SEMI-QUANTITATIVE PROCALCITONIN KIT FOR EVALUATING SEVERITY AND PREDICTING MORTALITY IN SEPSIS

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ABSTRACT

BACKGROUND

Sepsis is a life-threatening condition that arises when the body's response to infection causes injury to its own tissues and organs. Sepsis is caused by an immune response triggered by an infection. Most commonly, the infection is bacterial, but it may also be from fungi, viruses, or parasites. This study evaluates the semi-quantitative pro-calcitonin kit for evaluating sepsis severity and determines the mortality in affected patients.

MATERIALS AND METHODS

This study was a prospective study which was conducted in the Department of General Medicine, Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana conducted from July 2015 to September 2016.

RESULTS

The DIC, SOFA and APACHE II scores were found to be significant i.e. have P<0.01 between group A and C and between group B and C. There was a significantly higher procalcitonin concentrations in patients with severe sepsis and septic shock than in those patients with less severe disease. It was observed that there was an upward trend in pro-calcitonin concentrations in patients with septic shock. In the three group, a significant (P< 0.01) difference was observed with regard to numbers of patients and rates of severe sepsis, septic shock, DIC, and mortality.

CONCLUSION

For detecting the disease severity early in sepsis patients, semi-quantitative pro-calcitonin concentration testing can be used as a useful tool. It may also predict the mortality in septic patients at an early stage.

KEYWORDS

Sepsis, Disseminated Intravascular Coagulation, Acute Physiological and Chronic Health Evaluation, Sequential Organ Failure Assessment.

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BACKGROUND

Sepsis is a life-threatening condition that arises when the body's response to infection causes injury to its own tissues and organs. Common signs and symptoms include fever, increased heart rate, increased breathing rate, and confusion. There also may be symptoms related to a specific infection, such as a cough with pneumonia, or painful urination with a kidney infection.[1] In the very young, old, and people with a weakened immune system, there may be no symptoms of a specific infection and the body temperature may be low or normal, rather than high. Severe sepsis is sepsis causing poor organ function or insufficient blood flow. Insufficient blood flow may be evident by low blood pressure, high blood lactate, or low urine output. Septic shock is low blood pressure due to sepsis that does not improve after reasonable amounts of intravenous fluids are given.[2] Sepsis is caused by an immune response triggered by an infection. Most commonly, the infection is bacterial, but it may also be from fungi, viruses, or parasites. Common locations for the primary infection include lungs, brain, urinary tract, skin, and abdominal organs. Risk factors include young or old age, a weakened immune system from conditions such as cancer or diabetes, major trauma, or burns.[3] An older method of diagnosis was based on meeting at least two systemic inflammatory response syndrome (SIRS) criteria due to a presumed infection. In 2016, SIRS was replaced with qSOFA which is two of the following three: increased breathing rate, change in level of consciousness, and low blood pressure.[4] Blood cultures are recommended preferably before antibiotics are started, however, infection of the blood is not required for the diagnosis. Medical imaging should be used to look for the possible location of infection. Other potential causes of similar signs and symptoms include anaphylaxis, adrenal insufficiency, low blood volume, heart failure, and pulmonary embolism, among others. Sepsis usually is treated with intravenous fluids and antibiotics. Typically, antibiotics are given as soon as possible. Often, ongoing care is performed in an intensive care unit.

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If fluid replacement is not enough to maintain blood pressure, medications that raise blood pressure may be used. Mechanical ventilation and dialysis may be needed to support the function of the lungs and kidneys, respectively.[5] To guide treatment, a central venous catheter and an arterial catheter may be placed for access to the bloodstream. Other measurements such as cardiac output and superior vena cava oxygen saturation may be used. People with sepsis need preventive measures for deep vein thrombosis, stress ulcers and pressure ulcers, unless other conditions prevent such interventions. Some might benefit from tight control of blood sugar levels with insulin. The use of corticosteroids is controversial. Activated drotrecogin alfa, originally marketed for severe sepsis, has not been found to be helpful, and was withdrawn from sale in 2011. Disease severity partly determines the outcome. The risk of death from sepsis is as high as 30%, from severe sepsis as high as 50%, and from septic shock as high as 80%. The number of cases worldwide is unknown as there is little data from the developing world. Estimates suggest sepsis affects millions of people a year. In the developed world approximately 0.2 to 3 people per 1000 are affected by sepsis yearly, resulting in about a million cases per year in the United States. Rates of disease have been increasing. Sepsis is more common among males than females. The medical condition has been described since the time of Hippocrates. The two terms, "septicemia" and "blood poisoning", refer to the microorganisms or their toxins in the blood and are no longer commonly used. The pro-calcitonin concentration is useful as an early prognostic indicator quantitatively among patients with septic shock. Those patients who died in the intensive care unit had pro-calcitonin concentrations quantitatively higher at all assay time points when compared with those who survived to be discharged from ICU. Thus, research shows that quantitative pro-calcitonin measurements were correlated with semi-quantitative pro-calcitonin concentration ranges. This study evaluates the semi-quantitative pro-calcitonin kit for evaluating sepsis severity and determines the mortality in affected patients.

