Overuse of Zyvox Tied to Neuropathy

BY ALICIA AULT
Contributing Writer

WASHINGTON — Patients who develop neuropathy while taking the antibiotic Zyvox (linezolid), is made by Pfizer. Dr. Belen found 55 reports of neuropathy, and 10 with both optic and other areas affected. Fifty-two of the patients received 600 mg twice daily. The mean age was 51 years, with a range of 12-80 years. There were 24 male patients and 28 female, and 32 reports from the United States and 28 from overseas.

Neuropathies had not been observed in preclinical or clinical studies, but they began to appear in the postmarketing period. Pfizer added language to Zyvox’s label in December 2002 saying that neuropathies had been reported, but usually in patients treated for longer than the recommended maximum treatment period of 28 days.

The recommended duration of Zyvox treatment for complicated and uncomplicated skin and skin structure infections and community-acquired pneumonia is 10-14 days. For the indication of vancomycin-resistant enterococci (VRE), the recommended treatment is 600 mg intravenously or orally twice daily for 14-28 days.

But the median duration of treatment for patients who had neuropathies was 127 days—well beyond the recommended treatment period. The majority of patients with neuropathies had been taking Zyvox for 90-180 days. Dr. Belen said at the conference, sponsored by the American Society for Microbiology. Of the 55, nine patients recovered, nine had a partial recovery, and 15 had not recovered at the last reported follow-up. There were no outcomes reported for 22 patients.

Dr. Belen said she could not draw a conclusion that Zyvox was responsible for the neuropathies reported, since the adverse event report database is just a passive collector of information. The case series whose treatment was with one or more antibiotics. Eight received vancomycin, three received linezolid, and three received quinupristin/dalfopristin. Among the patients successfully treated with daptomycin, seven who had failed or could not tolerate vancomycin, which is often a first-line treatment for osteomyelitis.

The daptomycin treatment duration averaged 30 days, with a range from 21 to 42 days. “In general, the therapy was well tolerated, even for the longer treatment durations,” he said. The one patient in the case series whose infection was not resolved had a relapse during daptomycin therapy, “possibly as a result of underdosing,” he said.

Among the nine patients successfully treated with daptomycin were seven who had failed treatment with or could not tolerate vancomycin. Nine had undergone prior unsuccessful treatment with one or more antibiotics. Eight received vancomycin, three received linezolid, and three received quinupristin/dalfopristin. Among the patients successfully treated with daptomycin, seven who had failed or could not tolerate vancomycin, which is often a first-line treatment for osteomyelitis.

The daptomycin treatment duration averaged 30 days, with a range from 21 to 42 days. “In general, the therapy was well tolerated, even for the longer treatment durations,” he said. The one patient in the case series whose infection was not resolved had a relapse during daptomycin therapy, “possibly as a result of underdosing,” he said.

Among the nine patients successfully treated with daptomycin were seven who had failed treatment with or could not tolerate vancomycin. Nine had undergone prior unsuccessful treatment with one or more antibiotics. Eight received vancomycin, three received linezolid, and three received quinupristin/dalfopristin. Among the patients successfully treated with daptomycin, seven who had failed or could not tolerate vancomycin, which is often a first-line treatment for osteomyelitis.

The one patient in the case series whose infection was not resolved had a relapse during daptomycin therapy, “possibly as a result of underdosing,” he said. Because of renal dysfunction, the septic arthritis patient was started on alternate-day dosing and was not adjusted to daily dosing once renal function improved. During treatment, the patient developed an epidural abscess from 18 PA with reduced susceptibility to daptomycin.

Bone and joint infections are notoriously difficult to resolve, require prolonged treatment, and are associated with a high risk of recurrence. “Effective treatment requires the antibiotic to penetrate the site of infection at an adequate concentration to effectively kill the causative pathogen,” Dr. Finney noted. Because gram-positive organisms, particularly S. aureus, are the predominant cause of these infections, the possibility of drug resistance further complicates treatment. Vancomycin, a standard treatment for bone and joint infections, is not highly active against some gram-positive organisms, including S. au-

Daptomycin vs. Resistant Blood Infections

BY DIANA MAHONEY
New England Bureau

BOSTON — Daptomycin may be an effective option for difficult-to-treat gram-positive bloodstream infections, John Segreti, M.D., said at the annual meeting of the Infectious Diseases Society of America.

