introduction

Sepsis is known as an ancient problem in medicine (Angus, 2013; Sridharan, 2013). It is defined as Systemic Inflammatory Response Syndrome (SIRS) predisposed by infection. It is introduced as severe sepsis, if organ failure or hypotension is concomitant with it. Also if hypotension is resistant to fluid resuscitation, it is known as septic shock (Bone, 1992; Levy, 2003). Sepsis is listed as the 11th most common cause of death in USA by Center for Disease and Prevention in 2009 (Biron, 2015).

As sepsis and its complications are responsible for lots of death in Intensive Care Unit (ICU), (Prkno, 2013) deferment in diagnosis and treatment can lead to increase the mortality rate (Hegazy, 2014).

Diagnosis via clinical symptoms has been challenged due to low sensitivity and specificity (Castelli, 2006). Considering the use of factors like blood culture requires lots of time, which makes the recognition of novel biomarkers for rapid diagnosis, strongly needed. A perfect biomarker in this issue should have such characteristics: high level of sensitivity and specificity, getting fast results and low cost measuring. It would be authoritative determinant to show disease severity too (Hegazy, 2014).

Procalcitonin (PCT) is one of the presented biomarkers which proposed in this issue (Mohsen, 2015; Miglietta, 2015).

For the first time in 1993, PCT was known as a diagnostic factor in sepsis. It is now extensively considered as a diagnostic biomarker in bacterial infection. (Shi, 2015; Hoeboer, 2013). PCT is a 116 amino acid polypeptide which is created in thyroid gland cells in healthy subjects. It is broken by a specific enzyme to change into calcitonin as an active hormone. PCT is secreted by liver, pancreas, kidney, lung, spleen, colon and adipose cells in infective state (Cho, 2014).
As expressed in literature, serum concentration of PCT in healthy status is very small (Mohsen, 2015. Adamik, 2015). It was detectable within 2 hours after injection of bacterial endotoxin. This amount was raised up at 6-8 hours. After 12-48 hours this level was in plateau state (Mohsen, 2015).

Sequential Organ Failure Assessment (SOFA) score which evaluated the severity of disease is used as a factor in crucial state (Liu, 2015).

This score assess the function of respiratory, coagulation, hepatic, cardiovascular, renal and neurological systems (Yousef, 2013). According to the dysfunction of these organs, it is graded between 0-24 scores (Peres, 2002).

Studies on PCT as an acute phase reactant protein have been done broadly for prediction of severity and mortality in last years. It is thought high level of PCT is related to poor prognosis (Hegazy, 2014).

This study was designed in order to assign the correlation between PCT and SOFA score as a severity determinant among patients with severe sepsis and septic shock.

**Methods**

**Subjects**

This cross sectional study was performed on 60 adult patients admitted in Intensive Care Unit (ICU) in Imam Reza hospital, AJA University of Medical Sciences, Tehran, Iran between August 2014 and August 2015. All of our subjects certainly were diagnosed by sepsis or septic shock. Definition of sepsis and septic shock were consonant with the definition mentioned by the American College of Chest Physician/Society of Critical Care Medicine (ACCP/SCCM) consensus.

Assessment of severity of disease was performed by SOFA scores on day 1, 3 and 7.

We have excluded patients who had clinically non-infectious states such as: immune deficiency, burn, trauma, surgery, pancreatitis, liver failure, cardiogenic shock, Graft Versus Host Disease (GVHD), immunotherapy.

**Laboratory Assessment**

In order to measure the amounts of serum PCT on day 1, 3 and 7, blood samples were drawn from IntraVenous (IV) line. The amounts were measured by electrochemiluminometric assay using Elexis Kits, from the Roche Company, Germany.

**Statistical Analysis**

We used IBM SPSS STATISTICS (Version 23) to assess the gathered data. To find out the pattern of data distribution, Shapiro-Wilk test was utilized.

Comparison between the amounts of PCT in different groups according to SOFA score was evaluated by Kruskal-Wallis test. (Data distribution was non-normal)

Spearman coefficient was used to find out any correlations between PCT level and SOFA score. In this study statistical significance was defined as the amounts of P-Value less than 5 percent.

**Ethics**

This project was consonant with principles of declaration of Helsinki. Also it was authenticated by ethics committee of AJA University of Medical Sciences. Signing the informed consent was mandatory in order to enter the study.

**Results**

We have enrolled 60 patients to our study. The sex ratio was 36/24. The median of age among our subjects was 73 years (percentile 25: 61.5, percentile 75: 80). Median of weight was 66.50 kg (percentile 25: 60, percentile 75: 70). There were no significant correlations found between sex, age, and weight with neither of SOFA score and PCT levels in days 1, 3, and 7.

