Effective Health Care Program

Infectious Diseases and HIV/AIDS
Sepsis

Procalcitonin-Guided Antibiotic Therapy

Focus of Research for Clinicians

In response to a request from a national professional society regarding the use of procalcitonin in the clinical management of adult and pediatric patients with suspected local or systemic infection, a systematic review of comparative studies (randomized controlled trials and nonrandomized studies) was conducted. The patient populations included critically ill adults with suspected sepsis or other serious bacterial infections, neonates with suspected early neonatal sepsis, patients with upper and lower respiratory tract infections, children with fever of unknown origin, and postoperative patients at risk of infection. Pregnant women, patients with absolute neutropenia and other immunocompromised populations (solid organ and stem-cell transplant recipients, patients with advanced HIV infection/AIDS), and patients with chronic infections such as infective endocarditis were excluded from this review. The systematic review included 18 reports of eligible studies in over 6,000 patients published between January 1, 1990, and December 16, 2011. Outcomes including antibiotic usage, mortality, morbidity, adverse drug effects of antibiotic therapy, and hospital or intensive care unit (ICU) length of stay were assessed. The full report, listing all studies, is available at www.effectivehealthcare.ahrq.gov/procalcitonin.cfm. This summary, based on the full report of research evidence, is provided to assist in decisionmaking along with consideration of a patient's values and preferences. However, reviews of evidence should not be construed to represent clinical recommendations or guidelines.

Background Information

The early initiation and appropriate use of antibiotics are crucial factors in managing critically ill adult and pediatric patients with bacterial infections such as sepsis and in postoperative patients with suspected infections. The timely initiation and duration of use of appropriate antibiotics are also clinically relevant to managing bacterial upper and lower respiratory tract infections in the ambulatory care or hospital setting. A key challenge associated with antibiotic therapy is that the overuse and misuse of antibiotics can result in adverse effects and add to the increasing problem of antibiotic resistance. However, the duration of antibiotic therapy that is appropriate for these patient populations is often undefined, and clinical features are of limited help in guiding discontinuation of therapy.

Several serum biomarkers have been identified in recent years that have the potential to aid the diagnosis of local and systemic infections, differentiate bacterial and fungal infections from viral syndromes or noninfectious conditions, prognosticate outcomes, and ultimately guide management, particularly antibiotic therapy. Among these biomarkers, procalcitonin is the most extensively studied and is often used with algorithms to guide care in association with clinical impressions.

Procalcitonin is a precursor of the hormone calcitonin; its levels have been found to increase during infection and different degrees of inflammation. Some evidence indicates that procalcitonin, when compared with other biomarkers, is more specific for bacterial infections, with serum levels rising early after the onset of infection and falling rapidly as the infection resolves. In systemic bacterial infections, including sepsis, procalcitonin levels are generally $\geq$0.5 ng/mL, with higher levels associated with severe disease. In patients with suspected respiratory tract infection, a cutoff of >0.25 ng/mL is predictive of a bacterial infection, while a level <0.25 ng/mL signals resolution of the infection. The cutoff level of procalcitonin to identify postoperative patients with infection may be higher than that used for other patient groups due to cytokine release during surgery. In neonates, a nomogram accounting for the time from birth in hours is recommended for assessing procalcitonin cutoffs.

Earlier studies have investigated the potential roles of procalcitonin in diagnosing and managing local and systemic infections. However, its clinical role in diagnosing and managing patients with suspected infections remains unclear.

Conclusions

Procalcitonin guidance for antibiotic discontinuation reduced antibiotic usage in adult patients in ICUs without increasing mortality; however, there was uncertainty related to the evidence on mortality. The use of procalictonin to guide antibiotic intensification rather than discontinuation in adult patients in ICUs resulted in increased antibiotic usage, which was associated with increased morbidity. Furthermore, procalcitonin guidance for initiating and discontinuing antibiotic therapy significantly reduced antibiotic prescription rates and duration of use in patients with acute respiratory tract infections, including acute exacerbations of chronic obstructive pulmonary disease, community-acquired pneumonia, and acute bronchitis in the ambulatory care or hospital setting. Data to support a role for procalcitonin guidance in the pediatric population were lacking in the literature, but there was moderate-strength evidence showing that procalcitonin guidance resulted in reduced antibiotic usage in neonates with suspected early sepsis.