In a retrospective study, 31 patients were treated with daptomycin (Cubicin) for bacteremia and/or infective endocarditis at two medical centers. Of these, 24 achieved clinical resolution of the life-threatening conditions, including all 11 with methicillin-resistant Staphylococcus aureus (MRSA) infection, 6 of 7 with methicillin-sensitive S. aureus (MSSA) infection, and 5 of 11 with vancomycin-resistant enterococci (VRE).

Daptomycin was effective for 18 of the 22 bacteremias without endocarditis and for 6 of the 9 patients with infective endocarditis. The findings are particularly important in light of the increasing prevalence of serious infections involving gram-positive cocci and the increasing concern about antimicrobial resistance, especially in hospital intensive care units, said Dr. Segreti of Rush Medical College in Chicago.

Unfortunately, the gold standard for many serious gram-positive infections—vancomycin—is threatened. Its increased use for S. aureus infections leads to an increased risk for recurrent bacteremia and mortality.

“This may be a consequence of inadequate bactericidal activity of vancomycin, especially when treating some strains of S. aureus,” Dr. Segreti said. Daptomycin is a rapidly bactericidal agent than vancomycin, which is critical when treating bloodstream infections, especially in eradicating the vegetative mass associated with infective endocarditis,” he explained.

Between November 2003 and July 2004, 31 patients at Rush University Medical Center in Chicago and Fountain Valley (Calif.) Regional Hospital received 6 mg/kg daptomycin daily or every other day for bloodstream infections. Overall, 22 of the patients had been treated for MRSA bacteremia. The majority of the patients had culture-negative endocarditis. In 24 cases, the patients had received prior antibiotic therapy for their infections, including vancomycin in 18 patients and linezolid in 4, but they required a change in treatment because of limited success of the initial therapy or because of intolerable adverse effects.

Dr. Segreti and his colleagues in this investigation reported no financial interest in the manufacturer of daptomycin, Cubist Pharmaceuticals Inc.

BY DIANA MAHONEY
New England Bureau

BOSTON — Daptomycin may be an effective option for difficult-to-treat gram-positive bloodstream infections, John Segreti, M.D., said at the annual meeting of the Infectious Diseases Society of America.

Infectious Diseases

Daptomycin Looks Like a Possible Option for Treating Difficult Bone and Joint Infections

BY DIANA MAHONEY
New England Bureau

BOSTON — Daptomycin may be an effective option for difficult-to-treat gram-positive bone and joint infections, Michael S. Finney, M.D., said at the annual meeting of the Infectious Diseases Society of America.

These findings are particularly important in light of the increasing prevalence of serious infections involving gram-positive cocci and the increasing concern about antimicrobial resistance, especially in hospital intensive care units, said Dr. Segreti of Rush Medical College in Chicago.

Unfortunately, the gold standard for many serious gram-positive infections—vancomycin—is threatened. Its increased use for S. aureus infections leads to an increased risk for recurrent bacteremia and mortality.

“This may be a consequence of inadequate bactericidal activity of vancomycin, especially when treating some strains of S. aureus,” Dr. Segreti said. Daptomycin is a rapidly bactericidal agent than vancomycin, which is critical when treating bloodstream infections, especially in eradicating the vegetative mass associated with infective endocarditis,” he explained.

Between November 2003 and July 2004, 31 patients at Rush University Medical Center in Chicago and Fountain Valley (Calif.) Regional Hospital received 6 mg/kg daptomycin daily or every other day for bloodstream infections. Overall, 22 of the patients had been treated for MRSA bacteremia. The majority of the patients had culture-negative endocarditis. In 24 cases, the patients had received prior antibiotic therapy for their infections, including vancomycin in 18 patients and linezolid in 4, but they required a change in treatment because of limited success of the initial therapy or because of intolerable adverse effects.

Dr. Segreti and his colleagues in this investigation reported no financial interest in the manufacturer of daptomycin, Cubist Pharmaceuticals Inc.