Procalcitonin (PCT) is a biomarker for differentiating inflammatory response syndrome of sepsis (a Pilot study)

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A B S T R A C T

Sepsis is a serious condition that is associated with high morbidity and mortality rate. Although the true selection of antibiotics can reduce the overall mortality and morbidity of sepsis, the over usage and aberrant consumption of antibiotics can causes different side effects and antimicrobial resistances. The aim of this study was to determine the serum levels of Procalcitonin (PCT) and its role in differentiating the SEPSIS from patients with probable SIRS in patients referring to Tabriz Imam Reza hospital. In a cross-sectional study that performed the department of infectious diseases in Tabriz university of Medical Sciences on patients with SIRS, Procalcitonin levels were evaluated in for detecting the sepsis. The mean age of patients was 59.77 ± 22.21 years in the range of 19 to 91 years. 21 patients (60%) was male and 14(40%) was female. Of 35 studied patients, 45.71% of them had Sepsis and 54.29% of them had SIRS. Cut of point of Procalcitonin for differentiating inflammatory response syndrome (SIRS) of sepsis was 0.075 and sensitivity, Specificity, positive predictive value and negative predictive value was 81%, 79%, 76% and 83%, respectively. Checking the PCT is a method of high specificity and low sensitivity for the detection of bacterial infections, particularly in the case of a positive blood culture. It can be used in cases of suspected sepsis to begin antimicrobial therapy until blood culture results. The high cost of testing has prevented it from routine testing.

Introduction

Sepsis is a serious condition that is associated with high morbidity and mortality rate. However the clinical criteria of sepsis have low specificity and sensitivity. The rapid onset of antimicrobial therapy reduces morbidity and mortality (1).

Although the true selection of antibiotics can reduce the overall mortality and morbidity of sepsis, the over usage and aberrant consumption of antibiotics can causes different side effects and antimicrobial resistances (1). Regardless of its cause, SIRS (systemic inflammatory response syndrome) is considered as a major inflammatory process (1) the contributing factors include infections, burns, trauma, surgery and pancreatitis (2). Despite the use of modern antibiotics and regenerative therapies, sepsis is one of the main causes of death in severely ill patients (3).

Response to sepsis included some inflammatory and anti-inflammatory series of events (4). Diagnosis of sepsis and assessment of its severity is usually done with a series of signs and symptoms (4). However, rapid diagnosis and assessment of severity of sepsis is too important which causes the diagnosis of specific cause and treatment (5-6). Biomarkers can play an important role in this issue since this can point Presence or absence of sepsis and even its intensity (7-8).

The bio-markers can differentiate between viral and bacterial infections, fungal infections are from. Other uses include determining the prognosis of sepsis in selecting antibiotic therapy, evaluation and assessment of treatment of sepsis. Although the precise role of biomarkers in the management of sepsis remains unclear (9).

According to previous data from literature Procalcitonin (PCT) is more specific than CRP as a biological marker, but its value has still been questioned (10-11). Sepsis and septic shock are medical emergencies. Early diagnosis and proper treatment of this disease with early intervention has a significant impact on reducing mortality. Since the diagnosis of sepsis in patients with

inflammatory response syndrome with other causes are problematic and since some factor occur at one time and with regarding to the fact that rapid antibiotic therapy can effectively reduce the mortality and prevent economic costs. This study aimed at determining Procalcitonin to differentiate patients with SEPSIS and patients with SIRS (systemic inflammatory response syndrome). The aim of this study was to determine the serum levels of Procalcitonin and its role in differentiating the SEPSIS from patients with probable SIRS in patients referring to Tabriz Imam Reza hospital.

Materials and Methods

In a cross-sectional study conducted on patients with SIRS, Procalcitonin levels were evaluated in for detecting the sepsis. This pilot study was conducted on 35 adult patients older than 12 years admitted to hospital Imam Reza (AS) in Tabriz in 1391 and 1392 with SIRS and suspected sepsis all patients suspected for sepsis underwent blood, urine and CSF culture if necessary. Of all patients, blood samples were taken and after centrifuge during 4 minutes, plasma was separated for measuring the Procalcitonin serum level. The levels of Procalcitonin were measured using Lio isan Brahmas pct kit of Italy with immune assay quantitative method.

The inclusion criteria included of SIRS which is defined with the existence of 2 criteria: fever more than 38 degrees of centigrade , the respiratory rate more than 20 per minutes , pulse rate more than 90 per minute and WBC more than 12000 or fewer than 4000. The exclusion criteria included: noninfectious systemic inflammatory response like trauma, burning and myocardial infarction. The patients were completely followed up in two groups of sepsis and non-sepsis.