Table 1 shows the amount of PCT and SOFA Scores measured in day 1, 3 and 7 among all of our subjects. The Spearman coefficient showed a positive correlation between levels of serum PCT and SOFA score on days 1, 3, and 7.

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Table 2 shows the scatter plot and regression line in day 7.

In order to compare the level of PCT on days 1, 3 and 7 between different SOFA scores, we have classified our patients according to SOFA Score on days 1, 3 and 7 into 4 groups. Range of SOFA Score was defined in this way: Group1: 1-6, Group2: 7-12, Group3: 13-18 and Group4: 19-24.

None of subjects assorted in group 4. The most of our patients were categorized in group 2(43 patients). Group 1 and group 3 contained 8 and 9 patients respectively.

Kruskal-Wallis test did not reach to statistical significance in level of PCT between different groups on day 1 and 3, although it was statistically significant on day 7. (P= 0.028)
Table 1. PCT and SOFA score on day 1, 3 and 7.

<table>
<thead>
<tr>
<th></th>
<th>Median</th>
<th>Percentile 25</th>
<th>Percentile 75</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCT 1</td>
<td>0.82</td>
<td>0.40</td>
<td>2.9</td>
</tr>
<tr>
<td>PCT 3</td>
<td>0.75</td>
<td>0.31</td>
<td>1.66</td>
</tr>
<tr>
<td>PCT 7</td>
<td>0.50</td>
<td>0.30</td>
<td>1.23</td>
</tr>
<tr>
<td>SOFA 1</td>
<td>9</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>SOFA 3</td>
<td>8</td>
<td>7</td>
<td>11</td>
</tr>
<tr>
<td>SOFA 7</td>
<td>8</td>
<td>7</td>
<td>11</td>
</tr>
</tbody>
</table>

Table 2. Correlation between PCT and SOFA score

<table>
<thead>
<tr>
<th></th>
<th>Spearman Coefficient</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCT and SOFA score 1</td>
<td>0.260</td>
<td>0.045</td>
</tr>
<tr>
<td>PCT and SOFA score 3</td>
<td>0.292</td>
<td>0.023</td>
</tr>
<tr>
<td>PCT and SOFA score 7</td>
<td>0.507</td>
<td>&lt;0.001</td>
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</tbody>
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Figure 1. Scatter plot and regression line (day 7)
Discussion

Sepsis is a medically important condition that is known to become more prevalent in the last years. Studies in this field show that it could be introduce as a status with high amount of burden of disease (Sridharan, 2013). It is thought the secretion of PCT is predisposed by cytokines like Interleukin 6 (IL6) and Lipopolysaccharide (LPS) that effect on different organs in bacterial infection status (Sridharan, 2013).

Previous studies reported a controversial relationship between PCT and severity of sepsis. The present study was performed in order to evaluate the correlation between the level of serum PCT and SOFA score as a determinant of severity in severe sepsis and septic shock patients.

We used Spearman coefficient in order to analyze our data, which was introduced to find out any monotonic relationships.

Also considering that the presence of outliers through our data due to non-normally distribution, it seems use of Spearman could be accompanied with less bias (Zou, 2003).

According to Spearman coefficient our results showed a positive correlation between PCT and SOFA score on days 1, 3, and 7. These findings of our results were consistent with Chen et al, who expressed this correlation on days 5 and 7 (Chen, 2012) Hegazy et al. expressed this correlation from days 1 to 7 via Spearman coefficient. According to their report this correlation overally was became stronger in day 7 comparing earlier days (Hegazy, 2014).

Although, they introduced PCT as an early determinant for assessment of severity of disease, but according to our results, this finding is more relevant in day 7. In the study done by Huang et al, performed in 2013, the amount of PCT was compared between groups of survivors and non survivors in different days, which they found increasing levels of PCT on days 3, 5 and 7 (Huang, 2013).

Castelli et al reported a weakly positive correlation between PCT and SOFA score among a non-normally distributed population (Castelli, 2004). Another report published in 2006 showed a positive relationship between PCT and SOFA score among patients admitted in ICU. They reported this correlation was significantly stronger in group of patients with infection comparing with non-infected patients (Castelli, 2006).

We also found a significant correlation in serum levels of PCT among different groups categorized by SOFA score on day 7. Shi et al, who studied to evaluate the role of PCT in bacterial infections in the immunodeficient patients, reported the same type of correlation between SOFA score and PCT in the higher amounts of PCT (Shi, 2015).

Conclusion

Our findings suggest that PCT could be introduced as an ideal biomarker for assessing the severity of sepsis and also higher amounts of PCT could be associated with higher SOFA scores.

References


