

Comparative In Vitro Activity of Sch 20656, Netilmicin, Gentamicin, and Tobramycin

CHATRCHAI WATANAKUNAKORN

Department of Internal Medicine, University of Cincinnati College of Medicine, Cincinnati, Ohio 45267

Received for publication 3 May 1976

Sch 20656 and netilmicin (Sch 20569), two new semisynthetic aminoglycosides, were as active as gentamicin and tobramycin against *Enterobacteriaceae*. Against *Pseudomonas aeruginosa*, Sch 20656 was the least active, whereas netilmicin was active against many highly gentamicin-resistant isolates.

Due to the marked increase in the prevalence of serious infections caused by gram-negative bacilli in the past decade, the clinical use of aminoglycoside antibiotics has become widespread, resulting in steady increases in the number of gram-negative bacilli resistant to clinically available aminoglycosides. Continued efforts have been made by pharmaceutical manufacturers to develop new aminoglycosides effective against resistant gram-negative bacilli and with less toxic potentials.

Sch 20656 and netilmicin (Sch 20569) are two new semisynthetic aminoglycosides structurally similar to the gentamicin complex. In this study, the in vitro activity of Sch 20656 and netilmicin was compared with that of gentamicin and tobramycin against *Pseudomonas aeruginosa* and members of the family *Enterobacteriaceae*. A total of 337 clinical isolates were obtained from the Clinical Microbiology Laboratories of the Cincinnati General Hospital and the Cincinnati Veterans Administration Hospital. These consisted of *P. aeruginosa* (140 isolates), *Escherichia coli* (72 isolates), *Klebsiella* sp. (36 isolates), *Enterobacter* sp. (18 isolates), *Serratia* sp. (18 isolates), *Proteus mirabilis* (41 isolates), and indole-positive *Proteus* sp. (12 isolates). Many of the *P. aeruginosa* isolates were known to be resistant to gentamicin but susceptible to tobramycin (4).

The minimal inhibitory concentration (MIC) of Sch 20656, netilmicin, gentamicin, and tobramycin was determined by the agar dilution method recommended by the WHO International Collaborative Study on antimicrobial susceptibility testing (1). Mueller-Hinton agar (Difco Laboratories, Detroit, Mich.) was used. The inoculum was 0.002 ml of a 10^{-2} dilution of an 18-h culture (approximately 10^3 to 10^4 organisms), delivered by a Steers replicator (3). For

a given clinical isolate, the MIC of the four aminoglycosides was determined simultaneously by using the same inoculum.

The cumulative percent susceptibility of the organisms to the four aminoglycosides is listed in Table 1. Against *P. aeruginosa*, Sch 20656 was the least active, whereas netilmicin was less effective overall than gentamicin or tobramycin. However, at 32 $\mu\text{g/ml}$, more isolates (81.4%) were susceptible to netilmicin than to gentamicin (62.1%), and at 64 $\mu\text{g/ml}$ the percent susceptible was almost the same for netilmicin (93.6%) and tobramycin (98.6%). Of the 45 isolates with an MIC >64 μg of gentamicin per ml, the MIC of netilmicin was >64 $\mu\text{g/ml}$ for 6, 64 $\mu\text{g/ml}$ for 11, 32 $\mu\text{g/ml}$ for 19, and 16 $\mu\text{g/ml}$ for 9 isolates. The four aminoglycosides appeared to be equally effective against members of *Enterobacteriaceae* tested.

This study was supported by a grant from Schering Corp., Bloomfield, N.J., and by the Morton Hamburger Memorial Fund.

I thank Thomas Bannister for excellent technical assistance.

LITERATURE CITED

1. Ericsson, H. M., and J. C. Sherris. 1971. Antibiotic sensitivity testing: report of an international collaborative study. *Acta Pathol. Microbiol. Scand. Sect. B* 217(Suppl):1/90.
2. Schering Corporation. 1975. Informational material for the investigational drug Sch 20569. Schering Corp., Bloomfield, N.J.
3. Steers, E., E. L. Foltz, and B. S. Graves. 1959. An inocula replicating apparatus for routine testing of bacterial susceptibility to antibiotics. *Antibiot. Chemother.* 9:307-311.
4. Watanakunakorn, C., and T. Bannister. 1975. In vitro activity of tobramycin and gentamicin against *Enterobacteriaceae* and gentamicin-resistant, carbenicillin-resistant *Pseudomonas aeruginosa*. *Curr. Ther. Res.* 17:488-496.

TABLE 1. Comparative *in vitro* susceptibility of *P. aeruginosa* and *Enterobacteriaceae* to four aminoglycoside antibiotics

Determinants	No. tested	Cumulative % susceptibility at increasing concn ($\mu\text{g/ml}$)								
		0.5	1	2	4	8	16	32	64	>64
<i>P. aeruginosa</i>	140									
Tobramycin		1.4	7.9	44.3	70.7	86.4	90.0	96.4	98.6	100
Gentamicin		0	0.7	0.7	12.9	45.7	58.6	62.1	67.9	100
Sch 20656		0.7	0.7	1.4	1.4	3.6	11.4	47.9	87.1	100
Netilmicin		0.7	0.7	1.4	2.9	11.4	45.0	81.4	93.6	100
<i>E. coli</i>	72									
Tobramycin		1.4	38.9	80.6	91.7	91.7	94.4	98.6	98.6	100
Gentamicin		2.8	45.8	75.0	91.7	94.4	95.8	98.6	98.6	100
Sch 20656		0	19.4	69.4	93.1	95.8	98.6	98.6	98.6	100
Netilmicin		0	23.6	72.2	93.1	95.8	98.6	98.6	98.6	100
<i>Klebsiella</i>	36									
Tobramycin		2.8	83.3	91.7	94.4	97.2	97.2	97.2	100	100
Gentamicin		5.6	86.1	91.7	94.4	97.2	97.2	97.2	100	100
Sch 20656		2.8	83.3	91.7	94.4	97.2	97.2	100	100	100
Netilmicin		2.8	80.6	91.7	97.2	97.2	97.2	100	100	100
<i>Enterobacter</i>	18									
Tobramycin		11.1	77.8	88.9	100	100	100	100	100	100
Gentamicin		22.2	88.9	94.4	94.4	100	100	100	100	100
Sch 20656		0	50.0	94.4	100	100	100	100	100	100
Netilmicin		0	77.8	88.9	100	100	100	100	100	100
<i>Serratia</i>	18									
Tobramycin		0	0	55.6	88.9	94.4	100	100	100	100
Gentamicin		11.1	77.8	83.3	94.4	100	100	100	100	100
Sch 20656		0	72.2	83.3	94.4	100	100	100	100	100
Netilmicin		0	0	61.1	94.4	100	100	100	100	100
<i>P. mirabilis</i>	41									
Tobramycin		0	22.0	78.0	90.2	95.1	95.1	97.6	97.6	100
Gentamicin		0	24.4	68.3	90.2	95.1	97.6	100	100	100
Sch 20656		0	0	19.5	80.5	92.7	97.6	97.6	100	100
Netilmicin		0	0	17.1	90.2	95.1	97.6	100	100	100
Other <i>Proteus</i> sp.	12									
Tobramycin		0	8.3	33.3	83.3	83.3	83.3	91.7	91.7	100
Gentamicin		0	8.3	33.3	66.7	75.0	91.7	91.7	91.7	100
Sch 20656		0	8.3	50.0	66.7	75.0	83.3	91.7	91.7	100
Netilmicin		0	0	8.3	41.7	75.0	83.3	83.3	91.7	100