The firs group included patient's SIRS with sepsis and the second group included patients with sirs without sepsis.

Analytical methods

All the data from the patients was analyzed using the descriptive methods, the quantitative data was compared using independent sample t-test, ne way ANOVA and the non-quantitative data was compared using Chi-square and Fisher Exact Test, the p was considered meaningful in less than 0.05.

Ethical considerations

All the data from patients was kept confidential, the written consent was obtained from all patients before rolling in.

Results and Discussion

In this study, 35 patients admitted to the emergency department of Tabriz Imam Reza hospital that meets the criteria for systemic inflammatory response syndrome (SIRS) and suspected sepsis were studied. Finally, the clinical and laboratory follow-up of patients in both groups of Systemic Inflammatory Response Syndrome (SIRS) without evidence of bacterial infection and SIRS (SIRS) with evidence of bacterial infection (sepsis) were analyzed. The mean age of patients was 59.77 ± 22.21 years in the range of 19 to 91 years. The age distribution of patients is shown on chart 1. 21 patients (60%) was male and 14(40%) was female. 25 patients (71.4%) was resident in urban places and 10 patients (28.6%) was resident in rural places. The clinical and laboratory finding of patients upon the age and gender is shown in table 1 and 2.

As shown in Table 1 can there is a statistically significant difference between two groups with SIRS without evidences of

bacterial infections and sepsis in body temperature (P=0.008) systolic blood pressure(P=0.004) diastolic blood pressure(P=0.03). There was also a significant difference between two groups in Procalcitonin levels (p=0.001).

While there was no significant difference in other parameters like age, confusion, mechanical ventilation, pulse rate, respiratory rate, WBC , platelets and admission days. The under curve area was measured as 0.86 using ROC. The cutoff point for Procalcitonin for differentiating the SIRS and Sepsis was 0.75. The sensitivity, specificity, positive predictive value and negative predictive value were measured as 81%, 79%, 76% and 83% respectively. 9 patients (25.7%) were at light com at admission to emergency department.

Based on lab data, 29 patients (82.8%) had negative blood culture and 29 patients (82.9%) had negative urine cultures. The positive blood cultures included 4 cases (66.66%) E-coli, 1 case (16.66%) staph epidermidis and 1 case (16.66%) staph aurous.

The culture revealed 5 cases of positive E-coli and 1 case of enterbacter in urine cultures. The variety of Procalcitonin levels upon the outcome is shown in table 2 and 3. Distribution of Procalcitonin between two groups of patients was shown in chart 2. Distribution of Procalcitonin based on outcome of patients was shown in chart 3. ROC Chart of Procalcitonin in diagnosis of Sepsis of SIRS was shown in chart 4. The patients was divided into two groups after clinical and laboratory follow-up as patients with systemic inflammatory response syndrome (SIRS) without evidence of bacterial infection and systemic inflammatory response syndrome (SIRS) with evidence of bacterial infection (sepsis).

Table.1 Evaluation of studied parameters between two groups

	Group		P
	SIRS without Sepsis	SIRS with Sepsis	
Age	60.84 ± 22.30	58.50 ± 22.78	0.761
Respiratory Rate	23.84 ± 3.69	26.63 ± 6.93	0.163
Pulse Rate	93.89 ± 17.37	96.44 ± 15.21	0.651
Body Temperature	38.03 ± .82	38.84 ± .86	0.008
Systolic Blood Pressure	130.53 ± 23.15	110.31 ± 12.17	0.003
Diastolic Blood Pressure	77.63 ± 13.16	68.44 ± 11.21	0.035
WBC	23010.53 ± 56326.97	13793.75 ± 7529.54	0.521
PLT	240315.79 ± 129514.07	227000.00 ± 101258.09	0.002
Procalcitonin	0.67 ± .81	2.96 ± 2.39	<0.001

Table.2 Evaluation of studied parameters based on patients outcome

	Outcome		P
	Discharge	Death	
Age	59.17 ± 22.58	63.40 ± 21.88	0.699
Respiratory Rate	24.90 ± 5.87	26.40 ± 2.41	0.581
Pulse Rate	94.80 ± 15.52	96.60 ± 22.18	0.822
Body Temperature	38.45 ± .74	38.10 ± 1.75	0.439
Systolic Blood Pressure	119.50 ± 20.94	132.00 ± 22.53	0.230
Diastolic Blood Pressure	73.00 ± 12.84	76.00 ± 15.17	0.640
WBC	19773.33 ± 44884.26	12940.00 ± 4298.60	0.739
PLT	224700.00 ± 115439.53	291400.00 ± 113731.26	0.239
Procalcitonin	1.86 ± 2.17	0.82 ± 0.62	0.300

