

Procalcitonin in Sepsis..... indication, implication, procalcitonin guided antibiotic therapy and recent evidences.

DASH Sananta K

Criticalcareindia.com



Frontiers in Intensive care

What is Procalcitonin (PCT)?

Procalcitonin is a 116-plypeptide molecule. It is the precursor of Calcitonin, synthesized by 'C' cells of thyroid gland.

Is Procalcitonin produced normally in human beings? What are the triggers for PCT synthesis?

Procalcitonin is normally produced in human body but in low concentration (<0.1 ng/ml). It's production is regulated by the calcitonin-1 gene (CALC-1). During infection there is also upregulation of CALC-1 gene in non-thyroid tissues resulting in increased concentration of PCT.¹

PCT synthesis is triggered by bacterial endotoxin and cytokines. They prevent the final step of synthesis of Calcitonin (Conversion of PCT to Calcitonin).

What are the functions and uses of PCT?

Physiological functions²

- Pro-inflammatory properties-
 - It increases the expression of surface markers in neutrophil and lymphocytes.
 - It can increase the intracellular calcium concentration similar to pro-inflammatory cytokines.
- Anti-inflammatory properties

Criticalcareindia.com



Frontiers in Intensive care

www.criticalcareindia.com

- In-vitro test revealed PCT can decrease the pro-inflammatory factor TNF- α .
- Modulates expression of inducible nitric oxide synthase (iNOS).

Clinical utilities

1. Sepsis-

- Diagnosis of sepsis- Differentiating non-infectious from infectious etiology. Used predominantly as a biomarker for bacterial sepsis.³
- Prognosis in septic patients- Higher PCT level, more likely to be associated with sepsis related death.⁴
- Assessment of appropriateness of antibiotic therapy- A rapid decline in PCT indirectly confirms appropriate antibiotic therapy.

2. **Community acquired pneumonia (CAP)**- Used in assessment of severity of community acquired pneumonia. It was demonstrated that on admission PCT was a better predictor of CAP severity than both WBC count and CRP, and had a similar prognostic accuracy to CRB-65.⁵

3. **Ventilator associated pneumonia (VAP)**- PCT guided antibiotic therapy in VAP was found to be safe and led to increased antibiotics free days in patients with VAP in ICU.^{6,7}

4. PCT level guided antibiotic therapy-

Demonstrated significant decline in antibiotic usage, decreased ICU expenditure and increased antibiotic free days without significant effect on mortality.⁸

Non-infectious causes of high PCT

Trauma, surgery, burns, hyperthermia, neoplasms, pancreatitis, ischemic bowel disease and pulmonary oedema.⁹

Comparison between PCT and other biomarkers in Sepsis

PCT Vs C-reactive protein (CRP)-

Criticalcareindia.com



Frontiers in Intensive care

www.criticalcareindia.com

PCT is found to be more specific and sensitive than CRP in predicting inflammation due to bacterial etiology from non-bacterial etiology. (Sensitivity for PCT was 85% Vs 78% and specificity 83% Vs 60%).¹⁰

