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Cross-Resistance of *Pseudomonas* to Gentamicin and Tobramycin

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Clinical isolates of gentamicin-resistant organisms were found to be resistant to tobramycin, a new aminoglycoside antibiotic.

Tobramycin (nebramycin factor 6) is a new aminoglycoside antibiotic that is said to be from two to four times more active than gentamicin against strains of *Pseudomonas* (3). The purpose of this study was to determine the effect of this agent on *Pseudomonas* and other bacterial species resistant to gentamicin.

All of the organisms included in this study were recent clinical isolates. Of the 13 strains of *Pseudomonas* examined, 4 appeared to be clinically significant on the basis of their recovery from patients with urinary tract infection, wound sepsis, bacteremia, and chronic otitis media.

Minimal inhibitory concentrations of the drugs were determined by serial twofold dilution in Trypticase Soy Broth (Difco) and inoculation with approximately 10^5 organisms. The cultures were examined for turbidity after incubation at 37 C for 18 hr. Those showing no visible growth were subcultured on Trypticase Soy Agar. The lowest concentration from which subculture on agar was sterile was considered the minimal bactericidal concentration.

Cross-resistance between the two antibiotics was also studied by using strains of *P. aeruginosa* made resistant to gentamicin by serial transfer in increasing concentrations of the drug in Trypticase Soy Broth. After eight transfers, the minimal inhibitory concentrations for four strains rose from 3.125 to 6.25 μg/ml to 50 to 100 μg/ml.

Antimicrobial sensitivities were also determined by the standardized Kirby-Bauer technique (1) using discs containing 10 μg of tobramycin or gentamicin.

Pseudomonas strains resistant to 50 μg or more of gentamicin per ml were not inhibited by 25 μg of tobramycin per ml (Table 1). The minimal bactericidal concentrations were similar.

Cross-resistance between these agents was also demonstrated in 2 strains of *Citrobacter*, 3 of *Mima*, 5 of *Herellea*, 5 of *Providence*, and in 12 eugonic oxidase-positive, gram-negative rods.

Four strains of *P. aeruginosa* in which resistance to gentamicin was induced by serial transfer showed an increase in the minimal inhibitory concentration of tobramycin from 0.4 μg/ml to 12.5 μg/ml to 50 μg/ml. This represented a 30- to 120-fold increase in the minimal inhibitory concentration of tobramycin for each strain.

The results of sensitivity testing by the Kirby-Bauer method are also shown in Table 1. The zones produced by 10-μg discs of gentamicin and tobramycin were approximately equal in size. Two of the *Pseudomonas* strains appeared very sensitive to gentamicin (zone >12 mm) and tobramycin (zone >16 mm) when studied by this technique, despite apparent high-level resistance when studied by the broth-dilution method. Retesting and incubation for 48 hr failed to alter these results.

Our data indicate that clinical isolates of gentamicin-resistant bacteria are also resistant to tobramycin. A similar phenomenon was observed in strains of *P. aeruginosa* made resistant to gentamicin in vitro.

These results differ from those reported by Black and Griffith (2). They found that five strains of *Pseudomonas*, resistant to greater than 25 μg of gentamicin per ml, were sensitive to 0.5 μg of tobramycin per ml, suggesting a lack of cross-resistance between these drugs. The explanation for the discrepancy between our results and theirs is not apparent but may be related to strain differences.

Gentamicin solution and discs were provided by the Schering Corp. Tobramycin solution and discs were from Eli Lilly & Co.

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TABLE 1. *Susceptibility to tobramycin of Pseudomonas resistant to gentamicin*

Resistance to gentamicin	*Pseudomonas* strain no.	MIC[a] (μg/ml)		MBC[b] (μg/ml)		Zone diam. (mm)	
		Gentamicin	Tobramycin	Gentamicin	Tobramycin	Gentamicin	Tobramycin
Natural	6967	>100	>100	>100	>100	14	14
	2358	>100	>100	>100	>100	6	6
	5695	>100	>100	>100	>100	29	35
	5495	100	100	100	100	0	0
	865	100	100	100	100	0	0
	5827	50	25	50	50	18.0	18.0
	8482						
	6866	50	50	50	50	12.5	11.0
	6866	50	50	50	50	10	10
	171	>100	>100	>100	>100	0	0
	4589	100	100	>100	>100	0	0
	3887–43	>100	>100	>100	>100	6	6
	2016–50	>100	>100	>100	>100	6	6
Induced in vitro	288	50	12.5	50	25	8	10
	524	100	50	100	50	10	10
	900	50	12.5	100	25	14	14
	741	100	12.5	100	50	12	12

[a] Minimal inhibitory concentration.
[b] Minimal bactericidal concentration.

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