Brief Communication

Procalcitonin levels in salmonella infection

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Abstract

Aim: Procalcitonin (PCT) as a diagnostic marker for bacteremia and sepsis has been extensively studied. We aimed to study PCT levels in *Salmonella* infections whether they would serve as marker for early diagnosis in endemic areas to start empiric treatment while awaiting blood culture report. **Materials and Methods:** BACTEC blood culture was used to isolate *Salmonella* in suspected enteric fever patients. Serum PCT levels were estimated before starting treatment. **Results:** In 60 proven enteric fever patients, median value of serum PCT levels was 0.22 ng/ml, values ranging between 0.05 and 4 ng/ml. 95% of patients had near normal or mild increase (<0.5 ng/ml), only 5% of patients showed elevated levels. Notably, high PCT levels were found only in severe sepsis. **Conclusion:** PCT levels in *Salmonella* infections are near normal or minimally increased which differentiates it from other systemic Gram-negative infections. PCT cannot be used as a specific diagnostic marker of typhoid.

Keywords: Bacteremia, enteric fever, procalcitonin, *Salmonella*, sepsis, typhoid

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Introduction

Procalcitonin (PCT) levels have been used with success to diagnose bacterial sepsis early in the course of infective illnesses. PCT is produced in response to endotoxin or to mediators released in response to bacterial infections (interleukin-1beta [IL-1β], tumor necrosis factor-alpha [TNF-α], and IL-6). It strongly correlates with the extent and severity of bacterial infections. The normal level of PCT in a healthy individual is usually <0.1 ng/ml.[1] Also, it is suggested that levels of PCT would serve as an accurate marker for differentiating bacterial infections from viral infections.[2] In the present study, we intended to determine the utility of PCT levels as an early diagnostic marker of enteric fever in an endemic setting while awaiting blood culture report.

Materials and Methods

In our study, we prospectively studied adult patients with blood culture positive for *Salmonella typhi* (*S. typhi*) and *Salmonella paratyphi* (*S. paratyphi*) admitted between December 2011 and December 2013. On admission, all patients underwent detailed examination for their clinical features. Fever was defined as oral temperature >38.3°C. Tachycardia was defined as pulse rate >90 beats/min. Tachypnea was defined as respiratory rate >30/min. Abnormal white blood count was defined as <4000/mcL or >12,000/mcL. Hypotension was defined as systolic blood pressure <90 mmHg or diastolic blood pressure <60 mmHg. Patients were divided into groups as having bacteremia, sepsis, severe sepsis, and septic shock based on clinical evaluation using ACCM/SCCM/ESICM/ATS/SIS[1] criteria (2001). The patients were subjected to the usual blood investigations to

[1]Society of Critical Care Medicine (SCCM), the European Society of Intensive Care Medicine (ESICM), the American College of Chest Physicians (ACCP), the American Thoracic Society (ATS), and the Surgical Infection Society (SIS) criteria of sepsis (2001)

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ascertain the cause of pyrexia and *Salmonella* infection was confirmed in them using automated BACTEC blood culture system. The serum PCT levels were measured in these patients and samples were analyzed using an automated electrochemiluminescence based immunoassay kit (Elecsys Brahms PCT ThermoFischer, Berlin, Germany) on a Cobas e411 analyzer (Roche Diagnostics, Mannheim, Germany) whose analytic sensitivity was ≤0.02 ng/ml, and total precision (variation coefficient) was <3% at concentration levels 0.5 ng/ml. All kits used to estimate PCT levels were checked for quality standards using positive and negative controls in the laboratory. We divided patients into groups based on PCT levels [Table 1]. All patients included in the analysis were either treatment naive or off any antibiotics at least for 48–72 h before blood cultures and PCT were estimated in them. The patients who had blood culture negative for *Salmonella* were excluded from the study.

Results

On analysis of the 87 patients admitted with suspected enteric fever, 60 patients had proven *Salmonella* infections on blood culture. The patients were symptomatic with high-grade fever and toxemia for a median period of 5 days before seeking our medical help. The remaining 27 patients who had blood cultures negative for *Salmonella* were excluded from further analysis. Of the sixty blood culture positive patients, 33 were females, and 27 were males, the median age being 28.5 years. The blood cultures were positive for *S. typhi* in 52 cases (86.67%) and *S. paratyphi* - A in 8 cases (13.33%). Bacteremia was present in 32 patients (53.33%), sepsis in 25 (41.67%), severe sepsis in three patients (5%), and septic shock in none.