What are the drugs that can cause interference with PCT measurement?^{11,12}

Drugs that affect PCT measurement in all concentrations-

OKT₃ antibodies, mono and polyclonal antibodies, interleukins

Drugs that affect PCT measurement at higher concentrations-

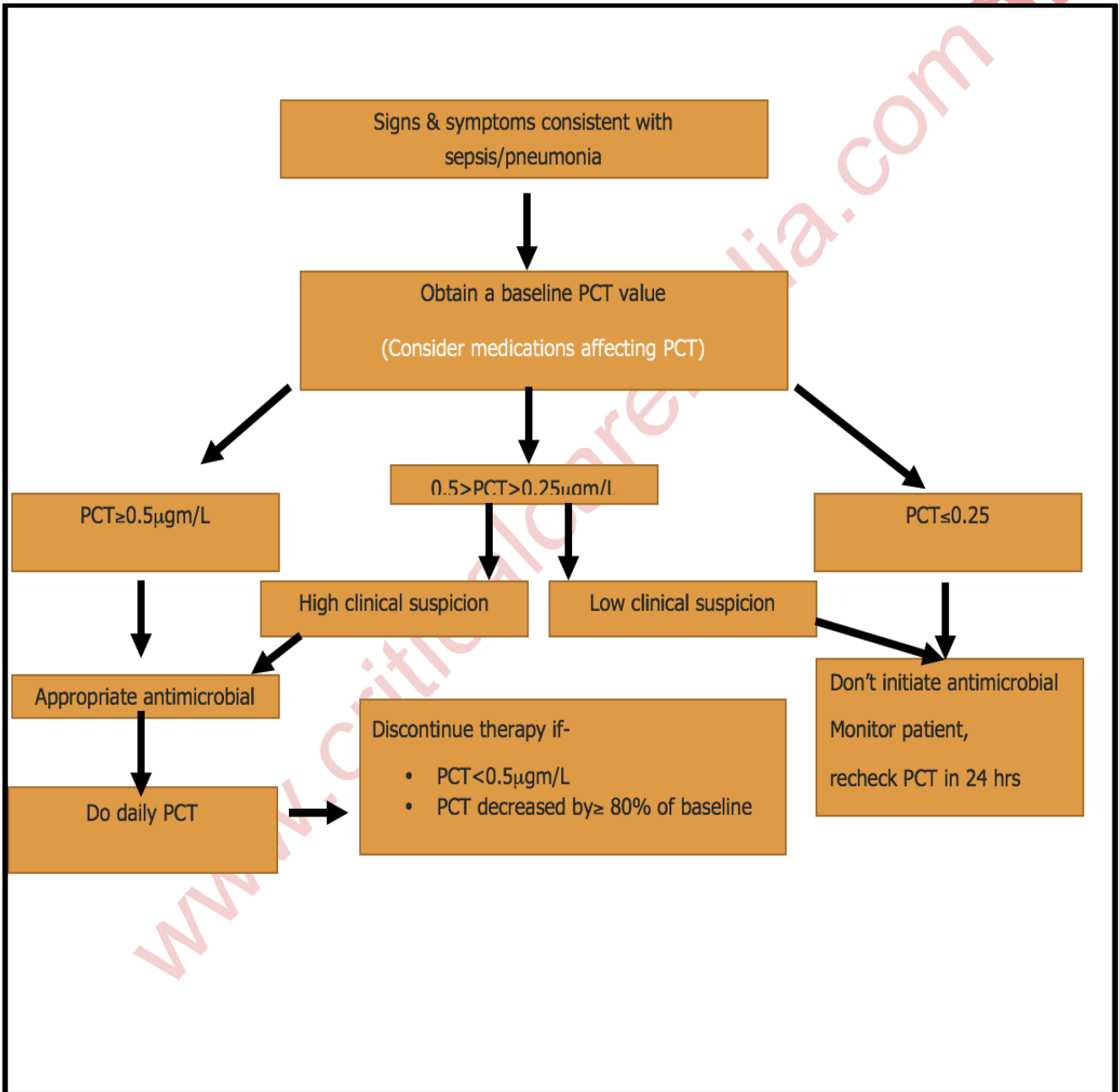
Antibiotics-Imipenem, Cefotaxime, Vancomycin

Catecholamine- Dopamine, Noradrenaline, Dobutamine

Others- Heparin, Frusemide



PCT guided antibiotic therapy in sepsis and pneumonia ^{1,13,14,15}



References

1. Jaime A. Foushee et al. Applying biomarkers to clinical practice: a guide for utilizing procalcitonin assays. *J. Antimicrob. Chemother.* (2012) 67 (11): 2560-2569.
2. Nakamura M et al. Procalcitonin: Mysterious Protein in Sepsis. *Journal of Basic & Clinical Medicine* 2013, 2(1):7-11.
3. Balci C et al. Usefulness of procalcitonin for diagnosis of sepsis in the intensive care unit. *Crit Care* 2003;7:85-90.
4. Giamarellos-Bourboulis EJ et al. Should procalcitonin be introduced in the diagnostic criteria for the systemic inflammatory response syndrome and sepsis? *J Crit Care* 2004;19:152-7.
5. Bauer TT, Ewig S, Marre R, et al. CRB-65 predicts death from community-acquired pneumonia. *J Intern Med* 2006;260:93-101.
6. Bouadma L, Luyt CE, Tubach F, et al. Use of procalcitonin to reduce patients' exposure to antibiotics in intensive care units (PRORATA trial): a multicenter randomized controlled trial. *Lancet* 2010;375:463-74.
7. Stolz D, Smyrniotis N, Eggimann P, et al. Procalcitonin for reduced antibiotic exposure in ventilator-associated pneumonia: a randomised study (ProVAP Study). *Eur Respir J* 2009;34:1364-75.
8. De Jong et al. Efficacy and safety of procalcitonin guidance in reducing the duration of antibiotic treatment in critically ill patients: a randomised, controlled, open-label trial. *Lancet Infect Dis* 2016. S1473-3099(16)00064-5.
9. Becker KL et al. Procalcitonin assay in systemic inflammation, infection, and sepsis: clinical utility and limitations. *Crit Care Med* 2008;36:941-52.
10. Simon L et al. Serum procalcitonin and C-reactive protein levels as markers of bacterial infection: a systematic review and meta-analysis. *Clin Infect Dis* 2005;40:1386-8.
11. Brahms. PCT sensitive KRYPTOR Assay Characteristics. <http://www.brahms-usa.com/assays>.
12. ThermoScientific/Brahms. Immunoluminometric Assay (ILMA) for the Determination of PCT (Procalcitonin) in Human Serum and Plasma. http://www.brahms-usa.com/manuals/AAL_PCT_LIA_USA_20050111.pdf
13. Dellinger RP et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med* 2013; 41:580-637.
14. Mandell LA et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis* 2007;44(Suppl 2):S27-72.
15. American Thoracic Society/Infectious Diseases Society of America: guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med* 2005;171:388-416.



www.criticalcareindia.com

Criticalcareindia.com



Frontiers in Intensive care

www.criticalcareindia.com