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Comparison of Susceptibility of Gentamicin-Resistant and -Susceptible "*Acinetobacter anitratus*" to 15 Alternative Antibiotics

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Fifty-four clinical isolates of "*Acinetobacter anitratus*" separated cleanly into gentamicin-susceptible (16 strains) and gentamicin-resistant (38 strains) subpopulations. When tested with a 10^4-CFU inoculum, gentamicin resistance was associated with a greater than fourfold increase in the MICs of norfloxacin, ciprofloxacin, A-56620, tobramycin, and amikacin for 50% of the strains. Antimicrobial agents with MICs for 90% of gentamicin-resistant strains in the susceptible range were ciprofloxacin, A-56619, A-56620, imipenem, SCH-34343, ceftazidime, aztreonam, carbenicillin, ticarcillin, and piperacillin. These agents may be useful alternative drugs for treating infections caused by aminoglycoside-susceptible and -resistant "*A. anitratus*."

Microorganisms of the genus *Acinetobacter* are potential pathogens in hospitalized patients with compromised host defenses. Approximately 70 to 90% of infections occur in patients who have undergone recent antibiotic therapy, tracheal, intravascular, or bladder instrumentation, surgery, or treatment in an intensive care unit (4). Although the incidence of aminoglycoside resistance in "*Acinetobacter anitratus*" may be nonexistent in some institutions (3, 6), in an earlier review of the susceptibility of isolates from the Massachusetts General Hospital from 1978 to 1980, resistance to gentamicin occurred in 29%. Tobramycin resistance and amikacin resistance were less common at 13 and 7%, respectively (5). Various reports (2, 3, 6, 7) have documented the susceptibility of *Acinetobacter* isolates to a wide range of antimicrobial agents, but few have compared aminoglycoside-susceptible and -resistant populations or the effect of the inoculum size of this organism on the MICs. Variability of the MICs of certain antibiotics dependent on inoculum size may occur with certain bacteria but not others (7), and therefore we undertook to examine this question by testing the susceptibility of 54 strains of "*A. anitratus*" to 16 antimicrobial agents, including 9 beta-lactam agents, 3 aminoglycosides, and 4 quinolones (8), at inoculum sizes of 10^4 and 10^6 CFU by a standard agar dilution test (1). Mueller-Hinton agar (BBL Microbiology Systems, Cockeysville, Md.) supplemented with calcium and magnesium (1) was inoculated, by using a Steers replicator device with Trypticase soy broth (BBL Microbiology Systems) cultures of each organism. The 10^6-CFU inoculum was from an undiluted overnight broth culture. The 10^4-CFU inoculum was prepared by adjusting an overnight broth culture to a 0.5 McFarland standard and making a 1:20 dilution. Standard reference strains *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, and *Staphylococcus aureus* ATCC 25923 were tested in each run to assure reproducibility. One hundred percent of the MICs recorded for these organisms after nine separate runs fell within one dilution of the modal MIC of each antimicrobial agent. The "*A. anitratus*" strains were recovered from hospitalized patients with a variety of clinical infections and did not wholly represent the nosocomial flora of patients in a specialized hospital unit, although a large proportion came from the intensive care and burn units, where there was a high rate of aminoglycoside resistance among gram-negative isolates. "*A. anitratus*" was identified to the species level by using API NFT (Analytab Products, Plainview, N.Y.) strips. The antibiotics, supplied as powders, were as follows: norfloxacin and imipenem (Merck & Co., Inc., Rahway, N.J.); ciprofloxacin (CIBA-GEIGY Inc., Basel, Switzerland); A-56619, A-56620, and cefsulodin (Abbott Laboratories, North Chicago, Ill.); gentamicin and SCH-34343 (Schering Corp., Bloomfield, N.J.); tobramycin (Eli Lilly & Co., Indianapolis, Ind.); amikacin and carbenicillin (Bristol Laboratories, Syracuse, N.Y.); ticarcillin (Beecham Laboratories, Bristol, Tenn.); piperacillin (Lederle Laboratories, Pearl River, N.Y.); aztreonam (E. R. Squibb & Sons, Princeton, N.J.); cefoperazone (Pfizer Inc., New York, N.Y.); and ceftazidime (Glaxo Pharmaceuticals, Ltd., Greenford, United Kingdom).

The quinolone agents and the carbapenems imipenem and SCH-34343 had the lowest MICs. The MICs of most agents for 50% of the strains increased fourfold or more with the larger inoculum (10^6 CFU). Considering concentrations achieved in serum by a given dose, imipenem was the most active of all the agents tested.

The "*A. anitratus*" strains separated cleanly into 16 gentamicin-susceptible strains for which the MICs were $\leq$4.0 μg/ml and 38 gentamicin-resistant strains for which the MICs were $\geq$32 μg/ml with the 10^4-CFU inoculum. The susceptibilities of gentamicin-susceptible and -resistant strains to alternative antibiotics are listed in Table 1. Compared to gentamicin-susceptible organisms, the MICs of norfloxacin, ciprofloxacin, A-56620, tobramycin, and amikacin for 50% of the gentamicin-resistant strains increased more than fourfold. Interestingly, there was a reverse shift with carbenicillin, ticarcillin, and piperacillin, the MICs for 50% of the gentamicin-resistant strains being more than fourfold lower than those for 50% of the gentamicin-susceptible strains. The following antibiotics had MICs for 90% of the gentamicin-resistant isolates in the susceptible range: ciprofloxacin, A-56619, A-56620, imipenem, SCH-34343, ceftazidime, aztreonam, carbenicillin, ticarcillin, and piperacillin. These antimicrobial agents may be useful alternative agents in the therapy of infections caused by aminoglycoside-resistant as well as -susceptible "*A. anitratus*."

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TABLE 1. Susceptibility of 54 strains of "*A. anitratus*" to 16 antimicrobial agents according to gentamicin susceptibility

Antibiotic	MIC (μg/ml)[a]					
	Range		50%		90%	
	GMS	GMR	GMS	GMR	GMS	GMR
Gentamicin	≤0.5–4	32–128	2	32	4	128
Tobramycin	≤0.5–32	≤0.5–≥512	2	32	16	32
Amikacin	≤0.5–8	32–≥512	4	64	8	128
Norfloxacin	4–64	4–≥128	8	32	16	64
Ciprofloxacin	≤0.25–2	1–8	1	2	1	4
A-56619	≤0.25–1	0.5–8	0.5	1	0.5	1
A-56620	≤0.25–1	0.5–8	0.5	2	1	2
Imipenem	0.5–1	1–4	1	2	1	4
SCH-34343	≤0.25–16	2–64	8	4	8	8
Ceftazidime	1–32	4–≥128	8	8	16	8
Aztreonam	4–≥128	8–≥128	32	16	64	16
Cefsulodin	2–64	64–≥128	64	≥128	64	≥128
Cefoperazone	8–≥128	8–≥128	64	32	≥128	≥128
Carbenicillin	≤2–128	4–≥1,024	32	8	64	32
Ticarcillin	≤2–64	4–512	32	8	64	16
Piperacillin	4–128	4–512	32	16	128	32

[a] 50% and 90%, MIC for 50 and 90% of the strains, respectively. GMS, Gentamicin-susceptible strains (MIC, ≤4.0 μg/ml), n = 16. GMR, Gentamicin-resistant strains (MIC, ≥32.0 μg/ml), n = 38.

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