# Steroids Gain Traction for Severe Pneumonia

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LISBON — The use of corticosteroids to reduce the morbidity and mortality of severe bacterial pneumonia is supported by results from two positive randomized trials, multiple observational studies, and animal models, Dr. Antoni Torres said at the 12th International Congress on Infectious Diseases.

However, the strategy is not ready for prime-time clinical practice or incorporation into treatment guidelines because the trials that produced the highly favorable results were relatively small, said Dr. Torres of the University of Barcelona. In addition, key questions remain, such as what level of systemic inflammation warrants adjunctive corticosteroid therapy, and when, how, and for how long steroids should be given, he added.

Dr. Torres said he anticipates answers to these questions will emerge from an ongoing randomized controlled trial he and his coworkers are conducting. The trial, which should be completed within a year, is restricted to community-acquired pneumonia (CAP) patients who are at high mortality risk and have a baseline C-reactive protein (CRP) level of at least 15 mg/mL, because there is evidence to suggest that reducing the inflammatory response in patients with a CRP below that benchmark may be dangerous.

Severe pneumonia is now recognized as an inflammatory state involving elevated pulmonary and circulating inflammatory cytokine levels. Steroids can modulate this inflammatory response, and the hypothesis under examination is that doing so will improve clinical outcomes.

Pneumonia is the community-acquired infection that most frequently leads to patients being admitted to the ICU. Up to 20% of patients with CAP are hospitalized, and one-quarter of those end up in the ICU.

Research interest in systemic inflammation in pneumonia has been driven by the fact that the mortality rate for severe CAP in the ICU setting has remained relatively steady at 20%-50% over the last 50 years, despite the availability of effective antimicrobial agents and excellent supportive measures, Dr. Torres said at the congress, which was sponsored by the International Society for Infectious Diseases.

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**DR. TORRES**

A prospective observational study by Dr. Torres and his coworkers involving 1,424 CAP patients hospitalized at 15 medical centers was among the work that fanned interest in the use of steroids in severe pneumonia and eventually led to randomized trials. In that study, 15% of the patients experienced empirical treatment failure, which was associated with an adjusted 11-fold increase in hospital mortality.

The independent risk factors for treatment failure included multilobar CAP, radiologic cavitation, pleural effusion, liver disease, leukopenia, and pneumonia risk class (Thorax 2004;59:960-5). However, it was the factors identified as protective against treatment failure, such as the influenza vaccination, initial treatment with a fluoroquinolone, and especially chronic obstructive pulmonary disease (COPD), that caught the researchers' attention. Dr. Torres and his coworkers hypothesized that COPD's protective effect might involve the use of steroids in affected patients.

The first randomized trial was a multicenter, double-blind, Italian study involving 46 patients with severe CAP on placebo or 200 mg of hydrocortisone as an IV bolus, followed by 7 days of therapy at 10 mg/hour.

The prolonged low-dose hydrocortisone group had significant reductions in mortality, duration of mechanical ventilation, chest x-ray scores, and length of hospital stay. Their CRP levels also dropped significantly (Am. J. Respir. Crit. Care Med. 2005;171:242-8).

The second randomized trial, conducted by other investigators, showed an initial bolus of methylprednisolone followed by a 9-day taper in patients on ceftriaxone and levofloxacin resulted in a significantly shorter time to resolution of pneumonia symptoms and sepsis, Dr. Torres said. Those results have not yet been published. ■