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PROCALCITONIN: A BIOMARKER FOR THE EARLY DIAGNOSIS OF SEPTICEMIA

Pathology

Manish Gupta Consultant Pathologist, Shalby Hospital, Jabalpur, MP, India

Mustafa Ali* Assistant Professor, Department of Pathology, Amaltas Institute of Medical Sciences, Dewas, MP, India *Corresponding Author

ABSTRACT

Introduction: Septicemia by definition is proliferation and multiplication of microorganism in the blood and it is one of the common causes of death in non-coronary Intensive Care Unit. It is a common cause of morbidity and mortality particularly in critically ill patients as well. Symptoms of septicemia include tachycardia, tachypnea, fever, altered total WBC counts etc. Rapid diagnosis of septicemia is critical in management of patients as sometimes death may be very imminent. Blood culture remains the gold standard for diagnosis of septicemia but a major limitation is unavailability of results rapidly as it takes approximately 48 hrs.

Method: Present study was a retrospective study considering one year data of patients admitted in a tertiary care hospital.

Result: 90 out of 140 had Procalcitonin above normal reference range and among these patients with raised procalcitonin level blood culture were positive in 69 patients.

Conclusion: Study concluded that Procalcitonin is rapid marker, and has high sensitivity and specificity in detection of septicemia and correlate well with blood culture reports.

KEYWORDS

Procalcitonin, Blood Culture, Septicemia

Introduction

Septicemia is the common cause of death in non-coronary Intensive Care Unit. It is a common cause of morbidity and mortality particularly in critically ill patients. Approximately, 30%–35% of patients with severe sepsis and 50%–55% of patients with septicemia dies within 2 hours. [1] Any type of microbes like bacteria, virus, fungi and parasites can cause septicemia, but bacterial causes the most common among all. [2-4] In septicemia, the microorganisms enter in to the blood circulation, proliferate and release various virulent factors into the blood circulation [5]. Symptoms of septicemia include tachycardia, tachypnea, fever, altered total WBC counts etc. Septicemia can be associated with hypoperfusion or dysfunction of at least one organ or multiple organ dysfunction syndromes [6]. Rapid diagnosis of septicemia is critical in management of patients. Blood culture remains the gold standard for diagnosis of septicemias. However a major limitation is unavailability of results within 48 hrs. Several clinical markers of infection have been used but most are found to be non-specific since they can be positive in localized infection or systemic inflammation of non-infectious origin. Hematological markers of infection like total and differential leukocyte counts may also be non-specific [7, 8, 9]. C reactive protein is most widely used acute phase reactant and a sensitive marker of inflammation however it cannot differentiate septicemia from other causes of inflammation. CRP gets elevated only 24 to 48 h after the infection is initiated, hence cannot be an early indicator [10, 11]. Many studies have been done on procalcitonin and most of them found procalcitonin as sensitive and specific marker of septicemia. It appears within 4-6 hours in circulation and thus helpful in the early diagnosis of septicemia.

Material and Method

The study was done in a retrospective manner including total 140 patients visiting a tertiary care hospital between April 2017 to March 2018 after clearance from the institutional ethical committee.

Relevant data on clinical features, laboratory findings including blood culture and Procalcitonin values were retrieved from the medical records of pathology and microbiology department. A diagnosis of septicemia was made as per the recommendations of the American College of Chest Physicians (ACCP) which included presence of any of the following two or more of the findings along with proven source of infection: Temperature >38°C or <36°C, Heart Rate >90/min, Respiratory Rate >20/min or PaCO2 <32 mmHg, Total leukocyte counts >12,000/mm3 or <4,000/mm3, or >10% bands. Patients with small cell carcinoma lung, medullary carcinoma of thyroid, cardiogenic shock, major surgical intervention, major trauma and severe burns were excluded from the study, as Procalcitonin can be nonspecifically elevated in these conditions.

Blood culture of all 140 patients was done by automated Bactec 9050 (BD Company). Procalcitonin was measured by fully automated immunoassay analyzer Biomeriux minividas based on ELFA technology. According to the manufacturers, the normal range of procalcitonin was 0.0 to 0.5 ng/ml and a value of Procalcitonin >0.5 ng/ml was pathological.

