Alter Pneumonia Strategies to Fight Resistance

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MONTREAL — In vitro pneumococcal resistance continues to have a substantial role in guiding antibiotic choices and disease management plans for patients with community-acquired pneumonia, according to Michael S. Niederman, M.D.

Many surveillance studies have revealed an increasing global prevalence of in vitro drug resistance among pneumococcal isolates obtained from patients with community-acquired pneumonia. Updated treatment guidelines reflect these findings by stressing the need for clinicians to keep in mind local antibiotic resistance patterns as well as patient risk factors for infection with drug-resistant pathogens, Dr. Niederman said at the Second International Conference on Community Acquired Pneumonia.

"Drug-resistant pneumococcus is more likely in certain at-risk populations, including people older than 65 years and those with immune suppression, exposure to a child in daycare, or a history of alcoholism, multiple medical comorbidities, or therapy with a β-lactam in the past 3 months," he said.

To minimize the opportunity for clinical failure of community-acquired pneumonia therapy related to antibiotic resistance, which can occur with any drug class, clinicians should be prepared to modify management approaches accordingly, stressed Dr. Niederman of the State University of New York at Stony Brook. One such consideration is to use focused instead of broad-spectrum therapy as appropriate, he said.

"Broad-spectrum agents such as quinolones are frequently used in situations where they are both not indicated and unnecessary," he said. For example, in one study of 100 consecutive emergency department patients who were discharged on quinolone therapy, 81 of the patients

Incidence Is Up For Some Strep Empyemas

SAN FRANCISCO — The incidence of pediatric pneumococcal parapneumonic empyema doubled in Utah and surrounding areas since introduction of the pneumococcal conjugate vaccine, Carrie L. Byington, M.D., said in a poster presentation at the annual meeting of the Infectious Diseases Society of America.

Activity of bacterial serotypes varies by geographical region. In the past decade, Utah has had one of the highest rates of pneumococcal parapneumonic empyema (PPE) in children due to *Streptococcus pneumoniae* serotype 1, which the vaccine does not cover, said Dr. Byington of the University of Utah, Salt Lake City, and associates.

A search of the Intermountain Health Care data warehouse found 776 cases of pediatric PPE between March 1996 and June 2005, 62% of which were treated at Primary Children's Medical Center, Salt Lake City. In the period 1996-2000, before introduction of 7-valent pneumococcal conjugate vaccine (Prevnar), the center saw 38 cases per year, compared with 72 cases annually between 2001 and 2004, a significant difference.

Among 295 cases of culture-confirmed invasive pneumococcal disease in children at the center, 74 were PPE, representing 18% of invasive pneumococcal disease in the prevaccine years and 32% since the vaccine.

The investigators retrieved and serotyped pleural and fluid isolates of *S. pneumoniae* from the 74 cases. The proportion of PPE due to serotypes covered in the vaccine decreased from 37% (9 of 24 cases) in the prevaccine era to 14% (7 of 50 cases) in more recent years.

Serotype 1 was the most common cause of PPE due to nonvaccine serotypes in both time periods, but disease due to other nonvaccine serotypes has become more common. Serotype 1 caused 11 (46%) of 24 PPE cases in the earlier period and 17 (34%) of 50 cases since the vaccine. Other nonvaccine serotypes caused only four cases (16%) of PPE in the prevaccine years but 26 cases (52%) of PPE in the postvaccine years.

The pneumococcal vaccine may need to be broadened to cover some of these serotypes, Dr. Byington suggested in an interview.

—Sherry Boschert

had inappropriate indications for the drug, and of the 19 in whom quinolone therapy was appropriate, only 1 was given the correct dose for the correct duration, he said (Arch. Intern. Med. 2003;163:601-5).

"This is the type of behavior that drives more resistance and has to be avoided," Dr. Niederman added.

Because recent prior therapy with β-lactams, macrolides, or quinolones predicts subsequent pneumococcal resistance to the agent that was used, "it is imperative that clinicians take a history of recent antibiotic usage and be prepared to choose an agent that differs from what was used previously," Dr. Niederman said. "This form of patient-specific antibiotic rotation only works if we have choices, which requires an understanding of the acceptable options for therapy."

For example, studies have shown that penicillin resistance probably has therapeutic significance only when MIC values are at least 4 mg/L.

"If β-lactam resistant pneumococcus is suspected, ceftriaxone [Rocephin] may be a reliable choice, while the cephalosporin cefuroxime [Ceftin] may be associated with increased mortality if used in the presence of in vitro resistance to this agent," he said.

In general, when managing patients at risk for drug resistance, "clinicians should choose a highly active antipneumococcal agent to minimize selection pressure for more organisms emerging with higher levels of resistance," Dr. Niederman said.

Patients not likely to have resistance should receive focused therapy with macrolides or ketolides, "reserving more potent agents for the appropriate setting," he added.

Ketolide use in particular "can improve the management of community acquired pneumonia in this era of pneumococcal antibiotic resistance by adding another choice to the heterogeneity of options," he said.

Studies have shown that telithromycin (Ketek)—the first ketolide available for clinical use—is an effective outpatient treatment for mild to moderate community-acquired pneumonia, even in older patients, those with higher pneumonia severity index scores, and those with bacteremia.

"The agent's rapid bactericidal effects appear to make short treatment durations feasible, and its mechanisms of action may avoid the induction of resistance, while maintaining good intrinsic activity against pneumococci, including those that are macrolide resistant," Dr. Niederman said. ■

Moxifloxacin Treats Aspiration Pneumonia

MONTREAL — The potent respiratory fluoroquinolone moxifloxacin is as safe and effective as combination ampicillin/sulbactam therapy for the treatment of aspiration-associated pulmonary infections, Sebastian Ott, M.D., reported in a poster presentation at an international conference on community-acquired pneumonia.

To compare the efficacy, safety, and tolerability of moxifloxacin (Avelox) with that of ampicillin/sulbactam (Unasyn) for the treatment of aspiration pneumonia and primary lung abscess, Dr. Ott of the Helios Chest Hospital Heckeshorn in Berlin and his colleagues enrolled 139 patients diagnosed with either condition in a multicenter, open-label trial.

Nearly 65% of the patients in the study were diagnosed solely with aspiration pneumonia, and definite or presumptive pathogens were isolated in 45 subjects, he said.

Of the 139 patients, 96 were treated according to protocol: 48 were randomized to receive 400 mg of moxifloxacin given intravenously once daily followed by oral moxifloxacin for 7-14 days or until complete resolution of radiologic and clinical signs of infection, and 48 received 1.5-3.0 g of ampicillin/sulbactam intravenously twice daily followed by oral administration for the same duration.

At the end of treatment, the overall clinical response rate for both groups was 67%. In the moxifloxacin group, 59% of patients with aspiration pneumonia and 80% of those with primary lung abscess had responded to the antibiotic treatment.

Among those who received ampicillin/sulbactam, 64% of the aspiration pneumonia patients and 82% of the primary lung abscess patients responded to treatment.

Both of the regimens were well tolerated to a similar degree, "even after long-term administration," Dr. Ott said. "The benefit of moxifloxacin is that its [once-daily] dosing is more convenient."

The findings of this study provide clinicians with an important therapeutic option to add to their toolbox for treating aspiration-related pulmonary infections, which are rare but potentially life threatening.

—Diana Mahoney