Role of Procalcitonin in the Management of Infected Patients in the Intensive Care Unit

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KEYWORDS

• Procalcitonin • Multiplex PCR • Respiratory panel • Antimicrobial stewardship
• Sepsis • Septic shock • Community-acquired pneumonia

KEY POINTS

- With available diagnostic "bundles," an etiologic agent or agents can be quickly identified in 70% or more of patients with severe community-acquired pneumonia (CAP).
- In patients with CAP and a serum procalcitonin (PCT) level $\leq$0.25 ng/mL, the likelihood of an invasive bacterial etiology is 5% or less.
- In patients with CAP, serum PCT levels can help determine if detected potential bacterial pathogens are colonizing or invading.
- Elevated serum PCT levels do not discriminate between the major categories of shock. However, a normal serum PCT eliminates a bacterial etiology of the shock in more than 95% of patients.
- For both severe CAP and bacteremic septic shock, sequential PCT levels assist in both assessing source control and determining the duration of antimicrobial therapy.

INTRODUCTION

Approximately 70% of patients admitted to critical care units are started on some type of antimicrobial therapy.[1–4] The most common indications are empiric therapy for suspected community-acquired pneumonia (CAP) or sepsis/septic shock. Of concern, the empiric therapy was continued beyond 3 days in one study and for more than 4 days in another.[3,5]

In critically ill patients, with ultimately documented severe bacterial pneumonia or septic shock, the aggressive early use of antibacterials can decrease attributable mortality.[6] When no microbial etiology is identified, clinical uncertainty drives the

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continuation of empiric antimicrobial therapy. The goal is to quickly define etiologic pathogens, or pathogens, so as to apply individualized focused therapy.

In patients with CAP, molecular diagnostics can rapidly detect potential viral and bacterial pathogens. The biomarker procalcitonin (PCT) can help clarify if a detected bacterial pathogen is colonizing or invading. As a consequence, empiric therapy can become specific therapy in an increasing number of patients.

In patients with shock, earlier detection and rapid speciation of blood culture isolates is increasingly available. Normal serum PCT levels strongly suggest the patient's hypotension is not due to invasive bacterial infection. Sequential PCT levels assist in documenting "source" control and allow individualization of the duration of antibiotic therapy.

SEVERE COMMUNITY-ACQUIRED PNEUMONIA

Standard Diagnostic Methods

Detection of the etiology, or etiologies of CAP results in a change from empiric to specific antimicrobial therapy. The higher the diagnostic yield, the better. The traditional diagnostic bundle for patients admitted to the intensive care unit (ICU) with CAP and hypoxemic respiratory failure consists of the following:

- Sputum, or if intubated, endotracheal tube aspirate, for culture and sensitivity
- Urine to test for presence of *Streptococcus pneumoniae* antigen, and *Legionella pneumophila*, serogroup 1 antigen
- Usually 2 blood cultures

If not intubated, it is not possible to collect a valid sputum in up to half or more of the patients.[7–10] Blood cultures are easily obtainable, but blood cultures are positive in fewer than 10% of the patients.[11] *S pneumoniae* antigen is found in urine in roughly 11% of the patients.[12] Using the urine antigen for detection, *L pneumophila* is found in 1% or less of the patients with CAP.[11,13] In short, the overall diagnostic yield with the standard bundle is less than 50%.[14,15]

Further, the turnaround time is slow. Urine antigen results return in 2 to 12 hours, sputum cultures in a minimum of 2 to 3 days, and blood cultures can take many days.[15]

Addition of Molecular Diagnostics

The diagnostic yield can be increased, with fast turnaround times, by adding molecular polymerase chain reaction (PCR) probes to the diagnostic bundle.

In 2 separate studies of patients admitted with CAP, the following tests were added to the previously discussed bundle:

- Anterior nasal swab for nucleic acid amplification test (NAAT) for *Staphylococcus aureus* (results within 24 hours)
- Nasopharyngeal swab for FilmArray Multiplex PCR panel for 17 viral strains and 3 bacteria (results within 2 hours)
- Nasopharyngeal swab for NAAT for *S pneumoniae* (results within 24–48 hours)

With the enlarged bundle, a potential pathogen was detected in 70% to 80% in 2 cohorts of patients enrolled over 2 respiratory winter seasons.[14,15]

Similar results with a slightly smaller diagnostic package were reported for patients with acute exacerbations of chronic bronchitis and other lower respiratory tract infections.[16]