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Procalcitonin versus CRP in determination of antibiotic during ICU admission

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ABSTRACT:
The management of antibiotic medications, its duration, assessment and indications are quite important in treating patient in the intensive care unit. When employing highly active drugs in intensive care, proper indications and therapy length are crucial (Nargis et al., 2014). Procalcitonin (PCT) and C-reactive proteins (CRP) are one of the first of inflammatory indicators to dicrease utilisation of excessive anti-biotics recently. These two measures are the only laboratory marker that could discriminate between a bacterial infection and a viral or non-infectious inflammatory reaction. All individuals with at least two concurrent systemic inflammatory response syndromes who needed antibiotic treatment for a known or suspected bacterial infection were included. Patients were randomly assigned to receive either conventional antibiotic therapy or PCT-guided
antibiotic therapy (control group). When clinical signs and symptoms of infection subsided and PCT dropped below 1 ng/ml, or when PCT was greater than 1 ng/ml but initially reduced by 25–35%, antibiotic treatment was discontinued in the PCT control group for three days to eight days, the control group received antibiotic therapy as normal care.
The study included 110 surgical intensive care patients who had received antibiotics for proven or suspected severe infections. For patients in intensive care, PCT monitoring has proven to be a helpful tool to direct antibiotic medication. This may encourage the best possible use of antibiotics, which benefits both the prevention of germ resistance and the expense of critical care.
Keywords : intensive care unit, procalcitonin, C - reactive protein

I. INTRODUCTION

Intensive care patient are particularly susceptible to consequences such as infections and sepsis more easily. Because clinical symptoms and traditional indicators are not always trustworthy markers for the diagnosis of sepsis and infection, biomarkers such as procalcitonin (PCT) or C-reactive protein (CRP) are often utilized as diagnostic tools to treat these individuals. However, in ICU patients, such as those undergoing elective surgery, levels of PCT, CRP, and other biomolecules may be increased, indicating early postoperative or posttraumatic inflammation, regardless of the diagnosis of sepsis or infection. Several studies have described the kinetics and degree of PCT during stay in ICU. At the same time, PCT and CRP stimulation in ICU is relatively well described and remain part of heated contribution considering the fact which diagnostic tool in helpful in reducing the stay of patient in ICUE. According to de Jong et al. (2018) PCT levels grow in extremely low pace than CRP levels, and the non-specific stimulation time is likewise much shorter. Therefore, PCT parameter is the best option for early identification of sepsis and surgical infection. On the same time it has been elaborated byBassetti et al. (2018) studies on CRP induction after polytrauma are rare and do not give detailed information on the induction of this protein in different degrees and types of trauma, such as PCT. In more accurate sense many scholars firmly believe that medical expert talk and discuss more about PCT due to obvious reasons such as early results mechanisms. In which regard, CRP get neglected and not many academics and practitioners utilize this diagnostic tool.

Purpose of the study

The purpose of this study is to describe the amount and duration of PCT and CRP induction in patients with different forms of acute and severe infections. We also examine time of stay of ICU patient with regard to utilization both of these tools. Tounderstand the mechanism of both diagnostic tool and to reach on unbiased conclusion we would use previous researches and studies to elevated the level of this review based paper.

Evaluation of PCR and CRP efficiency in ICU and severe trauma

The classic biomarker of infection with the greatest research is PCR. The liver produces this acute phase protein in response to IL-639

(Bréchot et al., 2015). Blood levels start to increase 4-6 hours following the inflammatory stimulation, rising twice every 8 hours, peaking between 36 and 50 hours, with a half-life of 19 hours. Although the CRP test is expensive, it is highly helpful in facilities with limited funding. In contrast to healthy controls, patients with community-acquired pneumonia had higher CRP levels and are able to distinguish the illness from COPD and heart failure ratio. In patients with severe infections, a decline in CRP is related to a better prognosis and recovery (Carr 2015). Lower respiratory tract infections are less common in primary healthcare settings where antibiotic therapy is guided by on-site CRP tests.

Several factors determine whether PCT is a more accurate measure than CRP. When individuals with life-associated pneumonia have bacteremia, 50 PCT is thought to be more accurate than PCR at predicting the condition. The study also indicated that PCT was considerably greater in patients with gram-negative bacilli infections than in people with gram-positive cocci. In an observational research, there was a strong connection between PCT and CRP in the same order, and PCR and PCT independently detected pneumonia caused by another asthma or COPD exacerbation. So it has been proposed that CRP might be helpful in directing antibiotic therapy in hospitalized patients with lower respiratory tract infections.

In study of Carr (2015) the clinical usefulness of PCT and CRP was investigated in discriminating between verified isolated viral pneumonia and mixed pneumonia (bacterial and viral) during the 2009 H1N1 pandemic.The detection of mixed bacterial pneumonia had an 84% bacterial sensitivity and specificity. PCT > 1.5 g/L infection rate are 69% and 63% for CRP> 100 mg/L respectively. The result of a sensitivity test indicate that 50% sensitivity to PCT and 50% sensitivity to PCR. Low PCT and low CRP suggested that a mixed bacterial infection was not likely to be the cause of the pneumonia.

