



Drug Monitor

ONLINE EDITION

Linezolid-tolerant Bacteremia

When antibiotics fail to curb persistent methicillin-sensitive *Staphylococcus aureus* (MSSA) or methicillin-resistant *S. aureus* (MRSA) bacteremia, consider antimicrobial tolerance, advise physicians from Winthrop-University Hospital, Mineola, NY and State University of New York, Stony Brook. Although *S. aureus* has been described in the medical literature as “tolerant” to several antibiotics, these physicians report on what they believe to be the first case of persistent MRSA bacteremia unresponsive to linezolid.

Their patient, a 68-year-old woman, came to the emergency department (ED) with swelling in her lower left leg. Her medical history included diabetes, hypothyroidism, rheumatoid arthritis, and anticardiolipin antibody syndrome. She also had had a cerebrovascular stroke. One month before her ED admission, she had developed deep vein thrombosis (DVT) and pulmonary embolism. Testing in the ED revealed new DVT and pulmonary embolism. Although she was taking warfarin, heparin was administered. On the third day, she had a new occipital stroke. Echocardiography showed no clear thrombi.

On the eighth day, her fever spiked to 102°F and she became delirious. The patient was given moxifloxacin. When the blood cultures grew MRSA, however, this drug was stopped and linezolid 600 mg IV every 12 hours was started. Two days later, repeat blood cultures remained positive for MRSA. A repeat echocardiogram showed no abscess or vegetations, and the patient remained febrile. Three days later, blood cultures still remained positive for MRSA.

At this time, since the more common causes of persistent MSSA/MRSA were eliminated (echocardiography and computed tomography ruled out abscesses and the patient did not have a central venous line catheter or implanted device), minimal bactericidal concentration (MBC) testing was requested. The test results suggested the patient's MRSA strain was susceptible to daptomycin and vancomycin but was tolerant of linezolid. Linezolid therapy was discontinued and daptomycin 12 mg IV every 24 hours was started. The patient's condition continued to deteriorate, however, and she died of a massive pulmonary embolism 18 days after admission.

The authors say that antibiotic tolerance is suggested by a wide discrepancy in the minimal inhibitory concentration (MIC) and the MBC. But, since MBC testing is not routinely ordered, antibiotic tolerance can be overlooked as an explanation for a patient's failed response to an appropriately dosed antibiotic. Based on the fact that the patient's MBC for daptomycin and vancomycin were very similar to the MIC, the treating physicians concluded that these drugs would treat the patient's MRSA strain adequately. The authors say, given their experience with other similar situations, high dose daptomycin might have been a successful treatment if there had been enough time for it to be effective.

Source: *Heart Lung*. 2008;37(5):398-400.
doi:10.1016/j.hrtlng.2007.12.001.

New Help for BPH

The FDA has approved silodosin (Rapaflo, Watson Pharmaceuticals,

Inc, Corona, CA) to treat the signs and symptoms of benign prostatic hyperplasia (BPH). Silodosin acts by blocking alpha-1 adrenoreceptors in the prostate, prostatic capsule, bladder base and neck, urethra, and prostatic urethra. This blockage allows the smooth muscles in those areas to relax and results in improved urine flow.

In two, 12-week, double-blind trials including 923 men, 466 were selected randomly to receive silodosin 8 mg/day. Those patients taking silodosin showed a statistically significant improvement in BPH symptoms and urinary flow rate compared with those taking placebo. Adverse effects included dizziness, diarrhea, orthostatic hypotension, headache, nasopharyngitis, and nasal congestion. The most common adverse effect—retrograde ejaculation—is not a safety concern, the FDA says.

The recommended dose of the new drug is an 8-mg capsule once daily; a 4-mg daily dose will be available for men with moderate kidney impairment. The drug is not recommended for men with severe kidney or liver impairment, and patients planning cataract surgery should notify their ophthalmologist that they are taking silodosin because of the risk of intraoperative floppy iris syndrome, a complication of alpha-1 adrenoreceptor blocker medications.

Prostate cancer and BPH cause many of the same symptoms, and the two diseases often coexist. Therefore, the FDA advises, patients thought to have BPH should be examined prior to starting therapy with silodosin to rule out cancer. ●

Sources: FDA news release. October 10, 2008.

Rapaflo [prescribing information]. Corona, CA: Watson Pharmaceuticals, Inc; September 2008.