Chart.1 Age distribution of patients
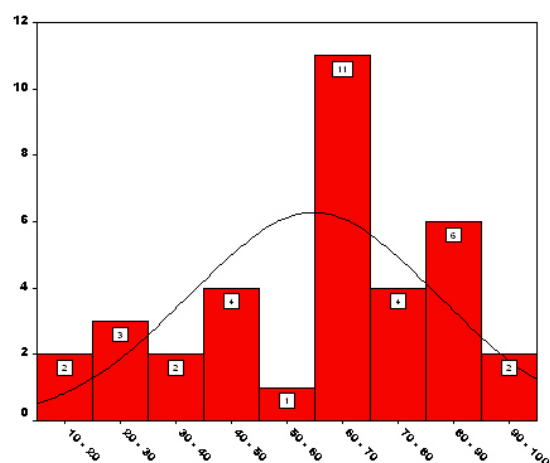
Table.3 Final diagnosis patients between two groups

	Group		Outcome	
	SIRS	Sepsis	Death	Discharged
Pneumonia	0	4	0	4
CVA	3	1	1	3
Cirrhosis and liver trans	1	0	0	1
Tumor necrosis	1	0	0	1
Brain tumor	3	0	2	1
Diarrhea	0	1	0	1
Heart failure	1	0	0	1
Bowel obstruction	1	0	0	1
Known	3	1	0	4
Encephalopathy	2	0	1	1
DVT	1	0	0	1
PTE	1	0	0	1
Meningitis	0	1	0	1
Kidney Transplantation	2	0	0	2
UTI	0	7	1	6
Vertebral Osteomyelitis	0	1	0	1

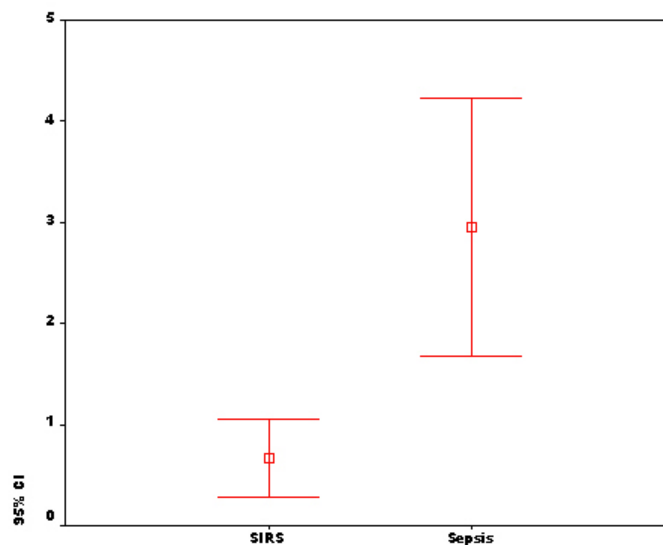**Chart.2** Distribution of Procalcitonin between two groups of patients

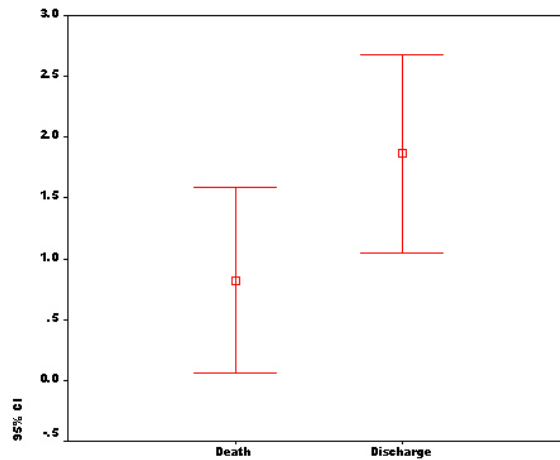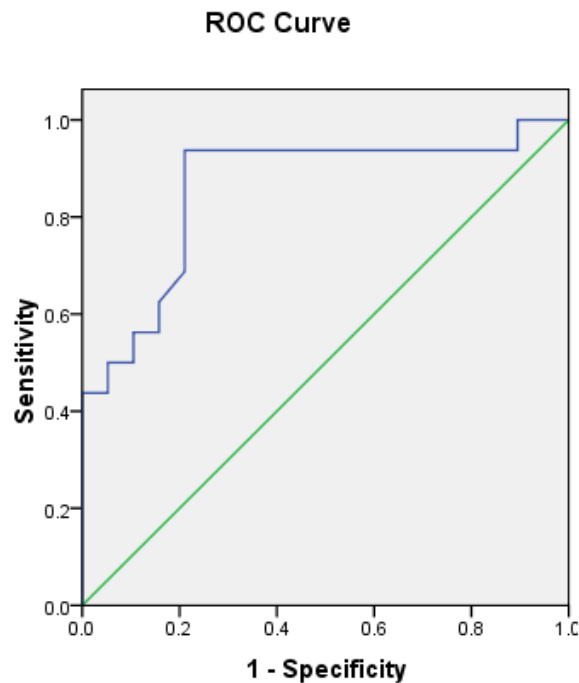**Chart.3** Distribution of Procalcitonin based on outcome of patients

Chart.4 ROC Chart of Procalcitonin in diagnosis of Sepsis of SIRS

Diagonal segments are produced by ties.

