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Serum Procalcitonin as Marker for the Diagnosis of Sepsis.

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ABSTRACT

Background: Objectives: In the last few years, serum procalcitonin has been used as an early maker of sepsis with varying results. In this study, we aimed to study the role of serum procalcitonin in establishing the diagnosis of sepsis. **Methods:** Blood samples were collected at admission from 60patients admitted to the Central Intensive Care Units at SCB Medical College,Hospital Cuttack from August 2016 to November 2017. Patients were categorized into different groups according to clinical symptoms of sepsis, bacteriological and laboratory parameters. Group I consisted of 20 patients with positive blood cultures and other biological tests which suggested infection. Group II consisted of 20 patients with negative blood cultures but had two or three of clinical signs of sepsis. The control group included 20 healthy patients with no clinical and biological data of infection. Sreum procalcitonin were determined by immunoluminometric assay method. **Result:** Mean levels of procalcitonin in septic patients (group I) were significantly higher than the other two groups (P<0.005). Sensitivity, specificity, positive predictive value and negative predictive value were determined for all markers and compared with each other. **Conclusion:** We conclude that serum procalcitonin is a better marker than CRP in the diagnosis of sepsis in children.

Keywords: C-reactive Protein, Sepsis, Procalcitonin.

INTRODUCTION

Sepsis, a syndrome of physiologic, pathologic, and biochemical abnormalities induced by infection, is a major public health concern, accounting for more than $20 billion (5.2%) of total US hospital costs in 2011.[1] The reported incidence of sepsis is increasing, likely reflecting aging populations with more comorbidities, greater recognition, and, in some countries, reimbursement-favorable coding. Although the true incidence is unknown, conservative estimates indicate that sepsis is a leading cause of mortality and critical illness worldwide. Furthermore, there is increasing awareness that patients who survive sepsis often have long-term physical, psychological, and cognitive disabilities with significant health care and social implications.[2] Clinical signs of systemic inflammation including changes in body temperature, tachycardia and routine laboratory tests like keukocytosis and C-reactive Protein (CRP) are used for diagnosis of sepsis.[3] Due to non-specific signs and symptoms of sepsis, the diagnosis of sepsis in patients is quite difficult and can be misleading because critically ill children often manifest systemic inflammatory response syndrome (SIRS) without infection.[4] Though CRP has been used as marker for diagnosis of sepsis in patients , elevated CRP levels can be seen in infection, in autoimmune disease, in surgery, meconium aspiration and recent vaccination. Also the CRP values do not rise significantly until almost 14-48 hr after the onset of infection.[5]

Procalcitonin (PCT) has been proposed as a marker of bacterial sepsis in critically ill adult patients. PCT is a precursor of calcitonin and a 116 amino acids protein.[6]

In contrast to calcitonin that has a short half – life of 10 min; PCT has a much longer half-life as 25-30 hr.[7] In healthy persons, PCT levels are barely detectable .

Bacterial lipopolysaccharide (LPS) has been shown to be a potent inducer of PCT release into the systemic circulation. Procalcitonin concentration starts to rise from 3-4 hr after an endotoxin challenge, peak about 6 hr, and remain increased for over 24 hr.[8]

In this study, we aimed to : investigate the value of PCT and CRP, in establishing the early diagnosis of sepsis in children.

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MATERIALS AND METHODS

This was a prospective observational study carried central Intensive Care Units at SCB medical

college,Hospital Cuttack from August 2016 to November 2017. Patients were excluded if they had chronic systemic inflammatory diseases, degenerative neurological diseases, primary or acquired immunodeficiency diseases, were on corticoid therapy, nonsteroidal anti-inflammatories or antibiotics for more than 24 hours, had suffered traumas or burns or were in postoperative care. Written consent was obtained from all patients. Sepsis clinical criteria: organ dysfunction is defined as an increase of 2 points or more in the Sequential Organ Failure Assessment (SOFA) score.For patients with infections, an increase of 2 SOFA points gives an overall mortality rate of 10%.Patients with suspected infection who are likely to have a prolonged ICU stay or to die in the hospital can be promptly identified at the bedside with qSOFA ("HAT"); i.e. 2 or more of:

- Hypotension: SBP less than or equal to 100 mmHg
- Altered mental status (any GCS less than 15)
- Tachypnoea: RR greater than or equal to 22

Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.

- Septic shock clinical criteria: Sepsis and (despite adequate volume resuscitation) both of:
- Persistent hypotension requiring vasopressors to maintain MAP greater than or equal to 65 mm Hg, and
- Lactate greater than or equal to 2 mmol/L

Before initiation of antibiotic therapy in children suspected of sepsis, blood samples for blood culture, PCT and CRP measurements were obtained by peripheral venous puncture.