MATERIALS AND METHODS

This study was a prospective study which was conducted in the Department of General Medicine, Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana. Institutional ethical committee approval was taken for this study. A written informed consent was taken from all the patients. This study was conducted from July 2015 to September 2016. Exclusion criteria was patients who had age of younger than 18 years, those patients with liver cirrhosis, patients receiving warfarin, and patients with traumatic injury. On admission, semi-quantitative pro-calcitonin concentrations and C-reactive proteins SOFA, APACHE II scores were measured. Body temperature, blood pressure, pulse rate, respiratory rate, white blood cell count, Glasgow coma scale, serum albumin level and anti-thrombin activity level were measured. After enrolment, all patients were followed up every 30 days and mortality was assessed. The statistical significance was determined by Chi-square test. P value less than 0.05 was considered significant.

RESULTS

In this study, 200 patients were selected. The patients were divided into three groups namely Group I consisting of 85 patients, out of which 45 with a pro-calcitonin concentration <0.5 ng/ml, 40 with pro-calcitonin concentration of ≥0.5 and <2 ng/ml; group II consisting of 40 patients and group III consisting of 75 patients.

Demographics	Group I	Group II	Group III
Number of Patients	85	40	75
Gender (Male/Female)	43/42	25/15	40/35
Age (Years)	76.38 ± 14.8	75.39 ± 12.7	77.91 ± 10.84

Table 1. Demographic Distribution in the Study

Table 1 shows that Male to Females were 43/42 in group I, 25/15 in group II and 40/35 in group III; Age in years were 76.38 ± 14.8 in group I, 75.39 ± 12.7 in group II and 77.91 ± 10.84 in group III.

Clinical Data	Group I	Group II	Group III
PCT level	<2	≥2, <10	≥10
Systolic BP (mmHg)	124.83 ± 21.84	118.24 ± 38.0	105.87 ± 59
Diastolic BP (mmHg)	72.5 ± 18.4	65.89 ± 18.42	59.57 ± 12.0
Mean BP	89.5 ± 14.8	80.24 ± 1.8	73.94 ± 19.8
Respiratory rate per minute	21.58 ± 5.4	24.89 ± 3.6	25.98 ± 5.8
Heart Rate per minute	93.71 ± 29.8	100.5 ± 14.9	103.87 ± 9.6

Table 2 shows that systolic BP in mmHg was 124.83 ± 21.84 in group I, 118.24 ± 38.0 in group II and 105.87 ± 59 in group III; diastolic BP in mmHg was 72.5 ± 18.4 in group I, 65.89 ± 18.42 in group II and 59.57 ± 12.0 in group III; mean BP in mmHg was 89.5 ± 14.8 in group I, 80.24 ± 1.8 in group II and 73.94 ± 19.8 in group III; respiratory rate per minute was 21.58 ± 5.4 in group I, 24.89 ± 3.6 in group II and 25.98 ± 5.8 in group III; heart rate per minute was 93.71 ± 29.8 in group I, 100.5 ± 14.9 in group II and 103.87 ± 9.6 in group III.

Clinical Data	Group I	Group II	Group III
Temperature ºC	38.6 ± 1.9	39.4 ± 1.4	39.6 ± 2.7
WBC (*1000/µL)	13.8 ± 1.7	13.9 ± 8.9	12.5 ± 3.9
Maximum C-reactive protein (mg/dl)	14.8 ± 5.4	16.9 ± 6.2	18.7 ± 4.8
Albumin (g/dl)	2.65 ± 0.11	2.47 ± 0.58	2.14 ± 0.89
Antithrombin activity	83.59 ± 15.7	75.24 ± 16.8	62.41 ± 14.8

Table 3. Clinical Data of the Study Patients

	Group I	Group II	Group III
DIC score	1.62 ± 1.25	1.78 ± 2.11	2.56 ± 3.14
APACHE II score	13.25 ± 5.4	14.28 ± 3.1	20.8 ± 4.2
SOFA score	1.7 ± 1.2	3.0 ± 7.4	5.5 ± 5.6

Table 4. DIC Score, SOFA Score AND APACHE II score of Each Group

DIC- Disseminated Intravascular coagulation,
APACHE- Acute Physiological and chronic health evaluation,
SOFA- Sequential organ failure assessment.

