

Steroids Gain Traction For Severe Pneumonia

BY BRUCE JANCIN
Denver Bureau

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 that answers to these questions will emerge from an ongoing randomized 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 evidence suggests 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.

Among community-acquired infections, pneumonia is the disease that most often leads to admission 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 at 20%-50% over



the last 50 years, despite the availability of effective antimicrobial agents, Dr. Torres said at the congress, which was sponsored by the International Society for Infectious Diseases.

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 pneumonia. 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).

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DR. TORRES

However, it was the factors identified as protective against treatment failure, such as 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).

A randomized trial conducted by other researchers showed that an initial bolus of methylprednisolone followed by a 9-day taper in patients on ceftriaxone and levofloxacin significantly sped up resolution of pneumonia symptoms and sepsis, Dr. Torres said. Those results have not yet been published. ■

'Switch Therapy' Deemed Safe In Elderly With Pneumonia

BY JANE SALODOF MACNEIL
Southwest Bureau

SAN DIEGO — Advanced age by itself should not be a barrier to switching a patient with community-acquired pneumonia from intravenous to oral antimicrobial therapy soon after the patient shows clinical improvement, Dr. Paulo Rossi said in a poster presentation at the International Conference of the American Thoracic Society.

An observational study of 2,648 adult patients at 40 hospitals in 13 countries showed that, regardless of age, about two-thirds were discharged within 24 hours of meeting the criteria for "switch therapy." Of 372 patients aged 85 years or older, 65% were discharged in this early time frame, as were 68% of 1,161 patients aged 65-84 years and 72% of 1,115 patients aged 18-64 years.

No deaths occurred in the youngest group after switch therapy, and mortality was low among the older groups: 9 deaths (1.6%) of the 554 switch-therapy patients in the 65-84 age group and 2 deaths (1.2%) of the 164 patients in the oldest cohort.

The study shows that frail elderly patients with community-acquired pneumonia (CAP) can handle switch therapy, said Dr. Rossi of S. Maria della Misericordia Hospital in Udine, Italy. "Even if they are over 90 they can, more or less," he said in an interview.

He and his coinvestigators reviewed records of CAP patients who were entered into the Community-Acquired Pneumonia Organization database from June 2001 to May 2005. The database includes hospitals in the United States, and the study coordinator was based at the University of Louisville (Ky.).

The study relied on American Thoracic Society guidelines for time to switch therapy. Patients had to meet four criteria to be considered candi-

dates for a switch: improvement in cough and shortness of breath; at least 8 hours without a fever; leukocytosis reduced by at least 10% from the previous day; and "tolerating oral intake with adequate gastrointestinal absorption."

The investigators considered patients to be candidates for hospital discharge once they met the above criteria for oral therapy, a diagnostic work-up was completed, any comorbidity was treated, and social needs were met. Any discharge within 24 hours of the patient's meeting the criteria for switch therapy was considered an early discharge.

Of the oldest patients, 90% were classified as being at high risk. Nonetheless, 51.6% met the criteria for switch therapy on or before the 6th day of hospitalization. In the middle group of patients, aged 65-84 years, 54.2% passed this goal by the 5th day, and in the youngest group, 57.1% passed this goal by the 4th day.

All told, the proportions of patients who met the criteria for switch therapy declined with age, going from 71% of the youngest group to 63% of the middle group to 56% of the oldest patients. The proportion of patients who were switched was similar across groups, however: 80% of the under-65 patients, 76% of the middle group, and 78% of those aged 85 and up.

After therapy was switched, the oldest patients were the least likely to require reestablishment of IV antibiotics. Just 2 (1.2%) of the 164 patients in the oldest group had to be switched back, vs. 20 (3.6%) of the 554 patients in the middle group and 46 (7.4%) of the 621 patients in the youngest group.

Older patients often have comorbidities that present a barrier to switch therapy but also put them at risk of nosocomial infection if they stay in the hospital, Dr. Rossi said. Hence, as stated on the poster, "for these patients an early discharge is potentially more important than in younger patients." ■

Pneumonia Tx Algorithm Cuts Nursing Home to Hospital Transfers

BY MARY ANN MOON
Contributing Writer

A strategy for on-site treatment—rather than automatic hospitalization—of nursing home residents who develop pneumonia reduced hospitalizations by more than half and substantially lowered treatment costs without damaging clinical outcomes, according to Dr. Mark Loeb of McMaster University, Hamilton, Ont., and his associates.

The researchers developed an algorithm, or "clinical pathway," for treating elderly nursing home patients who had pneumonia, and then tested it in a trial involving 661 patients at 20 facilities in southern Ontario. Patients with pneumonia who had a pulse of up to 100 beats/min, a respiratory rate of fewer than 30 breaths/min, systolic blood pressure of at least 90 mm Hg, oxygen saturation of at least 92%, and the ability to eat and drink were randomly assigned to receive usual care (347 subjects) or to be treated on-site (314 subjects).

For on-site treatment, a study nurse performed chest x-rays as needed, empirically administered oral levofloxacin once daily for 10 days, gave IV hydration as needed, administered oxygen as needed, and monitored vital signs. Subjects were transferred to a hospital if at any time they deteriorated to the point at which they no longer met the enrollment criteria.

Of the on-site treatment group, 34 patients (10%) required hospitalization, compared with 76 (22%) in the usual care group. After the data were adjusted for possible confounding factors, the mean rate of hospital admission was 8% for the on-site treatment group, compared with 20% for the usual care group. The mean number of days spent in the hospital was more than twice as many in the usual care group (1.74 days) as in the on-site treatment group (0.79 days), the researchers said (JAMA 2006;295:2503-10).

The results were similar when the analysis was restricted to patients with pneumonia confirmed by x-ray. In this subgroup, 18% of those in the on-site treatment group were

hospitalized, compared with 30% of the usual care group, and the mean admission rates were 9% vs. 29%, respectively.

There were no significant differences between the two groups in mortality, adverse events, health-related quality of life, or functional status. In contrast, the differences in health care costs were substantial.

The initial cost for the on-site treatment approach—which included oxygen therapy, hydration therapy, mobile x-rays, nursing care, and administrative costs—was \$87 (in Canadian dollars) per patient above the cost of usual care. However, this was more than offset by reductions in professional billings, transportation fees, and hospitalization costs, which amounted to \$1,103 (Canadian) in savings per patient. This would translate to \$1,517 savings per patient in U.S. dollars, Dr. Loeb and his associates said.

Their results also suggest that automatically transferring nursing home residents to a hospital when they develop pneumonia has little effect on their clinical outcomes or mortality, the investigators added. ■