Finally according to clinical symptoms of sepsis, microbiologic and laboratory results, patients were classified in to three groups:

1. Proven sepsis (n=20): positive blood culture and clinical symptoms of sepsis.
2. Suspected sepsis (n =20): with clinical symptoms but negative blood culture.
3. Control group (n=20): children with no clinical and biological data of infection were selected as the control group.

Statistical analysis

To compare means of the variables, one way ANOVA test was done by SPSS (version 16). Categorical variables between groups were analyzed using Chi-square test.

RESULTS

In this study, 20 patients with positive blood cultures and clinical sepsis (group I) and 20 patients with suspected sepsis (group II) and 20 healthy patients (group III) were enrolled.Blood culture were positive for all patient (group I). The identified bacteria included Staphylococcus aureus (n=7), coagulase negative staphylococcus (n=5) Streptococcus beta hemolytic group A (n=4), Escherichia coli (n=1), Pseudomonas aeruginosa (n=2) and Entrobacter (n=1).There was no statistical significance among the variable like age, sex and weight in all 3 groups

The mean of CRP and PCT is studied groups are shown in [Table 1]. There was a significant difference between the mean of CRP level of healthy controls and septic patients ($P<0.05$, It was also observed significant difference between septic and suspected newborns ($P<0.05$).

Table 1: The mean and standard deviation of CRP and PCT in different groups.

	Markers	Mean±SD	P-Value
CRP mg/l	Control group	5.36±3.87	P<0.05
	Proved sepsis	25.72±26.14	P<0.05
	Suspected sepsis	10.15±11.48	P<0.05
PCT ng/ml	Control group	0.68±0.49	P<0.05
	Proved sepsis	6.75±5.84	P<0.05
	Suspected sepsis	3.95±5.15	P<0.05

CRP concentration in 55% of proved sepsis group was higher than the cut-off value. But in suspected sepsis only 20% of cases and in the control group only in 8% of infants, CRP level was located higher than the cut-off value.

PCT level was significantly higher in septic and suspected patients in comparison with the normal healthy patients. ($P<0.05$). The optimum cut-off value was found to be 12 mg/l for CRP and 1.1 ng/ml for PCT.

DISCUSSION

In recent years measurement of procalcitonin and other inflammatory mediators have been reported as sensitive parameters for the early diagnosis of sepsis in patients and evaluating its outcome.[9] Varieties of proinflammatory cytokines plays a role in pathogenesis of bacterial sepsis. Production of interleukin – 6 occurs before procalcitonin. These cytokines seems to trigger the procalcitonin secretion from target cells.[10]

The increase in the serum concentration of CRP is rather slow during the first 24-48 hr of infection and this may negatively affect the sensitivity of the test. In addition, increase in CRP concentration in non-infected clinical conditions such as meconium aspiration, prolong rupture of membranes are thought to affect the specificity of the test.[11]

PCT has been investigated for its diagnostic role in neonatal sepsis. It has been reported that high concentration of plasma PCT was found in infants with severe infection, while PCT levels were very low in those with no infections.[12] Many authors found that procalcitonin is a promising marker for

the diagnosis of neonatal sepsis.[7,8] But some investigators questioned the diagnostic accuracy of PCT in detecting the sepsis in patients. In these studies, it was reported that serum levels is increased in non-infected neonates with perinatal asphyxia, intracranial hemorrhage, pneumothorax, or after resuscitation.[13] In the research of Chin Yi-ling et al (2004)sensitivity of 69.5% and specificity of 64.5% for PCT were obtained, compared to 67.25% of sensitivity and 93.9% of specificity for CRP.[14] Also, the results of study by Khoshdel et al (2008) showed that sensitivity, specificity and positive and negative predictive values of PCT level for sepsis were 87.5%, 87.4%,30.4% and 99.1% respectively.[15] The study of Zahedpasha et al (2009) in showed that PCT levels were remarkably high in neonates with proven sepsis and the levels dropped dramatically after treatment with antibiotics.[16]

In the present study, among 20 patients of proved sepsis, 4 cases has PCT levels less than 1.1 ng/ml (cut-off value). In the control group, among 20 patients, only 2 patients had procalcitonin higher than 1.1 ng/ml, perhaps due to physiological increase of proclacitonin, even in the absence of infection. Our results indicated that the sensitivity of procalcitonin (70%) was higher than CRP (45%) for the diagnosis of sepsis and PCT appears to be useful marker for the severity of infection in patients. Adib et al in their concluded that procalcitonin is a better marker than CRP in the diagnosis of neonatal sepsis.[17]

CONCLUSION

Plasma PCT levels on admission allowed sepsis and septic shock to be differentiated, with an even greater level of significance. The results suggest that PCT is valid for auxiliary diagnosis of septic conditions in patients and useful as an indicator of the severity of sepsis.

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