BENEFITS OF THE PROCALCITONIN AS A DIAGNOSTIC BIOMARKER OVER C-REACTIVE PROTEIN

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Abstract:
Both procalcitonin (PCT) and C-reactive protein (CRP) are biomarkers that are frequently utilized; however, the diagnostic benefits of each of these biomarkers vary. Despite the progress that has been made in critical care medicine, intensive care units (ICUs) continue to face the problem of identifying sepsis at an early stage and providing adequate treatment for it. In this regard, PCT, which is a revolutionary laboratory marker, has lately been demonstrated to be rather beneficial all over the world. PCT is proven to be superior to CRP in terms of accuracy in detection and in assessing the severity of sepsis. This is despite the fact that both markers are unable to differentiate between infectious and noninfectious clinical syndromes.

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Introduction:

D-dimers in the diagnosis of pulmonary embolism, natriuretic peptides in the diagnosis of acute heart failure, and troponin in the diagnosis of myocardial infarction are just a few examples of diagnostic biomarkers that have been successfully utilized in these various areas of medicine. Nevertheless, finding a timely diagnosis of bacterial infections continues to be a difficult task [1]. Mainly, there is a shortage of reliable clinical and/or microbiological parameters from specimens that are simple to obtain. These parameters have the potential to be utilized in the diagnosis of bacterial infections and in the elimination of other illnesses. Many of the current microbiological methods have a number of drawbacks, the most significant of which are diagnostic delays, such as those that occur with culture methods, suboptimal sensitivity for samples such as blood cultures, and low specificity due to contamination in samples such as sputum cultures. Other methods, such as lung biopsies, are not amenable to routine diagnostics because of their invasive nature. Further, inflammatory indicators, such as C-reactive protein (CRP) and white blood cells (WBC), do not have the ability to differentiate between bacterial infections and other types of infections [2].

There have been recent developments in biotechnology and the sequencing of the human genome that have presented us with chances that have never been seen before to improve our understanding of critical sickness and damage [3]. The discovery of infections at an early stage is considered to be of physiologic and clinical significance. When a potentially harmful process is discovered at an earlier stage, it is possible to undertake further preventative actions (i.e., the removal of a stimulus for injury) and possibly curative treatments at a more opportune and appropriate moment [4].

As a result of the fact that larger amounts of procalcitonin (PCT) are seen in severe bacterial infections in comparison to viral infections and nonspecific inflammatory disorders, procalcitonin has emerged as a promising marker for the detection of bacterial infections. As a result, PCT can be utilized to provide support for clinical judgments for the beginning or ending of antibiotic therapy. In the clinical setting, the utility of serum PCT levels is continuously developing [5]. Patients who have systemic infections are considered to be candidates for PCT, which is considered to be a viable candidate marker for making a diagnosis and for antibiotic stewardship [5].

PCT should be incorporated into clinical algorithms that are tailored to the specific type of infection as well as the clinical context and setting. This is vitally important, just as it is with any other diagnostic tool. Although ideal PCT level cutoffs have been established for certain types of infections and clinical situations, and their safety and efficacy have been demonstrated in randomized-controlled intervention trials, observational studies are the only ones that are available for other types of infections. In light of this, the clinical value and safety of utilizing PCT are still not fully understood [6].

Cell-reactive protein (CRP) is a cyclic homopentameric protein that has a role in the acute-phase reaction that occurs in sepsis. It binds phosphorylcholine, which is a component of teichoic acids in organisms that are gram-positive, and lipopolysaccharides, which are found in species that are gram-negative. Lysophosphatidylcholine, ribonucleoproteins, chromatin, and histones are all exposed in apoptotic cells, and CRP has the ability to bind all of these substances there. In order to activate the classical complement pathway and promote phagocytosis, it exerts its influence via interacting with the complement component C1q and the crystallizable anti-body fragment (Fc) receptors Fc-γRI and Fc-γRII [7]. Despite the fact that CRP expression has been observed in neurons, monocytes, lymphocytes, and atherosclerotic plaques, the liver is the primary organ in which it is demonstrated. TNF-α, interleukin (IL)-6, and IL-1β are the factors that stimulate the generation of CRP. 4–6 hours after stimulation, protein production commences, and it reaches its peak between 36 and 48 hours later, with a half-life of around 19 hours [8].

Review:

Resistance to antimicrobial agents has emerged as a significant concern that influences the results for patients and the overall resources available. Because of this, there is a need for more strict efforts to reduce the overuse of antibiotics. When PCT is used to guide diagnostic and therapeutic decisions in patients with infections in medical practice, there are two important issues that need to be considered in order to optimize diagnostic accuracy and patient safety. These issues are the functional assay sensitivity and cutoff ranges. There have been a variety of cutoffs reported. Similar clinical algorithms were utilized in all of the published research on antibiotic stewardship. These algorithms included recommendations for and against antibiotic treatment depending on PCT cutoff values employed in the trials. One of four antibiotic recommendations was defined by the algorithms. These recommendations ranged from "strongly discourage" and "discourage" to "recommend" and "highly recommend,"

respectively. The probability of a bacterial infection was taken into consideration when determining the PCT cutoff values, which were calculated from multilevel-likelihood ratio estimates collected from observational research. When the level of PCT drops to a level that is less than or equal to 0.1 ng/mL in the intensive care unit at our institution, it is considered to be an indication that the bacterial invasion has been fully eradicated and that it is safe to terminate antibiotic medication [9]. This method, as opposed to an arbitrary one-size-fits-all duration of therapy, has been successfully implemented by a number of research. Every single study that has been conducted up until this point in time on patients who have been diagnosed with sepsis or pneumonia has shown that the duration of antibacterial treatment can be significantly reduced when it is guided by sequential PCT levels [10].