DISCUSSION

Tsuneaki Kenzaka et al;[6] reported that in DIC, SOFA, and APACHE II scores, a significant difference was found between group A and group C and between group B and group C (P<0.01). Patients with severe sepsis and septic shock had significantly higher procalcitonin concentrations than did patients with less severe disease. It was observed that the rate of patients with septic shock with high pro-calcitonin concentrations showed an upward trend. A significant (P< 0.01) difference was observed between the three groups with regard to numbers of patients and rates of severe sepsis, septic shock, DIC, and mortality. In our present study, similar results were observed such as the DIC, SOFA and APACHE II scores were found to be significant i.e. have P<0.01 between group A and C and between group B and C. Aikawa N et al;[7] reported that in patients with systemic bacterial infection and those with localized bacterial infection, the concentrations of PCT were significantly higher than the concentrations in patients with nonbacterial infection or noninfectious diseases. In addition, PCT, endotoxin, IL-6, and CRP concentrations were significantly higher in patients with bacterial infectious disease than in those with nonbacterial infectious disease (P<0.001, P<0.005, P<0.001, and P<0.001, respectively). The cut-off value of PCT for the discrimination of bacterial and nonbacterial infectious diseases was determined to be 0.5 ng/ml, which was associated with a sensitivity of 64.4% and specificity of 86.0%. Areas under the receiver operating characteristic curves (POCs) were 0.84 for PCT, 0.60 for endotoxin, 0.77 for IL-6, and 0.78 for CRP in the combined group of patients with bacterial infectious disease and those with nonbacterial infectious disease, and the area under the ROC for PCT was significantly higher than that for endotoxin (P<0.001). In a study done by Ugarte H et al;[8] it was observed that the best cutoff values for ProCT and CRP were 0.6 ng/mL and 7.9 mg/dL, respectively. Compared with CRP, ProCT had a lower sensitivity (67.6 vs. 71.8), specificity (61.3 vs. 66.6), and area under the receiver operating characteristic curve (0.66 vs. 0.78, p <.05). The combination of ProCT and CRP increased the specificity for infection to 82.3%. In the infected patients, plasma ProCT, but not CRP, values were higher in nonsurvivors than in survivors. Delevaux I et al;[9] observed that PCT levels were >0.5 ng/ml in 39/60 (65%) patients in group I. In group II, three patients with a viral infection had slightly increased PCT levels (0.7, 0.8, and 1.1 ng/ml) as did two others, one with crystal arthritis and the other with vasculitis (0.7 ng/ml in both cases). All other patients in group II had PCT levels <0.5 ng/ml. In this study a value of PCT >0.5 ng/ml was taken as the marker of bacterial infection (sensitivity 65%, specificity 96%). PCT values were more discriminative than WBC and CRP in distinguishing a bacterial infection from another inflammatory process. Meisner M et al;[10] examined the validity of solid phase immunoassay at daily clinical routine conditions at five different hospitals in a prospective study. After development of the assay (200 microl plasma, 30 minutes incubation), PCT levels were categorized into four groups (< 0.5 microg/l; > or = 0.5-< 2 microg/l; > or = 2-< 10 microg/l; > or = 10 microg/l) according to the provided reference scale. Samples from patients with suspected elevation of PCT of different aetiology (n=237) were read by various analysers and compared with the results of the Lumitest PCT (B.R.A.H.M.S.-Diagnostic GmbH, Hennigsdorf, Germany). A total of 74.7% of measurements were categorized according to the results of the Lumitest PCT, 24.5% were read within the next lower or higher category. Using a +/- 10% range at the reference concentrations (20% at 0.5 microg/l), 82.7% of samples were correctly categorized and 16.4% within the next categories. Using a cut-off value of 2.0 microg/l, 92.0% (94.1% for ± 10%) of the results were correctly categorized.

CONCLUSION

For detecting the disease severity early in sepsis patients, semi-quantitative pro-calcitonin concentration testing can be used as a useful tool. It may also predict the mortality in septic patients at an early stage.

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