Pseudomonas cepacia Susceptibility to Sulbactam

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For 25 of 32 Pseudomonas cepacia isolates, predominantly from sputum of adult patients, agar dilution MICs of sulbactam were 2.5 μg/ml, and for only one was the MIC more than 80 μg/ml. Susceptibility was reliably predicted by response to a commercial sulbactam-ampicillin disk.

Pseudomonas cepacia was originally described as a plant pathogen but has been increasingly recognized as a cause of opportunistic infections in humans (2). Highly versatile metabolically, it can be isolated from soil, water, and the hospital environment, including a variety of medical devices and disinfectant solutions. Although P. cepacia has little capacity to invade the normal host, patients with altered defenses may develop serious infections, including endocarditis, bacteremia, meningitis, osteomyelitis, and pneumonia (5, 7). Patients with cystic fibrosis are especially prone to colonization and pulmonary infection (3).

In part, the success of P. cepacia is the result of its resistance to antibiotics. Isolates are routinely resistant to aminoglycosides, to polymyxins, and to antipseudomonal β-lactams such as ticarcillin. Some are susceptible to chloramphenicol (7), and most are susceptible to trimethoprim-sulfamethoxazole (4), but resistance to even these antimicrobial agents has been a problem in patients with cystic fibrosis (2). P. cepacia is also usually susceptible to ceftazidime, but use of ceftazidime for pulmonary infections in cystic fibrosis patients has produced disappointing results (1). Consequently, the discovery that P. cepacia was susceptible to sulbactam aroused interest.

Although it is used clinically mainly for its β-lactamase-inhibiting properties in combination with an otherwise β-lactamase-unstable penicillin such as ampicillin, sulbactam alone is active against Neisseria gonorrhoeae, Neisseria meningitidis, and some strains of Acinetobacter calcoaceticus (6). Activity against P. cepacia was discovered by chance when a 30-mm zone around a disk containing 30 μg of sulbactam was observed. Accordingly, 32 isolates of P. cepacia from the Massachusetts General Hospital Bacteriology Laboratory were collected between January and September 1988 and tested for susceptibility. Each isolate came from a unique patient. One isolate came from urine, one came from sinus irrigation, two came from postmortem lung samples, and the remainder came from sputum. All the patients were adults, and many were in intensive care units.

Sulbactam disks were made by adding 50 μg of sulbactam (kindly provided by Pfizer Inc., Groton, Conn.) in 20 μl to blank disks which were applied to a lawn of test organisms on Mueller-Hinton agar (Difco Laboratories, Detroit, Mich.) and incubated at 37°C overnight. With one exception, all strains had a zone 30 mm or greater in diameter around the sulbactam disk. Zone diameters around commercial (BBL Microbiology Systems, Cockeysville, Md.) sulbactam-ampicillin disks containing 10 μg of each agent were 24 mm or greater with three exceptions. One strain had no zone around either disk, while two others had indistinct zones of 20 mm or less around sulbactam-ampicillin but zones of 30 mm or more around the disk containing 50 μg of sulbactam alone.

Susceptibility was measured quantitatively by incorporating graded concentrations of sulbactam into Trypticase soy agar (BBL) plates and applying about 10^6 organisms from an overnight culture with a spotting device. The MIC for 25 strains was 2.5 μg/ml. The MIC for three strains was 5 μg/ml. For three others, including the two strains with indistinct zones around sulbactam-ampicillin disk, the MIC was 10 μg/ml. For the single strain with no inhibition zone by disk testing, the MIC was more than 80 μg/ml.

To establish whether organisms could mutate to higher levels of sulfactam resistance, 1 × 10^4 to 3 × 10^5 organisms were spread on Trypticase soy agar plates containing concentrations of sulbactam fourfold or more above the MIC for that strain. Two strains, for which the sulbactam MICs were 2.5 μg/ml, produced no mutants, but one strain, for which the sulbactam MIC was 10 μg/ml, yielded derivatives able to grow on 80 μg of sulbactam per ml at a frequency of 2 × 10^-6.

Since MICs for many isolates of P. cepacia are well below expected peak serum sulbactam levels of 68 μg/ml after an intravenous dose of 1.0/2.0 g of sulbactam-ampicillin (6), the effect of sulbactam treatment in a patient with sputum cultures persistently positive for P. cepacia was studied. The patient was a 57-year-old man who required mechanical ventilation and multiple courses of antibiotics after coronary artery bypass surgery. P. cepacia was first cultured from tracheal aspirates 4 weeks postoperatively and for 8 days was the predominant organism grown. The sulbactam MIC for this isolate was 2.5 μg/ml, and the organism was resistant to ampicillin. The patient was treated with 1.0/2.0 g of sulbactam-ampicillin every 6 h for 3 days. Rare P. cepacia was last cultured on day 2 of therapy, but for 6 weeks thereafter sputum cultures failed to grow the organism.

Further clinical experience will be required to evaluate the efficacy of sulbactam against P. cepacia in other patients, particularly those with cystic fibrosis in whom development of resistance could be a problem with prolonged administration. It must also be recognized that not all clinical isolates of P. cepacia are susceptible to sulbactam when first isolated and that some may become more resistant by mutation. Nonetheless, the susceptibility of P. cepacia to sulbactam illustrates the principle that for certain pathogens sulbactam can be useful for its own antibacterial activity as well as for its ability to inhibit β-lactamase.

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