PCT, which is the precursor of the hormone calcitonin, has been utilized as a biomarker to assist in the detection of bacterial infections or sepsis. Additionally, it has been utilized to differentiate bacterial pneumonia from viral pneumonia and chronic obstructive pulmonary disease (COPD). The clinical criteria for diagnosing sepsis overlap with those for diagnosing other sources of systemic inflammation that are not infectious. This makes the diagnosis of sepsis particularly difficult. In contrast, a delay in diagnosis can result in morbidity and mortality due to sepsis, while an early diagnosis enables therapeutic measures to be implemented in a timely manner. On the other hand, the growth of antibiotic resistance calls for a more strict effort to reduce the excessive use of antibiotics. In the case of acute respiratory tract infections, antibiotics are frequently administered, despite the fact that the vast majority of infections are caused by viruses rather than bacteria. This is especially true in cases where the infection is severe. There is an increasing body of evidence supporting the utilization of PCT-guided antibiotic therapy, which can be utilized for both the beginning and the ending of antibiotic treatment. As a component of the antibiotic stewardship program, clinical algorithms that have certain PCT cut-offs are utilized in a variety of clinical settings and patient types. Randomized controlled trials (RCT) have established the safety and efficacy of PCT guided antibiotic therapy in adults with respiratory tract infections and in critically sick patients. These randomized controlled studies provide the most compelling evidence for the use of PCT in therapeutic settings. When it comes to other kinds of infections, the evidence that supports the utilization of PCT measurement is restricted to observational studies, and the safety and benefits of this method are still not definitively established [11,12].

According to the findings of a meta-analysis of newborn sepsis prediction models conducted in 2015, medical professionals are not accurate when it comes to forecasting neonatal sepsis. Specifically, the range of specificity for the prediction models was between 18 and 73%, whereas the range of sensitivity was between 56 and 98%. Lethargy, pallor, and hypothermia, which are all clinical signs that are not particularly specific, had the greatest odds ratios related with sepsis [13]. When it comes to diagnosing neonatal sepsis, blood cultures are considered to be the gold standard. However, the positivity rate is low, and the results may be impacted by factors such as insufficient blood volumes, low-colony count bacteremia, prenatal antibiotic use, or pretreatment with antibiotics prior to the culture being obtained [14]. It is possible for up to sixty percent of blood cultures to provide a false negative result in conditions of low-colony count bacteremia. Given these considerations, the utilization of antibiotics for the purpose of ruling out sepsis episodes and culture-negative sepsis is ten to fifteen times higher than the utilization of antibiotics for culture-proven sepsis [14].

Biomarkers for the diagnosis of newborn sepsis have been advocated for decades, particularly to assist in excluding the possibility of infection and to prevent the administration of antibiotics [12]. With the use of biomarkers, it is possible to reduce the amount of antibiotics that are administered to patients who are suspected of having sepsis [13, 14]. This is despite the fact that the use of biomarkers can result in more blood sample, longer monitoring, and an increased length of hospital stay. In order to avoid missing even a single incidence of neonatal sepsis, an ideal marker would have a sensitivity that is nearly flawless, while also having a high specificity that would prevent false-positive tests that would result in unnecessary antibiotic exposure. C-reactive protein, also known as CRP, is the biomarker that receives the greatest attention in the neonatal intensive care unit for this particular purpose. On the other hand, an increasing number of research [15] support the use of procalcitonin (PCT) as a marker that is both more sensitive and specific in both youth and adult populations.

PCT was proven to be a valuable marker in the identification of a septic process, with a sensitivity of 78% and a specificity of 94% when compared with CRP [16]. This, in relation to the diagnostic performance of PCT, was discovered by a number of worldwide literatures. These studies implement a methodology that is more specific in its approach

to the objectives that are intended, and the sample size is significantly larger, which results in a statistical significance that is significantly higher. The PCT demonstrated the highest degree of accuracy (75.34%) in this investigation, along with a larger level of specificity (72.2%), positive and negative predictive values, a positive likelihood ratio, and a smaller negative likelihood ratio. On the other hand, it was discovered that the sensitivity of CRP in the diagnosis of sepsis was higher (85.45%) than that of PCT (76.36%). It is customary to assume that there have been significant shifts in the prior disease probability when the PLR is greater than 10.0 and the NLR is less than 0.1. When compared to CRP and complement proteins, procalcitonin showed a higher PLR and a lower NLR [17]. There have been a few studies that have revealed that PCT has a weaker diagnostic performance than CRP when it comes to distinguishing between sepsis and SIRS. In contrast to this, the majority of research have found that procalcitonin is a better marker to predict the severity of sepsis, as well as the prognosis or the subsequent course of the disease [17].

Conclusion:

PCT is by far the most widely assessed of the several sepsis and infection markers that have been proposed among the numerous markers that have been proposed. It is possible that this marker will assist medical professionals in making an earlier diagnosis, distinguishing infectious from sterile causes of severe systemic inflammation, and performing an assessment of the severity of systemic inflammation that is caused by bacterial infections. PCT is a topic that has a great deal more to teach us. The utilization of PCT, just like any other biomarker, need to be taken into consideration within the framework of the clinical workup. More specifically, it ought to take into account all the patient-related and therapy-related aspects that have the potential to interfere with the initial magnitude and course of this parameter. The clinical course, management, and outcome of critically sick patients who are being treated in intensive care units (ICUs) are all significantly influenced by the speed with which infections are identified. According to the findings of this investigation, both PCT and CRP demonstrated a limited diagnostic utility in critical patients when it came to determining potential infectious causes. However, when it comes to determining the clinical severity of a condition, procalcitonin is superior to C-reactive protein. It is recommended that procalcitonin be incorporated into diagnostic standards for sepsis as well as integrated into clinical practice in intensive care units across the United States.

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