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PROCALCITONIN VS C- REACTIVE PROTEIN AS A BIOMARKER FOR SEPSIS

Medicine

Dr. Mitali Madhusmita* PG Resident, Department of Medicine, Dr. D.Y.Patil Medical College, Navi Mumbai *Corresponding Author

Dr. Suranjana Basak PG Resident, Department of Medicine, Dr. D.Y.Patil Medical College, Navi Mumbai

Dr. Annanya Mukherji Professor, Department of Medicine, Dr. D. Y. Patil Medical College, Navi Mumbai

Dr. Priyanka Jadav Lecturer, Department of Medicine, Dr. D. Y. Patil Medical College, Navi Mumbai

KEYWORDS

Introduction:
Definitions for the terms of "SIRS", "sepsis", "severe sepsis" or "septic shock" have been proposed by the ACCP/SCCM Consensus Conference in 1992, and are now widely used. Systemic inflammatory response syndrome (SIRS) encompasses a variety of complex findings that result from systemic activation of the innate immune response. The clinical parameters include two or more the following: Fever (>38° C) or hypothermia (<36° C), increased heart rate (>90 beats/min), tachypnea (>20 breaths/min) or hyperventilation (PaCO2 < 32 mmHg), and altered white blood cell count (>12,000 cells/mm3 or <4000 cells/mm3) or presence of >10% immature neutrophils. Traditional markers of systemic inflammation, such as CRP, erythrocyte sedimentation rate (ESR) and white blood cell count (WBC), also have proven to be of limited utility in such patients due to their poor sensitivity and specificity for bacterial infection. Early diagnosis and appropriate therapy of sepsis is a daily challenge in intensive care units (ICUs) despite the advances in critical care medicine. Procalcitonin (PCT); an innovative laboratory marker, has been recently proven valuable worldwide in this regard.

Objectives:
This study was undertaken to evaluate the utility of PCT in a resource constrained country like ours when compared to the traditional inflammatory markers like C - reactive protein (CRP) to introduce PCT as a routine biochemical tool in regional hospitals.

Materials and Methods:
PCT and CRP were simultaneously measured and compared in 105 medico-surgical ICU patients admitted at Dr. D.Y.Patil Hospital Navi Mumbai from December 2016 to February 2017; according to the American College of Chest Physicians (ACCP) criteria based study groups.

Results:
The clinical presentation of 82% cases revealed a range of systemic inflammatory responses (SIRS). The diagnostic accuracy of PCT was higher (81%) with greater specificity (91%), sensitivity (86%), positive and negative predictive values (89% and 50%). Both serum PCT and CRP values in cases with sepsis, severe sepsis and septic shock were significantly higher from that of the cases with SIRS and no SIRS ($P < 0.01$).

Conclusion:
PCT is found to be superior to CRP in terms of accuracy in identification and to assess the severity of sepsis even though both markers cannot be used in differentiating infectious from noninfectious clinical syndrome. Procalcitonin has been identified as a promising biomarker that may provide added value to the clinical decision process, i.e. assist in diagnosis, assess prognosis, and assist in treatment selection and monitoring. This biomarker is now widely used in Europe and recently was approved by the FDA in USA for the diagnosis and monitoring of sepsis and evaluation of the systemic inflammatory response in the clinical arena.

Discussion:
PCT was first described as a marker of the extent and course of systemic inflammatory response to bacterial and fungal infections in 1993 by Assicot.[1] Ever since then Procalcitonin (PCT) has been examined extensively as a marker for systemic inflammation, infection, and sepsis, both singularly and in combination with other markers such as CRP, in adults and children in ICU setup. The predominant assay used in most studies has been an immunolum inometric assay, called the LUMItest, manufactured by Brahms. In recent years immunofluorescent assays were given preference. The only study reported in our country earlier was conducted on neonatal sepsis using a rapid semi quantitative immunochromatographic method.[2] The quantitative immunofluores cent assay is being practiced for the first time in this study.

In this study, cultures were positive in 53.4% of microbiological culture specimens ($n = 39$); *E. coli* being the major (35.8%) isolate followed by *Klebsiella*, *Pseudomonas* and *Acinetobacter*. This was in accordance with the reports of Karlsson *et al*. and Andreola *et al*. though the rate of positive culture was less than ours. Karlsson *et al*.[3] also reported of significantly higher PCT levels in positive culture cases compared to that of the negative ones. In our observation, both PCT and CRP levels were higher in cases with positive cultures though statistically insignificant ($P > 0.05$). In another Korean study the higher CRP levels associated with positive cultures showed greater statistical significance ($P < 0.001$) than PCT levels ($P < 0.05$).[4]

In the present study, plasma levels of PCT and CRP in patients with and without infection at different levels of SIRS were assessed. Patients with moderate to severe sepsis had higher PCT concentrations than patients with no/local infections ($P < 0.01$). The most recent studies with such reports are given by López *et al*., Ruiz-Alvarez *et al*., and Endo *et al*.[4]

Both serum PCT and CRP showed significant raise of the mean values along with increased severity of the clinical presentations in the study subjects. Significantly higher mean PCT and CRP values were observed in sepsis, severe sepsis and septic shock cases compared to SIRS and no SIRS when compared at the various severities of systemic inflammation and sepsis. However, a number of studies having not been able to demonstrate significant relations of PCT or CRP with severity raised controversies regarding their utility as prognostic markers. In this study the mortality was confined to the cases with PCT level of > 10 ng/ml even though the rate of mortality was low (16.6%)[5]

With regards to the diagnostic performance of PCT, various international literatures found PCT to be a useful marker in the diagnosis of a septic process with a sensitivity of 78% and a specificity of 94% comparing these values with CRP.These studies have a more precise methodology towards the desired objectives and the sample number is much greater for which the statistical significance was much better. In this study PCT showed highest level of accuracy (75.34%) with greater specificity (72.2%), positive and negative predictive

values, positive likelihood ratio as well as the smaller negative likelihood ratio. However, sensitivity of CRP in the diagnosis of sepsis was found to be higher (85.45%) than PCT (76.36%). By convention, marked changes in prior disease probability can be assumed in PLR exceeding 10.0 and NLR below 0.1.Procalcitonin had a higher PLR and lower NLR than did CRP and complement proteins. These results are in agreement with those of Clec'h *et al*., Ruiz-Alvarez *et al*. and others.

Few studies have reported of lower diagnostic performance of PCT than CRP in differentiating between sepsis and SIRS. In contrast to this, majority of studies have reported that procalcitonin was a better marker to estimate the severity, prognosis, or further course of the sepsis. This study was consistent to the others with a few minor limitations. First, serial PCT monitoring every day was avoided which may improve its performance as an aid for follow up of sepsis. Second, antimicrobial therapy may have an impact on PCT values which could not be explained with our study design.

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