Antibiotic Commonsense

"An investment in knowledge always pays the best interest." Benjamin Franklin

ANTIBIOTIC RESISTANCE Task Force

Volume 7, Issue 2 April 2013

Editor, Lois Lux

Tacoma - Pierce County Health Department
Healthy People in Healthy Communities
www.tpchd.org

Respiratory Tract Infections: Using Procalcitonin to Guide Antibiotic Therapy Decisions

Brittany Marshall, PharmD, BCPS, Good Samaritan Hospital, Antimicrobial Stewardship Team

Respiratory tract symptoms attributed to bacterial, viral, and non-infectious sources often manifest similarly making appropriate antibiotic utilization a challenge. Many practitioners elect to treat all these symptomatic patients with empiric antibiotic therapy even when the probability of bacterial infection is low. Given that antibiotic exposure is the most important modifiable risk factor for the development of microbial resistance and *C. difficile* infection, it is imperative that antibiotics be limited to patients who have bacterial infections.[1]

Background

Patients with heart failure or chronic obstructive pulmonary disease (COPD) exacerbations admitted to the hospital are often placed on antibiotics for pneumonia based on chest x-rays that report varying degrees of atelectasis or pulmonary venous congestion, and cannot rule out infiltrates. Even if there is little clinical evidence for pneumonia, such patients are often treated with a full course of antibiotics or longer.

Procalcitonin (PCT), a biomarker of bacterial infection, has been utilized both in both inpatient and outpatient settings to help determine the likelihood of a bacterial infection. PCT is converted to calcitonin before release into the serum and remains undetectable in the absence of bacterial infection.

In the presence of a bacterial infection, PCT is produced by many body tissues and released directly into the bloodstream.[2] This produces an elevation in PCT detectable within 4–6 hours from onset of infection which subsequently declines with immune control.[3]

In patients with viral infections, PCT release is inhibited by interferon-gamma and circulating levels remain low. Furthermore, non-specific systemic inflammatory responses do not result in elevated PCT.[3]

In a patient presenting with shortness of breath and a clinical evaluation consistent with heart failure, COPD exacerbation or other cause, a low PCT can be used to support the clinician's low suspicion of pneumonia and a decision to withhold antibiotics (Table 1), even if the chest X-Ray report uses the word "pneumonia" or "infiltrate".

Evidence

A growing body of evidence supports the use of PCT in assisting with antibiotic management of suspected respiratory infections, including pneumonia, bronchitis and exacerbations of chronic bronchitis.

A 2007 study randomized 226 adults hospitalized for a COPD exacerbation into two groups: (1) usual care or (2) therapy guided by PCT levels. In the second group, antibiotics were discouraged with PCT levels less than 0.1 ng/mL; were optional with levels 0.1 to 0.25 ng/mL; and were recommended with levels greater than 0.25 ng/mL.

Patients receiving care guided by PCT were less likely to receive antibiotics than those in the control group (40% vs. 72%, P < .0001). There was no difference between groups in days to the next exacerbation, exacerbations in the next six months, lung function, symptoms, or length of hospitalization.[4]

Table 1: PCT Interpretation for Patients with Respiratory Tract Infections

PCT (ng/mL)	Bacterial Infection?	Antibiotic?	Other Considerations and Overruling Criteria
> 0.5	Very Likely	Yes	Consider the Course of PCT If baseline obtained, consider repeat PCT in 1-3 days and discontinue antibiotics when PCT decreases > 80% of the peak level
0.25–0.5	Likely	Yes	
0.1–0.25	Unlikely	No	Consider initial antibiotics when pts are high risk: PCT <0.25: COPD GOLD III or IV
< 0.1	Very Unlikely	No	

The MultiCare Good Samaritan antimicrobial stewardship program has utilized PCT for the past two years after piloting a project in 2012 to assess the utility of PCT in adult patients receiving broad spectrum antibiotics for suspected respiratory tract infections. In this 2012 study, a PCT level was drawn when the history, signs, and symptoms (such as absence of fever and leukocytosis, or a chest x-ray indeterminate for pneumonia) suggested a non-bacterial etiology for the patient's presentation, or when an appropriate duration of antibiotic therapy had been met based on available national guidelines.