Result

Serum procalcitonin values and blood culture findings were evaluated in all 140 patients. On the basis of procalcitonin results patients were divided in six groups as shown in the table 1. Total number of positive blood culture and their percentage were also evaluated in each group as shown in table 1. Out of 140 patients procalcitonin was above the normal range (0.0 -0.5 ng/ml) in 90 patients and among these patients with raised procalcitonin level blood culture were positive in 69 patients. Thus sensitivity of procalcitonin was found to be 76.6%. Sensitivity was 100% in patient with procalcitonin level above 50.0 ng/ml. The percentage of positivity of blood culture was low in patients with procalcitonin level between 0.5 to 5.0 ng /ml. Among the 50 patients, in which the procalcitonin level was within the normal range blood culture was positive in only 2 patients. Thus specificity was found to be 96%. The most common organism isolated in patient with positive blood culture was Gram positive cocci as shown in table 2.

Table 1: Serum Procalcitonin values and blood culture findings

Serum Procalcitonin Values	0 – 0.5 ng/ml	0.5 – 5.0 ng/ml	5.0-10.0 ng/ml	10.0-50.0 ng/ml	50.0-200.0 ng/ml	>200.0 ng/ml
Total number of patients in number and percentage	50 (35.7%)	38 (27.14%)	15(10.7%)	20 (14.3%)	9 (6.4%)	8 (5.7%)
Blood Culture Positive in number and percentage	2 (4%)	22 (57.8%)	12 (80%)	18 (90%)	9 (100%)	8 (100%)

Table 2: Type of organism isolated and their percentage in blood culture positive patients

Type of Organism isolated	Gram positive cocci	Gram negative bacilli	Gram positive coccobacilli	Fungus
Percentage out of 90 patients	50%	33.3%	13.3%	3.3%

Discussion

In healthy persons, procalcitonin is produced by parafollicular C cells of thyroid, from a CALC-1 gene located on chromosome 11. It is

produced as precursor preprocalcitonin which is further modified to procalcitonin a 116 amino acid molecule. Calcitonin hormone is involved in the regulation of calcium and phosphorous [12]. Normally, all the procalcitonin is converted to calcitonin so that no procalcitonin is released into the blood circulation. Hence, the procalcitonin level in normal individuals is very low (0.05 ng/mL). Normally, CALC-1 gene in C cells of thyroid are stimulated by elevated calcium level, glucagon, gastrin or β-adregenic stimulations. In inflammation release of procalcitonin is independent of the above regulatory mechanism. In inflammatory conditions, procalcitonin is produced by two different pathways. First is the direct pathway induced by lipopolysaccharides or other toxic metabolite of microbes and second is the indirect pathway induced by inflammatory mediators like TNF-α or IL-6.

In the present study, on comparing the results of blood culture and procalcitonin by taking a cut off value of more than 0.5 ng/ml for procalcitonin as an indicator of septicemia, the sensitivity and specificity was found to be 76.6% and 96% respectively. In a study conducted by Sinha M et al.,they observed a sensitivity of 90% and specificity of 84% for a cut off value of procalcitonin more than 0.5 ng/ml. They also concluded that procalcitonin assay may avoid unnecessary antibiotic usage [13]. In another study conducted by Harbarth et.al, they observed a sensitivity of 97% and specificity of 78% when a cut off value of 1.1 ng/ml was used to diagnose septicemia and concluded that procalcitonin is a promising indicator of sepsis in patient presenting in the emergency department with the clinical signs and laboratory findings suggestive of severe infection [14].

In the present study, the common organism isolated was gram positive cocci and among the gram positive cocci it was Staphylococcus Aureus. Sinha M et al., also observed gram positive cocci as the commonest isolates [13]. Among the gram negative bacilli and gram negative cocobacilli the common organism isolated was found to be E.Coli and Acinetobactor Baumanii respectively.

On the basis of findings of study, slightly rise in the level of procalcitonin is not always indicative of septicemia, although value more than 10.0 ng/ml is highly suggestive of septicemia.

Conclusion

Septicemia is a medical emergency that require intensive management with specific antibiotic therapy and other supportive management. Delay in the diagnosis of septicemia may lead to poor outcome. Although blood culture is the gold standard in the diagnosis of septicemia as it not only confirms the diagnosis but also provides the information on effective antibiotics. Major limitation with the blood culture is unavailability of results for 24 to 48 hours. Rapid sepsis markers such as procalcitonin in the blood may help in overcoming the limitations of confirmation by blood culture.

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