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Estimation of Serum Level of Procalcitonin as the Reliable Marker for the Assessment of the Post Operative Infection after Surgery

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Abstract

Introduction: Reliable clinical and/or microbiological parameters from easy to obtain specimens that may be used to diagnose bacterial infections and rule out other infections not in need of antibiotic therapy have been largely lacking. In this perspective this prospective study was done prospectively with the intention of finding out the diagnostic power of PCT as a reliable marker to differentiate infectious from non-infectious wound discharge. *Material & Methods:* A total of 300 patients who had undergone surgical procedure with no other evidence of any infection. Patients who either had immunocompromised states or didn't give consent for inclusion were excluded from the study. Those patients who suffered from some other source of infection (respiratory or urinary infection) or any other septic foci, deviated from our study protocol, suffering from pre-op infection were excluded from the study. *Results:* On comparing the serum levels of prolactine there is significant rise in procalcitonin level in patients with confirmed surgical site infection on the day of discharge from the surgical site with a p value of <0.001. *Conclusion:* Using PCT, which mirrors the likelihood of bacterial infection and the severity of infection, to guide antibiotic therapy, is a persuasive, evidence-based approach to a more rational use of antibiotics.

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Introduction

Despite recent advances in surgical techniques and intensive care management, infectious complications and sepsis remain significant problem after surgery. There are a number of limitations to using conventional diagnostic markers for patients with clinical suspicion of infection. As a consequence, unnecessary and prolonged exposure to antimicrobial agents adversely affects patient outcomes, while inappropriate antibiotic therapy increases antibiotic resistance [1,2].

Despite the successful implementation of diagnostic biomarkers in different fields of medicine, accurate and timely diagnosis of bacterial infections remains a challenge. Reliable clinical and/or microbiological parameters from easy to obtain specimens that may be used to diagnose bacterial infections and rule out other infections not in need of antibiotic therapy have been largely lacking [3].

The main disadvantages of many current microbiological methods are diagnostic delays (for example, culture methods), suboptimal sensitivity (for example, blood cultures) and low specificity due to contamination (for example, sputum cultures), whereas others are not amenable to routine diagnostics due to their invasive nature (for example, lung biopsy). Inflammatory markers, such as C-reactive protein (CRP) or white blood cells (WBC), lack specificity for bacterial infections. This is partly explained by the heterogeneity of different infections and the complex interaction of different pro- and anti-inflammatory mediators of the host response aimed at combating invading pathogens during systemic infections, which depend on timing, type, extent and site of the underlying infection [4].

Among several markers of inflammation and sepsis, procalcitonin (PCT) and C-reactive protein (CRP) markers are being studied to investigate their accuracy for the diagnosis of bacterial infections. PCT is the prehormone of calcitonin, which is normally secreted by the C cells of the thyroid in response to hypercalcemia; under these normal conditions, negligible serum PCT concentrations are detected [5]. The mechanism proposed for PCT production after inflammation and its role are still not completely known. It is believed that PCT is produced by the liver and peripheral blood mononuclear cells, modulated by lipopolysaccharides and sepsis-related cytokines. CRP is an acute-phase reactant, and CRP level measurements are frequently used to aid in the diagnosis of bacterial infections. CRP is synthesized by the liver, mainly in response to IL-6, which is produced not only during infection but also in many types of inflammation. It binds to polysaccharides in pathogens, activating the classical complement pathway. The reported diagnostic accuracy of PCT and CRP for the diagnosis of bacterial infections has varied across studies [6].

Procalcitonin, a new innovative inflammation parameter is presently being evaluated in clinical studies. It has been shown to be increased markedly in patients with severe bacteria induced inflammation, septic shock, endotoxinaemia and multiple organ failure [7]. In contrast, severe viral infections or inflammatory reactions of non-infectious origin as well as autoimmune or allergic disorders do not or only very moderately increase procalcitonin serum levels. Because procalcitonin is observed at significantly higher concentrations in bacterial infections, it might assist differentiation between these infections and other aetiologies of critical illnesses. Furthermore, pro-calcitonin correlates with the severity of infection and sepsis and thus could serve as a useful marker for monitoring surgical high risk patients. Procalcitonin may serve as a valid and sensitive indicator for bacterial infection with important diagnostic potential in the peri-operative period and in intensive care medicine [8].

In this perspective this prospective study was done prospectively with the intention of finding out the diagnostic power of PCT as a reliable marker to differentiate infectious from non-infectious wound discharge.

Materials & Methods

This study was conducted in the general surgery department at Gujarat Adani institute of Medical Science, Bhuj, Kutch, Gujarat for a period of two years. Inclusion criteria included A total of 300 patients who had undergone surgical procedure with no other evidence of any infection. Patients who either had immunocompromised states or didn't give consent for inclusion were excluded from the study. Those patients who suffered from some other source of infection (respiratory or urinary infection) or any other septic foci, deviated from our study protocol, suffering from pre-op infection were excluded from the study. Ethical clearance was taken from ethical committee of the institute. Written consent was obtained from all the participant patient of the study. Only after the consent was obtained they were enrolled for the study.

The epidemiological and clinical factors for all the patients were noted as per the performa prepared by the experts of the field. Serous discharge from the wound site or presence of signs of inflammation like warmth, redness, induration at the operative site were in the follow up of the patient were further evaluated for the presence of infection at surgical site. Swab of the wound area was collected and had sent for Gram stain along with bacterial cultures. All the routine clinical and hematological work up were done to look for signs of infection including 4 hourly Temperature chart, pulse charting, WBC count, ESR and CRP levels. Patients of all age groups who had undergone surgery were prospectively included in this study.

