

THERAPEUTICS

Procalcitonin level-guided treatment reduced antibiotic use in exacerbations of COPD

Stolz D, Christ-Crain M, Bingisser R, et al. Antibiotic treatment of exacerbations of COPD: a randomized, controlled trial comparing procalcitonin-guidance with standard therapy. *Chest*. 2007;131:9-19.

Clinical impact ratings: GIM/FP/GP ★★★★★☆☆ Hospitalists ★★★★★★★ Infectious Disease ★★★★★☆☆ Pulmonology ★★★★★☆☆

QUESTION

In patients with an exacerbation of chronic obstructive pulmonary disease (COPD), does treatment guided by procalcitonin levels reduce antibiotic use more than does standard therapy based on current guidelines?

METHODS

Design: Randomized controlled trial.
Allocation: {Not concealed}†.*
Blinding: Blinded (physicians and nurses assessing outcomes {and data collectors}†).*
Follow-up period: 6 months.
Setting: A university hospital in Basel, Switzerland.
Patients: 226 patients with COPD exacerbation (a sustained worsening from the stable state beyond normal day-to-day variations and acute enough in onset to require a change in regular medication) who met post-bronchodilator therapy spirometric criteria for COPD within 48 hours of emergency department admission. Exclusion criteria included a reason other than underlying COPD for presenting signs and symptoms, psychiatric comorbid conditions, immunosuppression, asthma, cystic fibrosis, or presence of infiltrates on chest radiography.
Intervention: Treatment guided by procalcitonin level ($n = 113$) or standard therapy ($n = 113$). A procalcitonin level $< 0.1 \mu\text{g/L}$

indicated the absence of infection, and antibiotics were discouraged; antibiotics were encouraged if the procalcitonin level was $> 0.25 \mu\text{g/L}$. In the standard-therapy group, antibiotics were prescribed according to current guidelines by the attending physician, who was unaware of patients' procalcitonin levels.

Outcomes: Total antibiotic use at the index exacerbation and at 6 months. Secondary outcomes included improvement in symptoms, need for intensive care unit stay, length of hospital stay, mortality, exacerbation rate, and lung function.

Patient follow-up: 92% (mean age 70 y, 55% women) (intention-to-treat analysis).

MAIN RESULTS

At the index exacerbation, procalcitonin guidance reduced antibiotic use more than did standard therapy (Table) and allowed sustained reduction in antibiotic exposure at up to 6 months (relative risk 0.76, 95% CI 0.64 to 0.92). Groups did not differ for improve-

ment in symptoms (82% vs 84%, $P = 0.853$), need for intensive care unit stay (7.8% vs 10%, $P = 0.526$), length of hospital stay (9 vs 10 d, $P = 0.960$), mortality (4.9% vs 8.5%, $P = 0.409$), exacerbation rate (43% vs 40%, $P = 0.607$), or lung function (FEV₁ percent predicted 45 vs 47, $P = 0.176$). Reexacerbation rate and time to next exacerbation were similar between groups at 6 months.

CONCLUSION

In patients with an exacerbation of chronic obstructive pulmonary disease, treatment guided by procalcitonin levels allowed a reduction in antibiotic use without altering clinical outcomes.

Sources of funding: No external funding.

For correspondence: Dr. D. Stolz, University of Massachusetts Medical School, Worcester, MA, USA. E-mail dstolz@uhbs.ch.

*See Glossary.

†Information provided by author.

Treatment guided by procalcitonin levels vs standard therapy at index exacerbation of chronic obstructive pulmonary disease†

Outcome	Procalcitonin guidance	Standard therapy	RRR (95% CI)	NNT (CI)
Antibiotic use	40%	72%	44% (27 to 57)	4 (3 to 6)

†Abbreviations defined in Glossary; NNT and CI calculated from data in article.

COMMENTARY

Bacterial infections commonly cause acute exacerbations of COPD. Many patients with COPD exacerbations receive antibiotics, a practice supported by the findings of a recent systematic review (1). However, COPD exacerbations have other causes, such as viruses, for which antibiotics are not indicated. Inappropriate antibiotic use is costly, causes adverse drug events, and selects for resistant bacteria. A reliable method for detecting bacterial exacerbations of COPD would be useful.

Serum procalcitonin is a promising candidate. Previous studies indicate that serum procalcitonin levels differentiate systemic bacterial infections from nonbacterial disorders with reasonable accuracy over a wide age range and in a variety of clinical conditions (2). Available methodology is sensitive, quick, and reasonably priced (3).

Stolz and colleagues showed that a procalcitonin-driven protocol substantially reduced antibiotic use in hospitalized patients with COPD exacerbations without apparent clinical harm. These results are interesting and potentially important, but the intervention should not be widely implemented without further study. One issue has to do with the generalizability of findings from a single study center. More impor-

tant, we need stronger evidence that withholding antibiotics in patients with low procalcitonin levels does no harm. Obtaining that information will require a large trial in which patients with COPD exacerbations with low serum procalcitonin levels are randomized either to placebo or antibiotics.

*Dennis E. Niewoehner, MD
 Veterans Affairs Medical Center
 Minneapolis, Minnesota, USA*

References

- Ram FS, Rodriguez-Roisin R, Granados-Navarrete A, et al. Antibiotics for exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2006;2:CD004403.
- Simon L, Gauvin F, Amre DK, Saint-Louis P, Lacroix J. Serum procalcitonin and C-reactive protein levels as markers of bacterial infection: a systematic review and meta-analysis. *Clin Infect Dis*. 2004;39:206-17.
- Christ-Crain M, Stolz D, Bingisser R, et al. Procalcitonin guidance of antibiotic therapy in community-acquired pneumonia: a randomized trial. *Am J Respir Crit Care Med*. 2006;174:84-93.