

Procalcitonin algorithm for guidance in antibiotic therapy decisions in respiratory tract infections and sepsis

1) OVERVIEW: Procalcitonin (PCT) has been evaluated as a biomarker to assist the clinician in the diagnosis and treatment of bacterial infections. It has been studied most thoroughly for lower respiratory tract infections and sepsis.

- It is an amino acid precursor of calcitonin in which under normal circumstances is produced by thyroid C-cells. Serum concentrations are normally < 0.05ng/ml. In circumstances of systemic inflammation, particularly bacterial infections, PCT is produced in large quantities by many body tissues. It is detectable within 2-4 hours and peaks within 6-24 hours. Levels are not elevated in pure viral infections.
- Levels parallel the severity of the inflammatory insult or infection and individuals with more severe diseases have higher levels. Furthermore, PCT has some utility as a prognostic indicator with higher serum concentrations related to risk of mortality.
- Production is not impaired by neutropenia or other immunosuppressive states.
- PCT has some advantages over other biomarkers used in common clinical practice such as C-reactive protein (CRP) and white blood cell (WBC) count. The advantages include: increased specificity for bacterial infections, the rapidity of its rise after an insult, excellent correlation with severity of disease and the rapid decline with control of infection.

PCT monitoring has been shown to decrease antibiotic exposure and antibiotic associated adverse events in respiratory tract infections without worsening of clinical outcomes.

In septic patients, PCT serial monitoring protocols have been shown to reduce antibiotic treatment duration and exposure without harm to patients.

Current literature limits widespread use to assessing antibiotic regimens in pneumonia and sepsis.

2) ROLE IN THERAPY TO ASSIST IN DECISION MAKING:

- Differentiation of bacterial versus viral respiratory tract infection.
- Determination of antibiotic treatment length in respiratory infections and sepsis.
- Monitoring response to anti-infective therapy (source control) in sepsis and bacterial pneumonia.
- Diagnosis, risk stratification and monitoring of sepsis and septic shock.
- May assist in diagnosing bacterial infection in neutropenic patients.
- May assist in diagnosing septic arthritis (vs non septic)
- May assist in differentiating bacterial meningitis and viral meningitis

3) LIMITATIONS OF PCT

PCT MAY BE FALSELY ELEVATED IN THE FOLLOWING CONDITIONS:

- Newborns (<48-72 hours; after 72 hours, interpret levels as usual)
- Massive stress (severe trauma, surgery, cardiac shock, burns): Levels may be elevated for the 1st 3 days post event. In absence of infection, levels trend down after inciting event.
- Treatment with agents that stimulate cytokines (OKT3, anti-lymphocyte globulins, alemtuzumab, IL-2, granulocyte transfusion).
- Malaria and some fungal infections.
- Prolonged, severe cardiogenic shock or organ perfusion abnormalities.
- Acute graft vs. host disease.
- Medullary thyroid tumors and small cell lung CA (paraneoplastic production of PCT).
- ESRD/HD
- Pancreatitis due to sterile necrosis (but can also indicate a secondary bacterial infection).

PCT MAY NOT RISE IN THE FOLLOWING CONDITIONS:

- Localized bacterial diseases (skin abscess, osteomyelitis, etc.)
- Infections caused by organisms that lack a cell wall (Mycoplasma, Chlamydia, etc)

4) CONCLUSION:

PCT CAN BE USED TO ASSIST CLINICIANS IN DIAGNOSING BACTERIAL INFECTIONS AND DETERMINING LENGTH OF ANTIBIOTIC THERAPY BUT ANY DECISION SHOULD NOT BE BASED SOLELY ON LEVELS.

ALWAYS CONSIDER THE PATIENT'S CLINICAL CONDITION AND AN ID CONSULT

***References available on Antimicrobial Stewardship Website**

Antimicrobial Stewardship Committee 9/2016

REFERENCES:

1. Schuetz,P et al. Effect of Procalcitonin Based Guidelines vs Standard Guidelines on Antibiotic use in Lower Resp. Tract Infections. JAMA. 2009; 302; 1059-1066.
2. Schuetz,P et al. Procalcitonin Algorithms for Antibiotic Therapy Decisions. ARCH INTERN MED/VOL 171 (NO.15), AUG 8/22, 2011
3. De Jong,E et al. Efficacy and safety of Procalcitonin guidance in reducing the duration of antibiotic treatment in critically ill patients: a randomized, controlled, open-label trial. LANCET INFECT DIS, 2016 Feb 29. Pii; S1473-3099(16)00053-0
4. Schuetz,P et al. Role of Procalcitonin in managing Adult Patients With Respiratory Tract Infections. CHEST 2012; 141(4):1063-1073
5. Rajender Agarwal and David N. Schwartz. Procalcitonin to Guide Duration of Antimicrobial Therapy in Intensive Care Units: A Systematic Review. CLINICAL INFECTIOUS DISEASES, 2011; 53(4); 379-387
6. PrknoA et al. Procalcitonin-guided therapy in intensive care unit patients with severe sepsis and septic shock. A systematic review and meta-analysis. CRIT. CARE 2013 Dec 11; 17(6):R291.
7. Zsolt,B et al. Can Procalcitonin levels indicate the need for adjunctive therapies in sepsis? International Journal of Antimicrobial Agents 46 (2015) S13-S18.
8. Nicolas Brechot et al. Procalcitonin to guide antibiotic therapy in the ICU. International Journal of Antimicrobial Agents 46(2015) S19-S24
9. Hugle, T et al. Serum Procalcitonin for discrimination between septic and non-septic arthritis. Clin Esp Rheumatol 2008 May-Jun; 26(3): 453-6.