On evaluation of serum PCT levels, the median value for our patients was 0.22 ng/ml; values ranging between 0.05 and 4 ng/ml. The median levels of PCT in patients with bacteremia, sepsis, and severe sepsis were 0.19 ng/ml (range: 0.05 ng/ml - 0.36 ng/ml), 0.28 ng/ml (range: 0.1 ng/ml - 0.8 ng/ml), and 1.4 ng/ml (0.48 ng/dl - 4 ng/ml), respectively.

A vast majority, that is, 57 patients (95%) with *Salmonella* infections had near normal or just mild increase (<0.5 ng/ml) in serum PCT levels [Table 1]. Of these 57 patients with either normal or minimal rise in PCT levels, 32 patients had bacteremia, 24 patients had sepsis, and one patient had severe sepsis. A hig`h PCT level (>0.5 ng/ml) was noted in only 3 out of 60 patients. Of them, one had sepsis, and two had severe sepsis, the PCT levels being 0.8 ng/ml, 1.4 ng/ml, and 4 ng/ml, respectively.

Discussion

Most of the patients with high-grade fever and toxemia in India are commonly found to have viral infections such as influenza or dengue, parasitic infections such as malaria or bacterial infections such as enteric fever. In our study, we attempted to determine if PCT levels would serve as a marker for the early diagnosis of enteric fever in our setting.

A PCT cut-off value of 0.5 ng/ml or 0.4 ng/ml has been found to have 76% sensitivity and 70% specificity for diagnosing bacteremia in a metaanalysis.[3] Also, the PCT levels in Gram-negative bacteremia (median 8.9 ng/ml) were noted to be significantly higher than in Gram-positive bacteremia (median - 0.7 ng/ml) and fungal infections (median 0.58 ng/ml) in another study and similar other studies.[4,5]

PCT has been investigated in several studies in India, though most have focused on case reports or series looking at specific diagnoses such as scrub typhus, septic arthritis and osteomyelitis, H1N1, pancreatitis, pyelonephritis, meningitis, and respiratory tract infections.[6,7]

There is a paucity of literature where PCT levels have been prospectively analyzed specifically for enteric fevers. In our study, it was hypothesized that in patients with bacteremia and sepsis due to *Salmonella* infections PCT levels would be high, as has been seen with other Gram-negative infections but we came across an unexpected result.[2,4] The PCT levels in the majority

Table 1: Procalcitonin levels in patients with *Salmonella* infections

	Salmonella bacteraemia (total-32)	Clinical Sepsis (total-25)	Severe sepsis (total-3)	Septic shock	Percentage of cases out of total 60 cases
Procalcitonin levels in (ng/dl)					
< 0.05	1	0	0	0	1.67
0.05-0.5	31	24	1	0	93.33
0.5-2	0	1	1	0	3.33
2-10	0	0	1	0	1.67
>10	0	0	0	0	0
Total patients with near normal procalcitonin levels <0.5ng/dl	32	24	1	0	95

PCT: Procalcitonin

of cases with *Salmonella* bacteremia or sepsis were not significantly raised. Even among patients who had sepsis or severe sepsis, the PCT levels were high (>0.5 ng/ml) in only 3 patients (10.7%). The unexpectedly low levels of PCT (<0.5 ng/ml) were seen in the majority of infections except in those with severe sepsis despite demonstrable bloodstream infection in every patient.

S. typhi and *S. paratyphi* are thus unusual among the members of the Gram-negative enterobacteriaceae family since the bacteremia, endotoxemia and fever caused by them is typically without leukocytosis, having relative bradycardia and is without elevated PCT levels. The minimal rise of PCT levels in *Salmonella* infections, as seen in our study, may have resulted from the limited severity of systemic inflammatory response induced by these organisms, as this infection is primarily intracellular. The levels of TNF-α and IL-6 are also not much raised in enteric fevers as opposed to other Gram-negative infections which trigger the severe septic cascade.[8]

Conclusion

We conclude that PCT levels would not be a useful discriminator of bacteremia versus nonbacteremic infections in patients with undiagnosed fever in areas endemic for enteric fever. PCT levels have the poor diagnostic ability in the detection of *Salmonella* infections and hence its use should not be advocated to rule out bacterial infections in the tropical fevers. The rise in PCT levels may be indicative of host response to the infection rather than the presence of infection *per se*. The PCT levels can, however, help differentiate severe sepsis or septic shock from other stages of infection in typhoid.[9]

Limitation of our study: We did not have a control group in our study. Perhaps a study with a larger sample size and with evaluation of more markers of inflammation like C-reactive protein, erythrocyte sedimentation rate, TNF, ILs, and their complex interplay could more emphatically support our findings.

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Conflicts of interest

There are no conflicts of interest.

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