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Journal club critique

Procalcitonin testing has the potential to reduce unnecessary antibiotic use in patients with suspected lower respiratory tract infections

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Expanded Abstract

Citation

Christ-Crain M, Jaccard-Stolz D, Bingisser R, Gencay MM, Huber PR, Tamm M, Muller B: Effect of procalcitonin-guided treatment on antibiotic use and outcome in lower respiratory tract infections: cluster-randomized, single-blinded intervention trial. *Lancet* 2004, 363:600-607.[1]

Background

Lower respiratory tract infections are often treated with antibiotics without evidence of clinically relevant bacterial disease. Serum calcitonin precursor concentrations, including procalcitonin, are raised in bacterial infections, but not in viral infections.

Hypothesis

Procalcitonin (PCT)-guided treatment of suspected lower respiratory tract infection substantially reduces antibiotic use without compromising clinical or laboratory outcomes.

Methods

Design: Prospective, cluster-randomized, controlled, single-blinded intervention trial.

Setting: Medical emergency department of a 784-bed academic tertiary care hospital in Basel, Switzerland.

Subjects: 243 patients presenting to the emergency department who were admitted with suspected lower respiratory tract infection as the main diagnosis.

Intervention: Patients were randomly assigned to either standard care (n=199) or PCT-guided treatment (n=124). In the latter group, serum PCT concentrations were used to advise clinicians. Use of antibiotics was: strongly discouraged (PCT <0.1 μg/L), discouraged (≥0.1 and <0.25 μg/L), advised (≥0.25 and <0.5 μg/L), or strongly advised (≥0.5 μg/L). Re-evaluation was possible after 6-24 hours in both groups.

Outcomes: The primary endpoint was antibiotic use with analysis by intent to treat. Secondary endpoints included clinical and laboratory outcomes.

Results

Final diagnoses were pneumonia (36%), acute exacerbation of chronic obstructive pulmonary disease (25%), acute bronchitis (24%), asthma (5%), and other respiratory affections (10%). Serological evidence of viral infection was recorded in 141 of 175 tested patients (81%). Bacterial cultures were positive from sputum in 51 (21%) and from blood in 16 (7%). In the procalcitonin group, the adjusted relative risk of antibiotic exposure was 0.49 (95% CI 0.44-0.55; p<0.0001) compared with the standard group. Antibiotic use was significantly reduced in all diagnostic subgroups. Clinical and laboratory outcomes were similar in both groups.

Conclusion

PCT-guided therapy of suspected lower respiratory tract infection substantially reduced antibiotic use without compromising clinical or laboratory outcomes.

Commentary

As many as 75% of all antibiotic doses are prescribed for acute respiratory tract infections; of these, most are caused by viruses not bacteria.[2] Since antimicrobial resistance among bacteria is an important public health problem and indiscriminate use of antibiotics has been implicated as a predisposing factor, it would be useful to have a rapid and

sensitive method for determining the presence of bacterial infection to facilitate more judicious use of antibiotics.

Serum concentrations of PCT are elevated in bacterial infections, but not in viral infections. PCT levels have been used to determine the presence of bacterial infection in the setting of acute respiratory distress syndrome[3] and sepsis,[4,5] to reduce unnecessary antibiotic use in meningitis,[6] and to predict outcome in critically ill patients with ventilator-associated pneumonia.[7] The authors of the current study used a new, rapid, and highly sensitive PCT assay to assess the likelihood of bacterial infection and influence antibiotic use in patients presenting to the emergency department with suspected lower respiratory tract infection. The use of PCT to guide antibiotic use resulted in significantly fewer patients receiving antibiotics (44% vs. 83%, $p<0.0001$) and reduced antibiotic-related costs.

This was a very well done study. However, a few limitations should be noted. First, reducing antibiotic therapy can only be considered advantageous if withholding antibiotics does not worsen clinical outcomes. Although serious adverse outcomes, such as death, occurred with similar frequency in both study arms, meaningful differences could have been missed due to the relatively small sample size. Second, it is not clear how the authors chose the cut-offs they used to advise clinicians. Other cut-offs might have provided even better discrimination. Third, the authors did not state if any patients received systemic or inhaled steroids prior to initial PCT determinations. Steroids inhibit the secretion of numerous cytokines and other pro-inflammatory mediators, some which are strong inducers of PCT expression and secretion.[8,9] Steroid use conceivably could alter PCT levels enough to change antibiotic use recommendations. Whether the results of this study and the cut-offs used would be applicable to patients receiving steroids is unknown. Finally, circulating PCT concentrations may be increased by noninfectious conditions, such as congestive heart failure and cardiogenic shock[10] and may even be low in some cases of sepsis due to bacterial infection.[11] Therefore, PCT concentrations should not be used to definitively diagnose bacterial infection and should always be considered in the context of other clinical findings obtained by taking a thorough history and performing a careful physical examination.

Recommendation

Based on the results of this study, we conclude that PCT testing has the potential to reduce unnecessary antibiotic use in patients with suspected lower respiratory tract infections. Still, we cannot recommend its routine use until larger studies convincingly demonstrate equivalent clinical outcomes. Whether these results can be extrapolated to situations more relevant to intensivists, such as the evaluation of critically ill patients with suspected ventilator-associated pneumonia,[11] remains to be seen.

Competing interests

The authors declare that they have no competing interests.

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