Serum levels of procalcitonin were measured on the day of wound discharge from operative site. Collected serum was stored a temperature of -50 degree celcius and PCT was determined by ELISA method at the end of the study. Other potential sites of infection such as respiratory and urinary tract infections were ruled out by appropriate clinical examination and lab investigations. All the patients were followed up till surgical wound healing and all the patients with wound discharge along with growth of infective agent by culture were noted and were grouped as patients with wound infection (WI). Those patients who developed wound discharge with no growth of infective agent grouped as culture negative wound discharge. At the end of the study the serum samples from all patients of two groups were tested for the levels of Procalcitonin and the Mean levels of procalcitonin were compared between the two groups, values of PCT were assessed using the appropriate statistical analysis (Unpaired t test was used for the comparison of biochemical parameters). The values were analyzed using SPSS software version

19. AII statistical analysis was carried out at 5% level of significance and a p value < 0.05 was considered significant and results were drawn.

Results

Out of 300 patients minimum age of patient was 5 years and maximum age was 65myears. Max patient comprises of 10-20 age group 40%. Male comprises of 70% and males 30%. At the end of the study Patients were grouped as per the table:

On comparing the serum levels of prolactine there is significant rise in procalcitonin level in patients with confirmed surgical site infection on the day of discharge from the surgical site with a p value of <0.001.

Table 1: Division of participants into different groups

	Wound discharge	Normal Wound Healing
Culture Positive	25	-
Culture Negative	5	-
Total	30	270

Table 2: Frequency of distribution of different organisms found in culture

Culture of infective organism	Frequency
Negative culture	5
Pseudomonas	8
Klebsiella	6
MRSA	5
MRSA + Pseudomonas	3
CONS	3
Total	30

Table 3: Comparison of serum prolactin with culture positive and culture negative groups

Groups	Number of participants	Serum level	P Value
Culture negative	5	28.10	<0.01
Culture positive	25	350.18	
Total	30		

Discussion

Early identification of infections is still a challenge for clinicians. The general consensus is not to provide antibiotics for every suspected infection because of emerging issues with bacterial resistance [9]. Therefore, a marker specific for bacterial infection will be most helpful. Based on this meta-analysis, we observed that PCT levels were more accurate markers for bacterial infection than were CRP levels, both when differentiating bacterial infections from noninfective causes of inflammation and when differentiating bacterial infections from viral infections.

The kinetics of a prospective marker should be considered along with its sensitivity and specificity. PCT secretion begins within 4 h after stimulation and peaks at 8 h, clearing when the insult is under control. PCT is stable in samples, the assay is relatively easy to perform, with a moderate cost, and the result is available within 2 h. CRP secretion starts within 4–6 h after stimulation, peaking only after 36 h. The assay for determing CRP levels is easy to perform, often automated, and has a low cost [6,10].

As would be expected, none of the studies included in this review were completely free from all potential biases and limitations. Study population and patient selection were not fully reported; however, there was minimal withdrawal from the studies, minimizing selection bias. Few studies reported information on blinding and test reproducibility, which could potentially have altered the trustworthiness of the data. Results are susceptible to spectrum bias, because diagnostic tests may have different accuracies in distinctive phases of the disease. Classification bias in the original studies was possible, because even in the face of positive culture results, there is not always enough evidence to discriminate between infection and colonization [6].

PCT measurements were performed using the same commercially available specific antibody system. However, means of measuring CRP levels largely varied, with 8 different methods used among the 12 included studies. The implications of multiple assay methods are unknown in the final result of this meta-analysis. However, each study was included using its own best cutoff value, and the linear regression methods used in the analysis accounted for possible threshold differences between studies [11].

In our study most of the patients (20 out of 30) developed wound discharge on the post op day 4, four patients on day 7, four patient on day 8 and two on postop day 10 showed the appearance of wound discharge. Most of the patients (80%) who had a culture positive wound discharge had to undergo a second surgery in the form of wound exploration and debridement, whereas the remaining 30% patients improved with daily dressings and I/V antibiotics. Amongst those patients who had a culture negative wound discharge only 30% of patients required re-operation in the form of wound lavage and wound debridement.

Studies done in patients undergoing cardiac surgeries and major cancer surgeries have shown that serum procalcitonin to be an effective biochemical marker which can predict the development of early SSI's in these patients [12]. Most studies show that the procalcitonin levels increase in the immediate post –operative period but owing to its short half – life of 18 – 24 hours the levels start decreasing rapidly (Davidson et al., 2013; Oberhofer et al., 2006). A persistently high level and rising levels seen on the 3rd or 5th post-op day have shown a positive correlation with the development of early onset surgical site infection. These results prompted us to do this study in surgery patients to look for similar results and to identify if serum procalcitonin can be an effective marker in this subset of patients as well. We aimed to determine the diagnostic significance value of this marker so as to identify its accuracy and clinical significance in our subset of patients. On comparing the levels of serum PCT in all the patients who had developed wound discharge during the early post-op period we found that the levels of PCT in serum on the day of wound discharge were significantly higher in patients who had culture proven wound infection and had required a wound debridement as compared to the patients in whom no organism could be isolated from the discharge and most of whom improved with just observation over time. And this difference was also found to be statistically significant with a p value < 0.001.

Conclusion

Emerging bacterial resistance to antimicrobial agents calls for more effective efforts to reduce the unnecessary and prolonged use of antibiotics in self-limiting non-bacterial and resolving diseases. Patients and physicians share a common goal of improving symptoms from infection as fast as possible and often see antibiotics as the most expeditious intervention to achieve it. This one-size fits-all approach fails to consider the basic questions of who benefits from antibiotic therapy, and if treated, what would be the optimal duration. Using PCT, which mirrors the likelihood of bacterial infection and the severity of infection, to guide antibiotic therapy, is a persuasive, evidence-based approach to a more rational use of antibiotics.

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