Few CRP-based algorithms have been examined throughout the years, despite the fact that PCT-guided antibiotic treatment algorithms have been found to be effective in lowering the length of antibiotic treatment in multiple RCTs in various clinical situations. CRP and PCT were compared in an RCT in 2013 mentioned byPepper et al. (2019) in adult patients hospitalized to intensive care with severe sepsis or septic shock. On the basis of PCT or CRP mechanism, the decision to stop using antibiotics was made on basis of response, or final limb. Regardless of CRPor PCT levels, antibiotics were stopped in both groups on day 7 for patients whose infections had clinically improved. The fact should be highlight here which is necessary to develop the basic understanding that even if the withdrawal requirements were satisfied, antibiotics were provided for at least 7 days if patients had a baseline SOFA score of 10 or above. The findings revealed no discernible differences between the PCT (8.1 days) and CRP (7.2 days) groups in the length of antibiotic treatment. There was no difference in mortality and morbidity. These findings imply that a CRP-based approach for managing antibiotic resistance may be just as secure as PCT while being less expensive. However, it can be recommend that this foundation must be verified in a bigger investigation, though.

The ability to distinguish between bacterial and viral illnesses in pediatric and adult hospital patients has recently been tested using tumor necrosis factor-stimulated ligand (TRAIL) in conjunction with PCR and interferon-gamma-stimulated protein 10A in many settings. TRAIL, a protein, is increased in viral infections but down regulated in bacterial infections, in contrast to PCT. Therefore, it is not used in conjunction with bacterial indicators like PCT and CRP. The three indicators worked together to produce an AUC of 0.94 0.04 for differentiating between bacterial and viral illnesses. According to Lautzetal. (2016) a recent study, using three biomarkers to distinguish between viral and bacterial infections in young children (2–60 months) may help prevent the overuse of antibiotics in these kids. Antibiotics are generally not advised due to issues with bacterial resistance for all suspected infections. A particular marker for bacterial infection would therefore be very helpful (Zilahi et al., 2016). It can be assumed PCT levels are more reliable predictors of bacterial infection than CRP levels between bacterial infection caused by viral infection and bacterial infection and non-infectious inflammation.

Operating mechanism of PCT and CRP in severe infection

The usage and efficacy of PCT as a biomarker are extensively debated in the literature in two primary areas considering guidance for antibiotic therapy and as an early indicator of sepsis (distinguishing between bacterial and non-bacterial etiology). In recent years, PCT has become a potential biomarker for antibiotic cessation, particularly in critically sick patients who cannot be given the medication just to demonstrate its safety and efficacy (Rowland et al; Maseda, 2015).

In septic patients, PCT and CRP have been tested to observe which method is more

effective at directing antibiotic therapy while using less antibiotics. In a recent review conducted by Aloisio et al. (2019) it was discovered that there was no significant difference in overall sensitivity (P = 0.48) or specificity (P = 0.57) between PCT and CRP for diagnosing infection in critically ill individuals. A negative predictive value (NPV) of 75% (95% CI, 54-96%) was obtained by combining A2M and PCT (measured at baseline and after 72 hours), which was able to distinguish bacterial infection from other causes of inflammation along with postoperative sepsis and the systematic response syndrome (SIRS). However, several research have questioned the actual value of PCT in aiding medical professionals in making a diagnosis. Although Mazlan et al. (2021) and Aloisio et al. (2019) subsequently showed that PCT's use would improve clinical management by 28-day therapy model, in-hospital treatment, length of treatment, ICU stay, and overall length, they did validate PCT's role as a biomarker that can minimize the duration of antibiotic therapy. In a systematic review that included 16 randomized clinical trials, Mazlan et al. (2021) evaluated a PCT-guided antibiotic withdrawal strategy. This method was found to be associated with lower mortality (hazard ratio 0.89; 95% CI 0.83 to 0.97) and shorter antibiotic therapy (mean 1.31 days; 95% CI 2.27 to -0.35). They also discovered low-certainty evidence in favor of the clinical application of this PCT and came to the conclusion that it is challenging to attribute a survival benefit to a PCT-led strategy because the samples reported were taken from studies that did not always adhere to protocol (i.e., when PCT is combined with other biomarkers like CRP) .

In the Netherlands, a nation with low hospital and community antibiotic use, two recent publications assessed the cost-effectiveness of MDT-led drug withdrawal. A PCT-based algorithm for antibiotic abstinence has been demonstrated by Kip et al. (2018) as a practical method for reducing antibiotic exposure in intensive care patients. Moreover, the fact could not be neglected that if the cost-effectiveness of the PCT test and the non-PCT test would be evaluated to decide how long critically sick patients should receive antibiotic therapy practitioner would choose PCT instead of CRP. Although the PCT group's average length of antibiotic therapy would be shorter, each patient's annual treatment expenditures would be higher in the PCT group. This assumption has been supported by Peng et al. (2019) who suggested that 73,665 euros as opposed to 70,961 euros in comparison of both diagnostic tools. CRP use generally has a moderate effect on overall health care expenses.

