Procalcitonin Testing – Clinician Handout

SYNOPSIS AND RELEVANCE

Procalcitonin (PCT) is a biomarker associated with serious bacterial infections that may be used in conjunction with other laboratory data and clinical assessment to predominantly guide the early discontinuation of antibiotic therapy in the appropriate setting. Due to limited sensitivity and specificity, treatment decisions should not be made on the basis of PCT alone. This module will:

1. Educate healthcare providers about the appropriate use of procalcitonin with respect to institution-specific guidelines.
2. Educate providers to assess compliance with institution-specific guidelines.
3. Describe the consequences of overutilization and underutilization of procalcitonin with respect to use of antibiotics.

BACKGROUND

Procalcitonin is a 14.5 kilodalton (kDa) protein, derived normally from pre-procalcitonin produced in the C-cells of the thyroid, and ultimately converted to the calcium-regulating hormone calcitonin. Normally, levels of procalcitonin are very low, at <0.1 ng/mL. However, following bacterial infection and sepsis, levels rise rapidly, within 3-4 hours, generally in correlation with the degree of infection. Procalcitonin levels remain elevated until resolution of disease, with a half-life of approximately 24 hours.[1] In comparison with C-reactive protein (CRP), procalcitonin takes less time to rise and to peak, and is more specific for bacterial-based infections.

Procalcitonin was first recognized in 1993 as a marker of bacterial infection,[2] and has very high negative predictive values at very low levels. Since then, numerous studies have investigated the use of procalcitonin in various diseases, although most randomized controlled trials have focused on respiratory tract infections, sepsis, and post-operative infections, whereas other disease conditions have generally been relegated to observational studies only.[1,3-10] Early diagnosis and treatment of such conditions as sepsis and respiratory tract infections leads to decreased morbidity and mortality.[1] Proper use of antibiotics reduces the likelihood that new bacterial drug resistance will emerge and may avoid drug-related adverse events in patients.[11] However, early diagnosis of bacterial infection can be challenging due to current limitations of laboratory-based testing.

Although procalcitonin is a useful aid, numerous studies have shown that it, like many biomarkers, is not entirely sensitive or specific, and should never be used solely in the decision to start or stop antibiotics, but instead must be used carefully in the context of clinical history, physical exam, and other diagnostic studies.[1,9,12] As such, procalcitonin usage and subsequent decision making must be incorporated into established institution-specific clinical algorithms that differ based on patient population, disease context, and physical setting.[9,12] The current Food and Drug Administration (FDA) indications for use of procalcitonin include using it as an aid in the risk assessment of critically ill patients on their first day of intensive care unit (ICU) admission for progression to severe sepsis/septic shock, as an aid in assessing the 28 day risk of mortality for patients with severe sepsis/shock in the ICU, as an aid in decision making for starting/stopping antibiotics in patients with lower respiratory tract infections, and as an aid in decision making for discontinuing antibiotics in patients with confirmed or suspected sepsis.[1]

There is a fair amount of evidence for procalcitonin's use in antibiotic stewardship for patients with suspected or confirmed respiratory tract infections,[4-6,13,14] as well as for discontinuation of antibiotics in the setting of bacterial infection and sepsis.[3,7,8,13,15,18] Most such approaches, as studied in randomized controlled trials, utilize four different cutoff ranges as shown in the appendix, with these cutoff ranges generally ranging from 0.1 to 0.5 ng/mL.[3-5,8] Such approaches have been shown, in general, to mildly reduce the use of antibiotics in these patient populations without worsening clinical outcome.[2,3,6,8] Additionally, these different algorithms suggest serial testing at various time intervals after the initial procalcitonin value, to further guide antibiotic management.[3,5,6,8,14] Time intervals vary, but based on the half-life of procalcitonin, repeat testing should generally be limited to a time interval not less than every 24-48 hours after antibiotic administration, with consideration of stopping antibiotics, in the appropriate clinical situation, at

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certain low levels of procalcitonin (such as <0.5 ng/mL) or at a defined decrease from the initial procalcitonin level (such as <80% of the initial level).[16,17]

Procalcitonin continues to be studied, and further work will undoubtedly help define and refine further indications for the use of procalcitonin. To date, procalcitonin has been studied in only a limited manner in children and pregnant women, although some clinical uses appear valid.[1,18]Additionally, procalcitonin values can be elevated naturally in the setting of other conditions, such as trauma, burns, chronic kidney disease, carcinomas, shock, and cirrhosis, and therefore procalcitonin values must be interpreted carefully in the setting of patient history.[16,19]

Current assays for procalcitonin are based on immunoassay methodologies, and procalcitonin can now be measured on numerous different analyzers, with a lower limit of quantification that can range to well below 0.05 ng/mL.[1] Additionally, procalcitonin assays have a fast analytical turnaround time, such that in-house results can be available to providers within an hour of collection, depending on the laboratory's workflow.

INSIGHTS

1. Procalcitonin may be used in conjunction with other laboratory data and clinical assessments to manage patients with a suspected infection given its general availability in hospital labs, relatively fast turnaround time, and high negative predictive value.
2. Procalcitonin may be used as an aid in the risk assessment and antibiotic decision making of certain adult patient populations, including those with sepsis, but should not be used alone.
3. Procalcitonin usage and interpretation must be incorporated into institution-specific clinical algorithms.

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