Original Article

Procalcitonin as a prognostic indicator and as an early biomarker in grading of sepsis

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Abstract

Aims and objectives: To study the pattern of PCT rise in sepsis. To see whether PCT rises earlier than other sepsis markers in severe infections. To see whether PCT levels can be used in grading of the sepsis To see whether rise and fall of PCT levels has any prognostic significance. Introduction: PCT (Procalcitonin) is a novel biomarker used across the globe for diagnosis and grading of bacterial sepsis.PCT differentiates between infectious and non-infectious diseases and also helps in prognosis of sepsis and septic shock. **Materials and Methods:** 100 patients admitted in medical or surgical departments were included in the study. PCT estimation and so also other sepsis markers were done and compared. Grading of sepsis was done on clinical grounds and also on the basis of PCT levels. **Observations:** Median PCT values in entire group was 8.89 ng/ml, Normal PCT levels noted in 24 patients, Very high PCT values were noted in 4 patients, PCT values correlated well with degree of sepsis. PCT values above 7 ng /ml were associated with high mortality. Gram negative sepsis had high PCT values compared to Gram positive sepsis. Persistently elevated PCT values indicated that severity of sepsis was more and also showed high mortality in this class. Conclusions: PCT is an early biomarker of sepsis.PCT can be used as a prognostic indicator in severe sepsis PCT is very good tool in grading the sepsis along with clinical parameters.

Keywords: Procacitonin, Sepsis, Septic shock, SIRS.

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INTRODUCTION

Sepsis is an important challenge in both medical ICUS and surgical ICUS. Clinical acumen falls short sometimes in diagnosing early sepsis. This may delay the treatment and so also the choice of antibiotics. This may ultimately lead to increased mortality in hospitalised patients. There is always a threat of community acquired infection and also nosocomial infection in ICU admissions. The conventional sepsis markers lack both sensitivity and specificity. Even the specimen samples are sometimes contaminated and may yield different culture and sensitivity reports. The culture reports May be available only after 48 to 72 hours. This will prevent us from choosing the right antibiotic combination. This ultimately will increase the mortality even in tertiary care centres. This increased mortality may be because of virulent bacterial strains and also due to multiorgan failure. Successful treatment of sepsis is a team work and credit cannot be solely attributed to the treating physician. Procalcitonin is a good sepsis marker and need not be overemphasised. Rather we will take a step ahead and see whether PCT is useful in grading of the sepsis and also whether PCT can be used as a prognostic indicator. This exercise will enable us in good counselling of the patient and his relatives which can avoid many unwanted confrontation events. PCT is a novel biomarker which can differentiate between infectious and non-infectious diseases and also will segregate between bacterial and non bacterial infections. This will give sufficient grounds for rational use of antibiotics.PCT is a precursor of

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thyroid hormone and remains low in physiological states but following systemic bacterial infections PCT levels rise rapidly and peak in 6 to 12 hours after the onset of infection. With the control of infection PCT level fall to normal level. This makes it a good sepsis marker and also a good prognostic indicator. SIRS, Sepsis, and Septic Shock Criteria. Defines the severity of sepsis and septic shock. For patients under 18, please use the Pediatric SIRS, Sepsis and Septic Shock Criteria.

SIRS CRITERIA (≥ 2 MEETS SIRS DEFINITION)

1. Temp >38°C (100.4°F) or < 36°C (96.8°F)
2. Heart Rate > 90
3. Respiratory Rate > 20 or PaCO2 < 32 mm Hg
4. WBC > 12,000/mm>3, < 4,000/mm>3, or > 10% bands

SEPSIS CRITERIA (SIRS + SOURCE OF INFECTION)

1. Suspected or Present Source
2. Severe Sepsis Criteria (Organ Dysfunction, Hypotension, or Hypoperfusion)
3. Lactic Acidosis,
4. SBP <90 or SBP Drop ≥ 40 mm Hg of normal

SEPTIC SHOCK CRITERIA

1. Severe Sepsis with Hypotension, despite adequate fluid resuscitation
2. Multiple Organ Dysfunction Syndrome Criteria. Evidence of ≥ 2 Organs Failing

