NOTES

Comparative In Vivo Activities of Cefsulodin, Sulbenicillin, and Gentamicin Against *Pseudomonas aeruginosa*

MASAHIRO KONDO AND KANJI TSUCHIYA*

Central Research Division, Takeda Chemical Industries, Ltd., Osaka, Japan

Received for publication 22 February 1978

The in vivo activities of cefsulodin, sulbenicillin, and gentamicin were compared in mice infected intraperitoneally with *Pseudomonas aeruginosa*. In mice infected with sulbenicillin- and gentamicin-susceptible strains, cefsulodin was about 12 to 60 times more active than sulbenicillin and had an activity similar to gentamicin. In mice, the activity of cefsulodin was independent whether the strains were resistant to gentamicin or not, but it was considerably affected by resistance of the strains to sulbenicillin.

Cefsulodin [3-(4-carbamoyl-1-pyridiniumyl)-7β-(D-α-sulfo
dephenylacetamido)-ceph-3-em-4-carboxylate monosodium salt, previously named SCE-129] has a marked in vitro antibacterial activity against clinical isolates of *Pseudomonas aeruginosa*, including gentamicin-resistant strains. The activity of cefsulodin against sulbenicillin- and carbenicillin-resistant strains of *P. aeruginosa*, however, is inferior to that against susceptible strains (12). Furthermore, it has been reported by Tsuchiya et al. (13) that the activity of cefsulodin is greater in vivo than in vitro.

In the present study, the protective activity of cefsulodin in mice infected intraperitoneally with *P. aeruginosa* was compared to those of sulbenicillin and gentamicin. Cefsulodin was purchased from Shionogi Pharmaceutical Co. Three (N18, NC-5, U31) of the four sulbenicillin- and gentamicin-susceptible strains of *P. aeruginosa* were provided by Y. J. Honma, Institute of Medical Science, University of Tokyo, and the remaining one (SP) was available as a laboratory standard strain. One (TN 1362 = KB 333) of the three gentamicin-resistant strains of *P. aeruginosa* was supplied by M. Koike, Kyushu University, and the other two (TN 1351 = Ju 200; TN 1352 = Ju 376) by N. Kozakai, Juntendo Medical School. The three sulbenicillin-resistant strains (GN 3341, GN 3345, GN 3416) of *P. aeruginosa* were supplied by S. Mitsuhashi, Gunma University. The laboratory strains and clinical isolates were maintained in Dorset egg medium (Nissui) and on Trypticase soy agar (BBL), cultivated at 37°C overnight in King A broth, and suspended in 5% mucin (Laboratories Division of Wilson Pharmaceutical and Chemical Corp.). Four-week-old male SLC-ICR mice weighing 19 to 23 g were infected intraperitoneally with 0.5 ml of the bacterial suspension in 5% mucin. The challenge dose of each infection was about 100 times the number of organisms required to kill 50% of the challenge-control mice. Groups of five mice for each dosage level were treated subcutaneously with 0.2 ml of antibiotic solution at 0, 2, and 4 h after infection. All experiments were repeated four to five times. The 50% effective dose (in milligrams per kilogram) was calculated by the probit method from the survival rate of the animals recorded on day 5 after infection (5). Minimum inhibitory concentrations were determined by the agar dilution method (12).

In mice infected intraperitoneally with sulbenicillin- and gentamicin-susceptible strains of *P. aeruginosa*, the protective activity of cefsulodin was similar to that of gentamicin. *P. aeruginosa* N18 was highly susceptible to sulbenicillin as well as to cefsulodin in vitro, but in mice infected with this organism cefsulodin was about 12 times more potent than sulbenicillin. The in vitro activity of cefsulodin against *P. aeruginosa* SP, NC-5, and U31 was 8, 16, and 4 times that of sulbenicillin, respectively, but in mice infected with these strains cefsulodin showed 60, 40, and 18 times more activity than sulbenicillin. Similar observations were made in a comparative experiment of the protective activity of cefsulodin and carbenicillin in mice infected with *P. aeruginosa* (13) (Table 1). In mice infected with gentamicin-
resistant strains of *P. aeruginosa*, cefsulodin was 16 to 33 times more active than sulbenicillin. The 50% effective dose levels of cefsulodin and sulbenicillin in mice infected with gentamicin-resistant strains were similar to those obtained in mice infected with strains susceptible to sulbenicillin and gentamicin. The activity of cefsulodin in mice infected with sulbenicillin-resistant *P. aeruginosa* was inferior to that in mice infected with sulbenicillin-susceptible strains, but was similar to that of sulbenicillin in mice infected with sulbenicillin-susceptible strains.

Among gentamicin-resistant strains of *P. aeruginosa*, some are susceptible to amikacin (4), tobramycin (3), sisomicin (16), and netilmicin (8), but many are resistant to these aminoglycoside antibiotics. These aminoglycoside antibiotics also have been considered to result in otic- and nephrotoxicity, as gentamicin does (2, 6, 10). Recently reported semisynthetic penicil
lins such as ticarcillin (11), BL-P 1654 (15), mezlocillin (1), pibencillin (9), PC 904 (7), and piperacillin (14) are active against *P. aeruginosa* but ineffective against carbenicillin- and sulbenicillin-resistant strains. Cefsudozin had the same activity against both gentamicin-susceptible and gentamicin-resistant strains of *P. aeruginosa* in vivo. In mice, cefsudozin was also active against sulbenicillin- and carbenicillin-resistant strains. These results correlate well with those obtained in the in vitro experiments and suggest that cefsudozin might be a useful chemotherapeutic agent in the treatment of infections due to *P. aeruginosa*.

**LITERATURE CITED**