ICU anti biotic exposure

In the intensive care unit, serious infections and sepsis patient prescribed with both PCT-and CRPs as a primary component of antibiotic therapy. The Schuetz et al. (2018) research, which examined patients with suspected bacterial infections (73% of whom had a respiratory tract infection), including seven intensive care units given CRP instead of PCT. It has been suggested by the both are important in treating intensive care patient in which one diagnostic tool was used to start antibiotic medication, while another one was used to continue antibiotic therapy. PCT reduction 80% of peak or PCT 0.5 g/L were required conditions for stopping an antibiotic. The majority of the differences occurred at study entrance when patients got antibiotics despite a PCT 0.5 g/L, and algorithm compliance was lower than for samples. However, there were safety concerns since the odds ratio for 60-day mortality in the PCT group 1.09 (0.79-1.51), which was somewhat higher than CRP statistically. Another investigationVijayan et al. (2017) was carried out in a clinic with a low level of antibiotic use. In contrast to conventional therapy, which required 7 days of antibiotic administration, the PCT-guided strategy required only 5 days. Additionally, compared to the conventional care group (25% at 28 days and 40.9% in treatment), mortality in the PCT-led group was significantly lower (p0.05) at 28 days (19.6%) and 1 year (34.8%).However, a placebo-controlled research of sodium selenite and procalcitonin-controlled antibiotic therapy in severe sepsis found no evidence that this approach improved 28-day mortality in patients with severe sepsis.

COVID and diagnostic tools

Patients with mild COVID-19 rarely experience bacterial co-infections (Gutierrez-Pizarraya et al., 2022). However, given that risk factors for nosocomial infections, such as extended mechanical ventilation, are key aspects of critical illness, a considerable fraction of critically sick hospital patients develop secondary bacterial infections. The most frequent secondary bacterial infection is bacterial pneumonia, particularly respiratory tract pneumonia, but patients with severe COVID-19 are also at risk for bloodstream and urinary tract infections.

Contrarily, many COVID-19 patients do not have secondary bacterial infections and do not

require antibiotic therapy. Despite the low prevalence of bacterial infections, 58 percent of patients in 552 hospitals across 30 Chinese regions received antibiotic treatment.

Generally in intensive care patients with confirmed influenza A(H1N1) pdm09, lower PCT levels have a 94% negative predictive value for bacterial infection (Hamade and Huang 2020) . Several COVID-19 biomarker investigations have been carried out on hospitalized patients. According to early findings from China, the majority of COVID-19 patients do not have increased PCT values (> 0.5 g/L). Elevated readings were, however, more frequently seen in severe instances and in individuals who had passed away. The findings demonstrate that individuals with secondary bacterial infection are more likely than those without signs of bacterial infection to experience a poor clinical outcome. Although there is also an increase in CRP and PCT in a systemic response to COVID-19. In terms of antibiotic therapy, patients with low PCT can definitely start empiric antibiotic therapy. In patients with bacterial infections, CRP levels were likewise significantly higher. Thus, PCT measures performed on COVID-19 patients while they are hospitalized and waiting could aid in the detection of subsequent bacterial infections and more precise administration of antibiotics. The threshold for PCR's ability to diagnose secondary bacterial infections is very high. Prospective studies are required to rigorously track clinical and microbiological superinfecting, as well as antibiotic resistance, as the COVID-19 pandemic develops.

II. CONCLUSION

In this investigation of sepsis patients in the intensive care unit, it has been discovered that CRP is not more effective than the PCT-based diagnostic tool. The length of antibiotic medication is indicated by the serum CRP level is lengthy in comparison of PCT. A number of studies have recently sought to determine the objective criteria for the start and end of antibiotic therapy which we have also discussed in this paper. Regarding the administration of antibiotics based on PCT levels, it doesn't seem to put the patient at more danger and almost likely limits their exposure to these medications. CRP has been utilized in clinical settings for a long time and considered as anti-inflammatory marker. Unlike PCT, which is readily available but expensive ($39 for PCT each test from our service vs. $1 for CRP) numerous studies have demonstrated that there are fewer people who are affected by major infectious diseases. It has been discovered that the length of treatment in patients with severe sepsis or sepsis was brief in both groups, in addition to the lack of improvement of CRP in early stages of infection compared to PCT after antibiotic therapy (6-7 days on average). This is somewhat explained by researchers and practitioners published paper's protocol's usage of the conventional 7-day time span. The median length of antibiotic treatment in patients was shorter than in the control group in other trials comparing CRP guided protocols with conventional therapy.

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