Antibiotics Benefit Acute COPD

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To address this issue, Dr. Rothberg and his associates at Baystate Medical Center of Tufts University, Springfield, Mass., used a large database designed to measure quality of care and resource utilization to conduct a retrospective cohort study of patients hospitalized in 2001 for acute COPD exacerbations at 375 acute care facilities. Included were patients hospitalized for at least 2 days with either a primary diagnosis of COPD or a primary diagnosis of respiratory failure and a secondary diagnosis of COPD; to avoid confusion with asthma, only patients older than 39 years were included in the study.

Patients admitted directly to the intensive care unit were excluded, as were those who had other bacterial infections for which antibiotics would have been indicated.

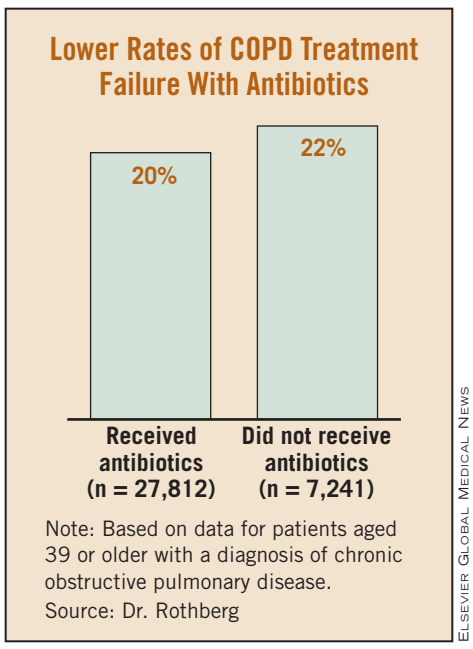
Of 35,053 patients who met the enrollment criteria, 79% (27,812) had received antibiotics (most commonly quinolones, cephalosporins, or macrolides) and 21% (7,241) had not.

Those given antibiotics were significantly younger (median age 70 years vs. 71 years), more likely to be in managed care (20% vs. 19%) and to be white (78% vs. 73%). They were less likely to have comorbidities including secondary pulmonary hypertension, sleep apnea, alcohol abuse, renal failure, and heart failure. (Because the database was so large, even seemingly small differences often reached statistical significance, Dr. Rothberg noted.)

Patients who received antibiotics appeared to have more severe disease, since significantly more had been given steroids (87% vs. 74%), an arterial blood gas measurement (58% vs. 53%), sputum testing (13% vs. 5%), and short-acting bronchodilators (55% vs. 50%). They also received more methyxanthines, loop diuretics, and morphine. The two groups were equally likely to have been given nutritional supplements and to have been prescribed continuous positive airway pressure or bilevel positive airway pressure.

Length of stay was significantly greater for the antibiotic group (4.92 days vs. 4.65 days), as was total cost ($4,361 vs. $4,277).

Adverse events, including allergic reactions, diarrhea, and treatment for *Clostridium difficile* infection after day 3, were not increased in the antibiotic-treated group.



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The unadjusted odds of treatment failure (in-hospital mortality, mechanical ventilation after day 2, and all-cause readmission within 30 days) were significantly lower for those treated with antibiotics (20% vs. 22%), with an odds ratio of 0.88. However, because this wasn't a randomized trial, there was a need to control for selection bias—that is, patients who received antibiotics were likely to have been sicker than those who did not. To control for that, a propensity model was used to predict the likelihood of receiving antibiotics, based on patient factors such as demographics, comorbidities, prior COPD admissions, diagnostic tests and treatments (e.g., arterial blood gas, steroids), physician specialty, and hospital factors such as size and teaching status.

Even after adjustment for both the propensity score and covariates, receiving antibiotics still resulted in a lower risk for treatment failure (odds ratio 0.87). The adjusted risk of mortality was also lower, with an odds ratio of 0.85, but the number of deaths was too small for that value to reach statistical significance, Dr. Rothberg said.

"We really tried to adjust for everything that we could. Having such a large data set allowed us to adjust for just about everything at the physician and the hospital level. … No matter how we looked at it, we were still left with a benefit for antibiotics." Future work will address whether there are differences between the antibiotic classes, he said.

This study was funded internally by Baystate Medical Center's Division of Healthcare Quality. ■

Noninvasive Ventilation Is a Must For Most Inpatients With COPD

BY MARY JO M. DALES
Editorial Director

SAN DIEGO — Noninvasive positive pressure ventilation should "absolutely" be used for nearly every patient hospitalized for an acute exacerbation of chronic obstructive pulmonary disease, said Dr. Daniel D. Dressler, director of education for the section of hospital medicine at Emory University, Atlanta.

"Learn how to use this therapy," Dr. Dressler advised at the annual meeting of the Society of Hospital Medicine. Although contraindicated in COPD patients who have malignant arrhythmias, refractory hypoxemia, cardiac or respiratory arrest, or hemodynamic instability, adding noninvasive positive pressure ventilation (NPPV) to usual care has been shown in a Cochrane meta-analysis of 14 clinical trials to save one life for every 10 COPD inpatients treated and to avoid intubation for 1 of every 4 patients treated, compared with usual care alone. Further, NPPV has been shown to lower the average length of stay by 3.2 days.

