Procalcitonin for Detection of Systemic Inflammation

Background Information

Procalcitonin (PCT) is the prohormone of calcitonin. In the normal state procalcitonin is synthesized primarily in the C cells of the thyroid gland, where it undergoes intracellular cleavage to produce calcitonin. As a result, circulating levels of PCT are very low or undetectable in healthy donors. However, in response to severe systemic inflammation such as seen with severe bacterial infection, PCT is expressed in numerous tissues throughout the body, resulting in increased levels of circulating PCT. Unlike many inflammatory molecules, PCT is relatively stable in blood, with a half-life of 24-36 hours, which allows it to serve as a useful monitor for the presence and resolution of systemic inflammation.

Clinical Indications

The majority of published uses for PCT have focused on its role as an aid in the diagnosis and monitoring of a variety of serious infectious diseases, including severe bacterial sepsis, septic shock and pneumonia. A large body of literature has focused on the use of PCT in the ICU setting, and the intended use in the FDA clearance of the current assay is "in conjunction with other laboratory findings and clinical assessments in the risk assessment of critically ill patients on their first day of ICU admission for progression to severe sepsis and septic shock."[1]

PCT's diagnostic potential also has been evaluated in many other clinical situations, including emergency department admissions, neonatal sepsis, pneumonia, FUO in neutropenic patients and rheumatologic diseases. Results from these studies have been variable, with PCT's sensitivity and specificity as a diagnostic marker varying widely depending on the specific characteristics of the study population.[2]

In contrast to the use of PCT for diagnosis of sepsis, an emerging area of interest has focused on the use of PCT to monitor response to antibiotic therapy. Because of PCT's relatively short half-life in blood, levels will drop in a matter of days once the underlying infectious stimulus has been removed. Various groups have looked at the use of algorithms based on changes in PCT levels to titrate the duration of antibiotic treatment in septic patients as well as in patients with respiratory infections.[3-5] While initial results in this area have been promising, further work is needed to determine how best to integrate PCT measurements into routine clinical practice.

Interpretation

Reference range: < 0.07 ng/mL.

Based on studies in ICU patients, procalcitonin levels > 2.00 ng/mL at time of ICU admission represent an elevated risk of progression to severe sepsis and/or septic shock; levels < 0.50 ng/mL represent a lower risk of severe sepsis and/or septic shock.

Levels < 0.50 ng/mL do not exclude infection as early stage (< 6 hrs) localized infections or systemic infections can be associated with low concentrations.

Levels 0.50 - 2.00 ng/mL should be interpreted in the clinical context of the patient as a variety of non-infectious conditions such as burns, trauma, surgery and severe cardiogenic shock can cause procalcitonin elevations.[1]

Limitations of the Assay

Serious, non-infectious stresses such as trauma, burns or surgery can lead to a rise in PCT in the absence of sepsis.

Patients with medullary carcinoma of the thyroid may show increased PCT levels in the absence of sepsis.

PCT may not be elevated in patients with localized infection, or in samples taken shortly (< 6 hrs) after initial infection.

Methodology

Procalcitonin is measured using the Vidas® PCT assay (bioMérieux, Durham, NC), a one-step immunoassay sandwich method with fluorescent detection. Patient sample is dispensed into wells containing anti-PCT antibodies labeled with alkaline phosphatase. This mixture is cycled in and out of a solid-phase receptacle (SPR) several times, allowing the antigen to bind with immunoglobulins fixed to the wall of

the SPR to form a sandwich. Detection is accomplished by cycling a fluorescent substrate for alkaline phosphatase (4-MUP) in and out of the SPR and measuring the amount of fluorescence produced. The intensity of fluorescence is proportional to the concentration of PCT present in the sample.

References

1. VIDAS BRAHMS PCT package insert. 30-450-01.
2. Tang BMP *et al*. *Lancet*. 2007;7:210-17.
3. Bouadma L, Luyt CE, Tubach F *et al*. Use of procalcitonin to reduce patients' exposure to antibiotics in intensive care units (PRORATA trial): a multicentre randomised controlled trial. *Lancet*. 2010;375:463-474.
4. Kopterides P, Siempos II, Tsangaris I, Tsantes A, Armaganidis A. Procalcitonin-guided algorithms of antibiotic therapy in the intensive care unit: A systematic review and meta-analysis of randomized controlled trials. *Crit Care Med.* 2010, Aug 19.
5. Schuetz P, Christ-Crain M, Thomann R, Falconnier C, Wolbers M, Widmer I, Neidert S, Fricker T, Blum C, Schild U, Regez K, Schoenenberger R, Henzen C, Bregenzer T, Hoess C, Krause M, Bucher HC, Zimmerli W, Mueller B; ProHOSP Study Group. Effect of procalcitonin-based guidelines vs standard guidelines on antibiotic use in lower respiratory tract infections: the ProHOSP randomized controlled trial. *JAMA*. 2009, Sep 9;302(10):1059-66.

Test Overview

Test Name	Procalcitonin
Reference Range	procalcitonin < or = 0.07 ng/mL
Specimen Requirements	1 mL serum; Tube/container: Gold, no additive SST
Minimum Specimen Requirements	0.5 mL
Special Notes	Refrigerate for transport; freeze if sample will not be received within 48 hours
Ordering Mnemonic	PROCAL
Billing Code	84522
CPT Code	84145

Technical Information Contact:

Cathy Means, MT (ASCP)
216.444.9033
meansc@ccf.org

Scientific Information Contact:

Belinda Yen-Lieberman, PhD
216.444.8844
yenb@ccf.org