

Procalcitonin in Diagnosis of Post-Operative Bacterial Meningitis: A Promising but Limited Role

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Procalcitonin (PCT) levels increase in inflammatory states following infection, tumor, burn, trauma, or surgery [1]. Many clinical studies have found that PCT levels significantly increase in patients with bacterial or fungal infection [2, 3]. Conversely, in cases of viral infection or inflammation caused by autoimmune diseases, PCT levels do not increase. Indicators related to existing inflammation, such as C-reactive protein (CRP) and white blood cell count, do not specifically respond to bacterial infection [4]. However, PCT could be a useful tool for diagnosis of sepsis since it has shown high specificity in the diagnosis and expectation of prognosis of bacterial infections in numerous studies [5].

PCT production is stimulated by the actions of interleukin (IL)-1 β , tumor necrosis factor- α , and IL-6, which are secreted according to the extent of bacterial infection, but is attenuated by interferon- γ , which is produced during viral infection. In addition, PCT levels increase within 6–12 hours in the presence of a stimulus, and fall to approximately half of the initial concentration within a day of the infection with improvement [6].

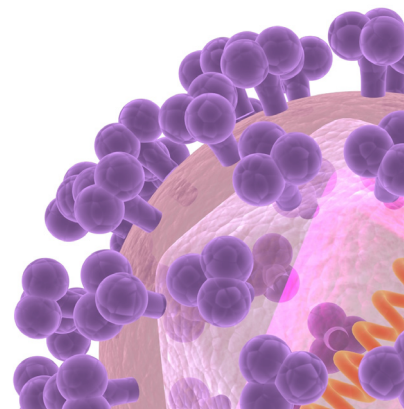
Choi et al. [7] investigated the use of PCT as a biomarker for the discrimination of non-bacterial meningitis from bacterial meningitis after brain surgery. In their study, neither type of meningitis was distinguishable by analysis of PCT alone. Many studies have investigated the utility of PCT for the differential diagnosis of bacterial meningitis and viral meningitis; such research has been prompted by the fact that PCT levels significantly increase in most cases of bacterial meningitis [8], probably due to the pathogenesis of bacterial meningitis differing from that of viral meningitis. Bacterial meningitis arises from nasopharyngeal colonization by invasive bacteria and associated bacteremia, and subsequent bacterial penetration of the blood-brain barrier. Therefore, community-acquired bacterial meningitis can cause systemic infection, which explains the increase in PCT levels in bacterial meningitis. In contrast, a study in patients with ventricle-peritoneal shunt infection, a non-systemic infection, did not show increased levels of PCT; this result was due to the fact that, in the absence of systemic infection, bacteria entered the meninges directly through the wound. Another reason for the inability

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ty of PCT to differentiate between bacterial and non-bacterial meningitis after brain surgery and trauma is due to the fact that surgery itself kills the cells that stimulate PCT production. As a result, the difference in PCT level between surgical patients and patients with post-operative bacterial meningitis may be negligible, due to the false-positive elevation in PCT levels after surgery.

There have been many observational studies and randomized controlled studies on the usefulness of PCT as a diagnostic tool. In a study of patients with coagulase-negative *Staphylococcus* bacteremia, PCT level was able to discriminate true bacteremia from contamination at a PCT cut-off level of 0.1 µg/L with a sensitivity of 100% and a specificity of 80% [9]. In studies of intra-abdominal infection, PCT was evaluated in patients with fever to determine its usefulness in differentiating infection from rejection after liver transplantation. In those studies, PCT was a useful diagnostic tool because PCT levels were elevated to 2.2 µg/L or higher in patients with post-operative infection, while levels were not increased in patients with graft rejection. However, graft rejection after anti-thymoglobulin injection stimulated the synthesis of PCT, leading to false-positive cases [10]. In addition, in a study of patients with neutropenic fever, PCT was a meaningful marker in the differential diagnosis and prognosis of infection.

Randomized clinical studies on the use of PCT as a guide for antibiotic treatment have shown that PCT can assist when making decisions about when to start and stop antibiotics; this information is also useful in terms of antibiotic stewardship. The risk of respiratory infection in the emergency room was evaluated according to PCT level (cut-offs at < 0.1, 0.1 to 0.25, 0.25 to 0.5, and > 0.5 µg/L), and levels were able to guide the initiation and termination of antibiotic therapy [3]. Using a PCT algorithm, it was found that low-risk patients with systemic infection or chronic obstructive pulmonary disease and patients with acute exacerbation could have their antibiotics suspended if they had a low PCT level. When a PCT algorithm was applied for intensive care unit patients with sepsis to estimate the severity of infection (patients were categorized into groups with PCT values < 0.25, 0.25–0.5, 0.5–1, and >1 µg/L), it was found that antibiotic therapy could safely be stopped in those whose PCT levels became normal or fell to by at least 80–90% [3, 5]. In an intervention study (the first of its type) that used PCT level as a guide for treatment in patients with different types and severities of respiratory infection, the group that was provided with PCT level guidance re-

ceived shorter durations and reduced dosages of antibiotics [5]. In studies of respiratory infections that tended to be associated with excessive antibiotic prescriptions in the primary care setting, antibiotic use was reduced in both the PCT-guided group and the controls, and the clinical outcomes were similar [4].

With the emergence of multidrug-resistant bacteria due to increased long-term use of antibiotics, PCT is being investigated for its usefulness in reducing unnecessary antibiotic use. PCT levels can discriminate bacterial infection from non-bacterial inflammation in systemic infection. Further research on PCT-guided diagnosis is required to allow better differentiation between infection and inflammation after surgery, especially in critically ill patients.

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