Comparative In Vitro Activity of Sch 29,482, a New Oral Penem, Against Neisseria gonorrhoeae

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Sch 29,482 is a new oral β-lactam (penem) antimicrobial agent with a broad spectrum of antibacterial activity against both gram-negative and gram-positive bacteria (10). It is stable to the action of most bacterial β-lactamases (10). The purpose of our study was to evaluate the in vitro activity of Sch 29,482 against β-lactamase-negative and β-lactamase-positive Neisseria gonorrhoeae strains. Because Sch 29,482 is an oral antimicrobial agent, we compared its activity with five other oral agents currently under investigation or in use for gonococcal infections.

Standard powders with known potency were obtained from the following sources: Sch 29,482, Schering Corp., Bloomfield, N.J.; norfloxacin, Merck Institute for Therapeutic Research, Rahway, N.J.; roxsoacin, Sterling-Winthrop Research Institute, Rensselaer, N.Y.; ampicillin, Bristol Laboratories, Syracuse, N.Y.; erythromycin, Abbott Laboratories, North Chicago, Ill.; and tetracycline, Pfizer Inc., New York.

A total of 142 N. gonorrhoeae strains were tested. One hundred β-lactamase-negative strains were collected during 1980 through 1981 from patients with anogenital infections at the Hennepin County Medical Center, Minneapolis, Minn. Forty-two β-lactamase-positive strains were obtained from the following sources: W. Harrison, Naval Regional Medical Center, San Diego, Calif.; Centers for Disease Control, Atlanta, Ga.; W. Hall, Veterans Administration Medical Center, Minneapolis, Minn.; and Minnesota Department of Health, Minneapolis.

The identity of the isolates was confirmed by growth on Thayer-Martin agar, Gram stain, positive oxidase reaction, and utilization of glucose but not of maltose, lactose, or sucrose. The organisms were frozen in Mueller-Hinton broth containing 15% glycerol and stored at −70°C. N. gonorrhoeae isolates were tested for β-lactamase activity by an acidimetric method (9).

The minimal inhibitory concentrations (MICs) of Sch 29,482, norfloxacin, roxsoacin, ampicillin, erythromycin, and tetracycline were determined by an agar dilution technique (7). Twofold dilutions of the antimicrobial agents, from 8 to 0.004 μg/ml, were distributed into Mueller-Hinton agar supplemented with 2% hemoglobin and 1% IsoVitaleX. The frozen gonococcal isolates were thawed and grown overnight on chocolate agar and then suspended in tryptic soy broth until the turbidity matched that of a 0.5 McFarland standard. One microliter of a 1:10 dilution of the adjusted suspension (104 CFU) was inoculated onto the antimicrobial agent-containing plates with a Steers replicator. The plates were incubated for 18 to 24 h at 35°C in a CO2 atmosphere. The minimal inhibitory concentration was defined as the lowest concentration of the antimicrobial agent that inhibited visible growth on the agar surface.

The MICs for the six antimicrobial agents against N. gonorrhoeae are shown in Table 1. Sch 29,482 was highly active against both β-lactamase-negative and -positive isolates; 90% of the isolates were inhibited by Sch 29,482 at a concentration of ≤0.06 μg/ml. Norfloxacin and roxsoacin were essentially equal to Sch 29,482 in activity against both N. gonorrhoeae groups.

The currently available oral antimicrobial agents erythromycin and tetracycline were less active than Sch 29,482, norfloxacin, and roxsoacin against both groups of isolates. Ampicillin inhibitory activity was dependent on β-lactamase production by N. gonorrhoeae. Good activity was demonstrated against β-lactamase-
negative isolates. As expected, β-lactamase-positive isolates were highly resistant to ampicillin.

Several new cephalosporins have been shown to be effective in N. gonorrhoeae infections, including those due to β-lactamase-positive strains (1, 3, 6, 8). However, these antimicrobial agents are available only in parenteral form and are not preferred by some patients with gonorrhea. The currently available oral antimicrobial agents ampicillin, erythromycin, and tetracycline are not effective in β-lactamase-positive N. gonorrhoeae infections. It is desirable to have alternate oral therapy available for these infections.

In our study, MICs of Sch 29,482 against N. gonorrhoeae are similar to those reported by others (2; C. Thornsberry and C. N. Baker, Program Abstr. Intersci. Conf. Antimicrob. Agents Chemother. 21st, Chicago, Ill., abstr. no. 747, 1981). Of the six oral antimicrobial agents tested in our study, Sch 29,482 was found to be as active as norfloxacin and roxsoxacin. Norfloxacin and roxsoxacin are related to nalidixic acid and are currently undergoing clinical trials in gonococcal infections (5; Y. Nishimura, H. Kishi, O. Tsukada, T. Tominaga, and T. Niijima, Program Abstr. Intersci. Conf. Antimicrob. Agents Chemother. 20th, New Orleans, La., abstr. no. 76, 1980). After a single oral dose of 1.0 g, Sch 29,482 gave a peak serum level of 22.7 μg/ml, with a half-life of 1.30 h (4). This level is markedly greater than the MIC of Sch 29,482 required to inhibit all N. gonorrhoeae strains tested in our study, suggesting that Sch 29,482 would be effective in the oral therapy of gonococcal infections. However, clinical trials to verify the efficacy of Sch 29,482 in treating gonococcal infections are warranted.

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