One-hundred twenty-two (122) patients with suspected respiratory tract infection were reviewed over three months, with 36 meeting the criteria for a PCT level. Of patients with a low PCT value, 48% had all antibiotic therapy discontinued after discussion with the physician, while 13% had therapy narrowed, for example, to azithromycin or doxycycline alone for COPD exacerbation.

Only 10% of recommendations to stop therapy were rejected by the attending physician. The remaining patients were discharged prior to follow-up on PCT levels. At follow-up 30 days post-discharge, one patient had been readmitted with a respiratory related complaint.

Limitations of Procalcitonin

False positive and false negative results can occur with any test and clinical context should guide interpretation of PCT results (Table 2). PCT and associated cut-offs have only been validated, with safety and efficacy shown, for a few infection sources. Primarily observational studies are available for other infectious sources, and thus the clinical benefit and safety of using PCT remains undefined.[3]

Summary

If used in the proper clinical settings, PCT can be very helpful in supporting decisions not to give antibiotics or to withdraw them at an early point. Decisions regarding antibiotic therapy should not be based solely on PCT. PCT should be used within the clinical context of the situation, taking into account the possible sites of infection, the likelihood of bacterial infection based on clinical data, and the severity of illness.

Antibiotics are grossly overused. They are prescribed when they are not indicated; broad therapy is used when narrow is preferred; and, excessive durations are used when treatment is indicated. Tools like PCT can help reduce this overuse of antibiotics. For patients with a low probability of a bacterial infection, a single PCT level and a decision to withhold antibiotics based on the cutoff ranges shown in Table 1 appears to be an appropriate and safe approach in this setting.[2] If antibiotics are started, a second low PCT within 12–24 hours can be used to support a decision to stop antibiotics at an early point, limiting their harmful effects.

Table 2: Conditions that can affect PCT levels[5]

False Positives
• Significantly compromised renal function, especially ESRD/ hemodialysis
• Acute respiratory distress syndrome
• Chemical pneumonitis
• Newborns (<48-72 hours; after 72 interpret levels as usual)
• Acute malaria, systemic fungal infections
• Massive stress (burns, severe trauma, surgery, cardiac shock)
• Medullary thyroid cancer, small cell lung cancer
• Some forms of vasculitis and acute graft vs. host disease
• Treatment with agents which stimulate cytokines
• Prolonged, severe cardiogenic shock or organ perfusion abnormalities
False Negatives
• Early in the course of infection
• Localized infections (i.e. empyema, osteomyelitis, localized abscesses)
• Subacute endocarditis

References

1. Liew YX, et al., Use of procalcitonin (PCT) to guide discontinuation of antibiotic use in an unspecified sepsis is an antimicrobial stewardship program (ASP). Eur J Clin Microbiol Infect Dis. 2011 Jul;30(7):853-5.
2. Schuetz P, et al., Procalcitonin algorithms for antibiotic therapy decisions: a systematic review of randomized controlled trials and recommendations for clinical algorithms. Arch Intern Med. 2011 Aug 8;171(15):1322-31.
3. Schuetz P, et al., Procalcitonin for diagnosis of infection and guide to antibiotic decisions: past, present and future. BMC Med. 2011 Sep 22;9:107.
4. Stolz D, et al., Antibiotic treatment of exacerbations of COPD: a randomized, controlled trial comparing procalcitonin-guidance with standard therapy. Chest. 2007 Jan;131(1):9-19.
5. Christ-Crain M, Müller M. Procalcitonin in bacterial infections–hype, hope, more or less? Swiss Med Wkly 2005 Aug 6;135(31-32):451-60.

Contact

Lois Lux **llux@tpchd.org**
Phone: **(253) 798-6416**
Fax **(253) 798-7666**