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Review Article

PROCALCITONIN AS A DIAGNOSTIC TEST FOR SEPSIS: A MINI REVIEW

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ABSTRACT

Sepsis is the systemic response to infection by microbial organisms. A differential diagnosis of infection caused by either bacteria or other microbial organisms is essential for effective treatment and prognostic assessment. Current clinical laboratory methods in the diagnosis of bacterial infections are either non-specific or require longer turnaround times. Procalcitonin (PCT) is a biomarker that exhibits greater specificity than other proinflammatory markers (eg, cytokines) in identifying patients with sepsis and can be used in the diagnosis of bacterial infections. In this article, we review the current knowledge of PCT and its use in the clinical laboratory setting**.** Procalcitonin is a promising marker for identification of bacterial infections. We assessed the accuracy and clinical value of procalcitonin for diagnosis of sepsis in critically ill patients.

Keywords: Procalcitonin, Biomarker, Sepsis.

INTRODUCTION

Procalcitonin (PCT) is a peptide precursor of the hormone calcitonin, the latter being involved with calcium homeostasis. It is composed of 116 amino acids and is produced by parafollicular cells (C cells) of the thyroid and by the neuroendocrine cells of the lung and the intestine.

The level of procalcitonin in the blood stream of healthy individuals is below the limit of detection (10 pg/mL) of clinical assays[1]. The level of procalcitonin rises in a response to a proinflammatory stimulus, especially of bacterial origin. In this case, it is produced mainly by the cells of the lung and the intestine. It does not rise significantly with viral or non-infectious inflammations. With the derangements that a severe infection with an associated systemic response brings, the blood levels of procalcitonin may rise to 100 µg/L. In serum, procalcitonin has a half-life of 25 to 30 hours. Remarkably the high procalcitonin levels produced during infections are not followed by a parallel increase in calcitonin or a decrease in serum calcium levels.

Diagnosis and prognosis of sepsis

Measurement of procalcitonin can be used as a marker of severe sepsis caused by bacteria and generally grades well with the degree of sepsis[2], although levels of procalcitonin in the blood are very low. PCT has the greatest sensitivity (85%) and specificity (91%) for differentiating patients with systemic inflammatory response syndrome (SIRS) from those with sepsis, when compared with IL-2, IL-6, IL-8, CRP and TNF-alpha[3]. Evidence is emerging that procalcitonin levels can reduce unnecessary antibiotic prescribing to people with lower respiratory tract infections[4]. Currently, procalcitonin assays are widely used in the clinical environment[5].

Diagnosis of bacteremia

A meta-analysis reported a sensitivity of 76% and specificity of 70%[6]. Diagnosis of bacteremia and septicemia in adults and children (including neonates). Diagnosis of renal involvement in urinary tract infection in children. Diagnosis of bacterial infection in neutropenic patients. Diagnosis, risk stratification, and monitoring of septic shock. Diagnosis of systemic secondary infection post-surgery, and in severe trauma, burns, and multiorgan failure. Differential diagnosis of bacterial versus viral meningitis. Differential diagnosis of community-acquired bacterial versus viral pneumonia. Monitoring of therapeutic response to antibacterial therapy.

Prognosis of pneumonia

A cluster randomized trial found that the procalcitonin level can help guide antibiotic therapy. In this trial, "on the basis of serum procalcitonin concentrations, use of antibiotics was more or less discouraged (<0.1 µg/L or <0.25 µg/L) or encouraged (≥ 0.5 µg/L or ≥0.25 µg/L), respectively[7]". However, an earlier nonrandomized, observational study reported "limited, prognostic value" of procalcitonin measurement[8].

Procalcitonin levels may be useful to distinguish bacterial infections from nonbacterial infections. Trials from 2008 and 2009 have shown that they may help guide therapy and reduce antibiotic use, which can help save on cost of antibiotic prescriptions and drug resistance[9,10].

Clinical Information

Procalcitonin (ProCT) is a 116 amino acid precursor of calcitonin (CT). ProCT is processed to an N-terminal 57 amino acid peptide (CT [32 amino acids] and a 21 amino acid C-terminal peptide, catacalcin [CCP-1]). Expression of this group of peptides is normally limited to thyroid C cells and, to a small extent, other neuroendocrine cells. CT is the only hormonally active of these peptides. CT is secreted by C cells in response to hypercalcemia and inhibits bone resorption by osteoclasts, minimizing oscillations in serum calcium and calcium loss.

During severe systemic inflammation, in particular related to bacterial infection, the tissue specific control of CT-related peptides expression breaks down and ProCT and CCP-1 (referred collectively to as ProCT) are secreted in large quantities by many tissues. CT levels do not change.

Noninfectious inflammatory stimuli need to be extremely severe to result in ProCT elevations, making it a more specific marker for severe infections than most other inflammatory markers (cytokines, interleukins, and acute-phase reactants). ProCT elevations are also more sustained than those of most other markers and occur in neutropenic patients. This reduces the risk of false-negative results.

ProCT becomes detectable within 2 to 4 hours after a triggering event and peaks by 12 to 24 hours. ProCT secretion parallels closely the severity of the inflammatory insult, with higher levels associated with more severe disease and declining levels with resolution of illness. In the absence of an ongoing stimulus, ProCT is eliminated with a half-life of 24 to 35 hours, making it suitable for serial monitoring. Finally, the dependence of sustained ProCT elevations on ongoing inflammatory stimuli allows identification of secondary septic events in conditions that can result in noninfectious ProCT elevations, such as cardiac surgery, severe trauma, severe burns, and multiorgan failure. ProCT levels should fall at a predictable pace in the absence of secondary infection.

Reference Values

Adults and children > or =72 hours: < or =0.15 ng/mL

Children < 72 hours: <2.0 ng/mL at birth, rises to < or =20 ng/mL at 18-30 hours of age, then falls to < or =0.15 ng/mL by 72 hours of age.

CONCLUSION

Procalcitonin is a helpful biomarker for early diagnosis of sepsis in critically ill patients.

Nevertheless, the results of the test must be interpreted carefully in the context of medical history, physical examination, and microbiological assessment.

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