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Clinical Bottom Line

Procalcitonin Guidance for Antibiotic Therapy in Adult Patients in the ICU*

- Using procalcitonin guidance to discontinue antibiotic therapy reduced antibiotic usage. ●●●
- Using procalcitonin guidance to discontinue antibiotic therapy did not increase morbidity, as indicated by ICU length of stay. ●●○
- Using procalcitonin guidance to discontinue antibiotic therapy did not increase mortality. ●○○
- Procalcitonin-guided intensification§ of antibiotic therapy was associated with greater duration of use and increased total exposure to antibiotics. ●●○
- Procalcitonin-guided intensification of antibiotic therapy was associated with increased morbidity, including increases in ICU length of stay, days on mechanical ventilation, and days with abnormal renal function. ●●○

Procalcitonin Guidance in Patients With Various Respiratory Tract Infections† in the Ambulatory Care or Hospital Setting*

- Procalcitonin guidance reduced antibiotic duration of use and prescription rates (●●●) and was associated with a reduction in total antibiotic exposure (●●○).
- Procalcitonin guidance did not increase mortality, hospital length of stay, or ICU admission rates. ●●○
- Evidence related to the effect of procalcitonin guidance on antibiotic-associated adverse events was insufficient. ○○○

Procalcitonin Guidance in Pediatric Patients

- Procalcitonin guidance reduced the use of antibiotic therapy for suspected early neonatal sepsis. ●●○
- Evidence was insufficient to determine if procalcitonin guidance reduced antibiotic usage in children aged 1–36 months with fever. ○○○

Procalcitonin Guidance in Postoperative Patients

- Evidence was insufficient to determine if procalcitonin guidance can identify postoperative patients at risk of developing infections who might benefit from pre-emptive antibiotic therapy. ○○○

* In the studies that used procalcitonin-based algorithms, physicians could consider other clinical information and over-ride the algorithms based on their judgment.

§ Antibiotic intensification consisted of change in antibiotic regimen or broadening the spectrum of antibiotic therapy.

† Respiratory tract infections included acute exacerbations of chronic obstructive pulmonary disease, community-acquired pneumonia, bronchitis, sinusitis, tonsillitis, or pharyngitis.

Strength of Evidence Scale

High:	●●●	High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.
Moderate:	●●○	Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
Low:	●○○	Low confidence that the evidence reflects the true effect. Further research is likely to change the confidence in the estimate of effect and is likely to change the estimate.
Insufficient:	○○○	Evidence either is unavailable or does not permit a conclusion.

Applicability of Findings of This Review

This systematic review found that procalcitonin guidance for antibiotic discontinuation reduces antibiotic usage for adult patients in ICUs, making the evidence applicable to clinical practice regarding antibiotic discontinuation in this setting.

About 75 percent of all antibiotics prescribed in the ambulatory care setting are for acute respiratory tract infections, most of which are viral and do not benefit from antibiotic treatment. This systematic review found that procalcitonin guidance for initiating and discontinuing antibiotic therapy for patients with respiratory tract infections in the ambulatory care or hospital setting significantly reduced antibiotic prescription rates and duration of use.

Certain populations were excluded from the studies of procalcitonin guidance reviewed in this report. Thus, findings from this review should not be extrapolated to these high-risk groups.

Gaps in Knowledge and Future Research Needs

- Assessing the effect of using procalcitonin guidance in patients who are immunocompromised is an important research need.
- Future studies are needed to assess procalcitonin-guided initiation and discontinuation of antibiotics in pediatric populations in both inpatient and outpatient settings.
- Future studies are needed to assess the effect of procalcitonin-guided antibiotic usage and total exposure on antibiotic adverse reactions, superinfections, or the development of antibiotic resistance.
- More research is needed regarding the effects on mortality of reduced antibiotic usage resulting from procalcitonin-guided antibiotic therapy.
- For a more pertinent comparative effectiveness approach, different comparators should have been selected, such as antibiotic stewardship programs and structured implementation of practice guidelines.

Ordering Information

For electronic copies of this clinician research summary and the full systematic review, visit www. effectivehealthcare.ahrq.gov/procalcitonin.cfm. To order free print copies, call the AHRQ Publications Clearinghouse at 800-358-9295.

Source

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