There remains controversy over the sensitivity and specificity of these criteria, even though they have been largely adopted for the purpose of research and in clinical practice. SIRS is commonly used as a screening tool in the emergency department to identify patients at risk for Severe Sepsis.. Clinical judgment remains important since a significant number of patients presenting to emergency departments will meet criteria for Sepsis but do not require further screening or management. Patients that present with two or more SIRS criteria and a suspected or confirmed infection should be screened for Severe Sepsis. Currently many institutions encourage or even mandate obtaining a lactic acid level on these patients. A lactate ≥ 4 mmol/L is considered the cut-off value for the diagnosis of severe sepsis and the initiation of Early Goal Directed Therapy (EGDT). Patients who meet the above criteria but are persistently hypotensive despite the initiation of intravenous fluid resuscitation are in Septic Shock and aggressive resuscitation measures should be initiated immediately. Early initiation of broad spectrum antibiotics and aggressive resuscitative measures have been shown to decrease mortality in patients with Severe Sepsis and Septic Shock. The early recognition of these conditions is therefore of the utmost importance. SIRS criteria are mostly used as a screening tool to identify patients that may need further workup for sepsis and severe sepsis. In the emergency department it is a triage tool that helps determine patient acuity and identify patients that are potentially septic and in need of further screening. Severe Sepsis and Septic Shock are universally accepted as indications to initiate sepsis management protocols such as Early Goal Directed Therapy. Having clearly defined criteria for SIRS, Sepsis, Severe Sepsis, and Septic Shock is also important in order to standardize clinical research, as well as institutional protocols for the management of these conditions.

MATERIALS AND METHODS

The period of study was limited to 15 days of indoor stay of the patient (this is because surgical /orthopaedic patients may remain hospitalised for more than 15 days). Written consent was obtained from the patient/ relatives to be included in the study. The cost of PCT test was borne by the institute. Ethical clearance was obtained from the IEC before going for the study.

Sample size: 100 patients admitted in Bharati hospital for sepsis on medical side or surgical side who meet the criteria of sepsis were included in the study. The sepsis criteria were decided on the basis of SIRS, Sepsis, and Septic Shock Criteria. Attempt was made to categorise the patients in mild, moderate and severe sepsis. Initial workup included following tests

1. Complete haemogram /ESR
2. BSL levels
3. BUL levels
4. Serum keratinize
5. Specimen staining and culture.
6. Blood cultures
7. CRP levels
8. Chest X-ray
9. Abdominal USG
10. CT/MRI as and when needed
11. Procalcitonin levels.

Grading of sepsis was done clinically and values of PCT were compared with it and observations were made. Even observations were made by comparing PCT levels with other laboratory findings. The end observation results were divided in to following categories.

1. Recovered fully
2. Recovered partially
3. Status quo
4. Deteriorated and progressed to multiorgan failure
5. Death.

OBSERVATIONS AND RESULTS

Out of 100 patients in the study 76had elevated levels of PCT. Median age of presentation was 55.8 years. 27 admissions were late arrivals. 36 admissions had surgical cause for sepsis. 64 admissions had medical cause for

sepsis. PCT values were more elevated in gram negative sepsis. PCT values greater than 10 were associated with high mortality. Out of 100 admissions 62 recovered with some residual sepsis persistent on 15th day. 22 patients did not show any significant improvement on 15th day also. 16 patients died due to multiorgan failure before 15th day of admission. Renal failure and ARDSwere invariably associated with critically ill patients. Out of 100 patients 27 had uncontrolled diabetes. The BSL values in them were above 255mg%. 18 patients had hypertension. 57 patients had renal derangements (altered urea and creatinine levels). Anaemia was present in45 patients. Leucocytosis was present in 90 patients.