Ten patients (54.29%) in SIRS group and 16 patients (45.71 %) in sepsis group. In the hospitalization period, 5 patient's intubation mechanical ventilation, 5 patients expired and the others discharged. The mean admission days were 8.74 ± 5.22 days in the range of 2 to 24 days. The final diagnosis of patients based on outcome is shown in table 3.

With regard to the importance of the issue and the existing challenges in the diagnosis and treatment of patients referring with SEPSIS and the importance of its

differentiation from the SIRS, we studied the diagnostic value of Procalcitonin as a biomarker in diagnosis of SPESIS from the SIRS.

The research in the analysis and information of Iran revealed only a limited number of studies in this area found that has been used in order to compare the results. Because most cases of sepsis are caused by bacterial infections, often using culture methods for detection is considered the gold standard, but this method is not sufficiently sensitive and specific. In cases of severe sepsis or septic shock, the result is negative in more than 50 % of the cases. In addition, at least 24 hours is required to earn the culture results which can delay the diagnosis and the effective action (12).

So, there is a clear need for a reliable diagnostic method for differentiating sepsis from systemic inflammatory response syndrome. So, the Procalcitonin can be used for screening and differentiating the SEPSIS from the Systemic inflammatory response syndrome, on the other hand the rapid administration of antibiotics can reduce the mortality and in absence of infections, the reliable biomarker can prevent unnecessary economic costs and their inappropriate usage (13). In a study by Oliver and colleagues in 2000 on 33 patients in ICU with positive SIRS and suspected SEPSIS, it is concluded that Procalcitonin levels in patients with SEPSIS (16.8 *ng*) was significantly higher that its levels in SIRS (P=0.003). They have also concluded that the sensitivity of Procalcitonin in differentiating the sepsis from SIRS is 86% and its specificity is 54% in the Procalcitonin level of 3.3 ng/ml (14).
In another study, Procalcitonin has been found to be a better biomarker in diagnosing and detecting the severity of illness and the probability of mortality. This marker is on the top of the markers used in beginning the

antimicrobial therapy which can use in early on time antibiotic therapy and reducing inappropriate antibiotics.

In a study by Hiks and his colleagues in 2013 that conducted on 66 patients with SIRS , serum Procalcitonin levels on admission in patients with sepsis patients was at an average 0.32 ng/ ml and 0.18 ng/ml in patients with SIRS without evidences of bacterial infection it was significantly higher in patients with SIRS (p=0.04). (15). In a prospective study conducted in 2000 by Brunkhorost and colleagues in using the Procalcitonin to differentiate SIRS from severe sepsis and septic shock, respectively, the concluded that Procalcitonin is not a reliable criterion for differentiating SIRS from sepsis (13). According to the results of various studies on the prognostic value of Procalcitonin in differentiating the sepsis from SIRS it can be can concluded that the criteria is very weak in the diagnosis of suspected cases of sepsis.

In our study, 16 patients (45.71 %) of patients was suffering from sepsis and 19 (54.29 %) had SIRS without evidences of bacterial infections. Among the criteria for SIRS, systolic and diastolic blood pressure was meaningful comparing to 3 other criteria (body temperature, respiratory rate, and number of white blood cells) in patients diagnosed with sepsis. In our study, as similar to other studies, levels of white blood cells and platelets was not significant in differentiating sepsis from SIRS.

Unlike the study of Brunkhorost and colleagues, in our study, in accordance with the studies of Oliver and Hiks, the serum Procalcitonin levels were significant in differentiating the sepsis from systemic inflammatory response syndrome. As was shown, the diagnostic role of Procalcitonin and making decisions based on their serum

levels is still controversial, and further studies are recommended.

Conclusions

Checking the PCT is a method of high specificity and low sensitivity for the detection of bacterial infections, particularly in the case of a positive blood culture. It can be used in cases of suspected sepsis to begin antimicrobial therapy until blood culture results. The high cost of testing has prevented it from routine testing.

Suggestions

Based on the findings of present study, Procalcitonin is a very useful biomarker in differentiating the sepsis from SIRS m but further studies with more cases seems to be necessary.

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