Dr. Dressler advised starting NPPV in the emergency department if possible, since "early intervention likely improves outcomes." Monitor these patients closely with arterial blood gases at 30-60 minutes after initiating or changing NPPV settings. Don't wait 2 hours before taking these measures.

The usual starting pressure level is 10/5 cm of water pressure, and the settings are titrated upward to tolerance with the assistance of the respiratory therapist, he said.

Based on the Cochrane review, those who respond best to NPPV are patients with pH values less than 7.3. But that finding largely may reflect the level of care at individual hospitals rather than the likelihood that the therapy was poorly tolerated by individual patients. In a recent study of COPD patients with pH values of 7.35 and higher, NPPV did not reduce the risk of death or intubation, but it did speed up reduction in the partial pressure of carbon dioxide (pCO_2) and reduced average length of stay from 10.2 days to 5.5 days (Eur. J. Intern. Med. 2007;18:524-30).

Antibiotic treatment for nearly all hospitalized patients with COPD exacerbations also reduces length of stay and is strongly supported by evidence, according to Cochrane analysis. On average, treating eight patients will prevent one death, and treating three patients will prevent one treatment failure.

The evidence for the choice of antibiotic is not great, however, and not all hospitalized patients with COPD exacerbations are likely to need antibiotic therapy. Among the tests investigators are examining, as tools to guide antibiotic prescribing, are measures of procalcitonin levels, with values less than 0.1 ng/mL discouraging the use of antibiotics and values exceeding 0.25 ng/mL encouraging the use of antibiotics. When compared with patients treated empirically by their physicians, outcomes did not differ for those treated based on procalcitonin levels, but using the test did have the desired result of reducing antibiotic use. One had to test four patients in order to avoid prescribing antibiotics for one patient. The procalcitonin test is not broadly available and is estimated to cost about $250, but Dr. Dressler predicted more use of this test in the next 2-4 years.

The evidence is similarly strong for prescribing systemic steroids and inhaled bronchodilators for these patients. Oxygen obviously is prescribed as well, despite a lack of studies showing it to be appropriate for COPD exacerbations among inpatients.

During hospitalization and at discharge of COPD patients, Dr. Dressler advised tobacco cessation counseling and, if not previously administered, a pneumonia vaccine and an annual influenza vaccine. Prophylaxis for venous thromboembolism is standard during the hospital stay.

Patients' home medication regimens should be augmented with a long-acting β-agonist and corticosteroid inhaler. Single agents have been shown to reduce the risk of exacerbations, but they have not been shown to reduce mortality. Combination therapy has been shown to reduce exacerbations and avoids one death for every 53 patients treated. ■

Noninvasive Ventilation Eases End-of-Life Dyspnea

TORONTO — Noninvasive mechanical ventilation alleviated respiratory distress in end-stage cancer patients in a randomized study that compared this palliative modality with the administration of oxygen, Dr. Stefano Nava reported at an international conference of the American Thoracic Society.

"In end-stage cancer we concentrate on relieving bodily pain with morphine, but we overlook the pain of the respiratory system, which is dyspnea," said Dr. Nava, chief of the respiratory critical care unit at Instituto Scientifico di Pavia (Italy).

Oxygen is routinely administered along with morphine in this situation, but there has never been a randomized trial evaluating any technique for easing respiratory distress in these patients and there is no evidence that oxygen is actually beneficial, he said.

To address this uncertainty, the trial was undertaken in six European centers, comparing noninvasive mechanical ventilation (NIV) using a face mask to oxygen administered via nasal cannula. NIV involves the use of positive pressure to aid in breathing, as does conventional mechanical ventilation, but does not require intubation, Dr. Nava explained.

For enrollment in the study, patients had to have acute respiratory failure and distress, with a Borg dyspnea score greater than 3 and a respiratory rate exceeding 25 breaths per minute.

A total of 126 patients were randomized. All of them had solid cancers, and mortality was 80%, as expected, Dr. Nava said. Clearly, survival was not increased. "In fact, we explain to patients that NIV may unduly prolong life, even if only for a few hours," he said.

Overall, there was a similar degree of relief in both groups, but the effects were more rapid with NIV. Borg dyspnea score in the NIV group fell significantly from 6.9 on admission to 5.7 at 1 hour, to 4.7 at 3 hours, and to 3.9 at 24 hours. By comparison, a significant decrease from 6.7 on admission to 5.5 was seen only at 3 hours and to 4.8 at 24 hours in the oxygen group.

Morphine use also was lower in the NIV group in the first 24 hours, at 12.2 mg/day, compared with 19.6 mg/day in the oxygen group. "This is important for patients, as it allows the sensorium to remain clearer and they are able to say goodbye and sign papers if necessary, which are not trivial things," Dr. Nava commented in a press briefing.

With NIV, the mask is worn only intermittently, so the patient also can drink and eat if able. In Europe, NIV is now used for up to 40%-50% of ventilated patients in the intensive care unit, but it has not yet been widely adopted in North America, he said.

—Nancy Walsh