Table 1

Grades	Leucocyte count	Number of patients
Mild	11,000 to 14,000 cells/cmm	9
Moderate	14,000 to 20,000 cells /cmm	24
Severe	More than 20,000 cells /cmm	57

Table 2

Procalcitonin Range	Number Of Patients
Less than 0.15 ng /ml	24
Between 0.16 to 3 ng /ml	30
Between 3 to 8 ng /ml	42
Above 8 ng/ml	04

Procalcitonin level <0.10 ng/mL. No systematic inflammatory response noted in them. Procalcitonin level 0.10 – 0.49 ng/mL. Minor or no significant inflammatory response. Local inflammation and local infections noted. Procalcitonin level 2.00 – 9.99 ng/mL. Severe systemic inflammatory response due to sepsis, High risk for progression to severe system icinfection. Procalcitonin levels >10ng/ml were exclusively due to severe bacterial sepsis or septic shock.

ADMISSION CATEGORISATION OF PATIENTS

Total number of admissions 100. Patients admitted on medical side are 64. Patients admitted on surgical side 18. Transfers received from surgical floors 18. Total number of 100.

AETIOLOGICAL CATEGORISATION OF SEPSIS

1. Respiratory system ----------27%
2. Cellulitis/ abscess/ gangrene------24%
3. Genitourinary tract----------09%
4. Abdominal infections----------30%
5. Others----------10%

LABORATORY SEPSIS MARKERS

1. Raised ESR ----------88%
2. Raised CRP ----------67%
3. Leucocytosis was present in------ 90%

Table 3

Grades	Leucocyte count	Number of patients
Mild	11,000 to 14,000 cells/cmm	9
Moderate	14,000 to 20,000 cells /cmm	24
Severe	More than 20,000 cells /cmm	57

Pus culture done in 29 case. Sputum culture done in 27 cases. Abdominal fluid culture done in 12 cases. Blood culture done in 47 cases. Catheter tips culture done in 02 cases

In totality the culture report analysis was as follows

GM negative organisms grown in 57% case. GM positive organisms grown in 04% cases. Mixed infections noted in 07% cases.

Median procalcitonin levels in entire group was 8.89 ng/ml(Less than 0.1 ng/ml was taken as normal). The minimal elevated level was 0.2 ng/ml. The maximal elevated level was 100 ng/ml. Median PCT level was8.89 ng/ml. In our study there was a linear correlation between other sepsis markers and PCT level meaning that PCT levels were significantly high in patients with severe sepsis where other biomarkers also indicated the same trend.

Table 4: A comparison of total leucocyte count and PCT level was done which yielded following results

Total Leucocyte Count	Procalcitonin Levels (Median Valuesin This Group)
Upto 9000/cmm	3.3
From 9000 to 20000	4.2
20000 and above	7.4

PROCALCITONIN and culture report comparison

Gram negative sepsis ---median PCT value was 4.8. GRAM positive sepsis---median PCT value was 3.9. Mixed infections – median PCT values was 4.3

REPEAT PCT LEVELS MEASUREMENT

Done in 11 patients who clinically had severe sepsis and even lab parameters suggested severe sepsis with multiorgan failure. Initial PCT and repeat PCT levels are shown in following table.

Table 4

Number	Initial PCT level	PCT level on 13th day
1	3.9	3.2
2	4.3	3.9
3	2.7	1.7
4	4.3	4.1
5	5.4	3.7
6	6.8	6.0
7	10.8	8.7
8	11.7	9
9	12.4	13.4
10	2.7	2.6
11	6.6	4.2

If we compare head to head the initial values and later values in these patients it clearly shows that in proven sepsis the PCT values marginally fall provided that the patient is on good antibiotic choice in full therapeutic doses. The PCT levels may continue to fall as you keep on treating the patients. These eleven selected patients had an eventful course and five out of them died because of multiorgan failure. These five patients also had high initial PCT levels with marginal fall in PCT on 13th day. On the contrary one of them had increased PCT value than the initial value. This clearly indicates that PCT values alter marginally in advanced sepsis may marginally increase or decrease or may remain unaltered and may point out to a bad prognosis.

CONCLUSIONS

PCT is a very good biomarker of sepsis. PCT is an early biomarker of sepsis. PCT can be used as a prognostic indicator in severe sepsis. PCT is very good tool in grading the sepsis along with clinical parameters. There is a linear correlation between PCT levels and leucocyte count in severe sepsis. Very high PCT values are associated with multiorgan failure and high mortality.

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