ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Nov. 1979, p. 641-643
0066-4804/79/11-0641/03$02.00/0

Vol. 16, No. 5

LY127935, a New Beta-Lactam Antibiotic, Versus *Proteus, Klebsiella, Serratia,* and *Pseudomonas*

D. J. FLOURNOY[1,2]* AND FRED A. PERRYMAN[2]

Clinical Microbiology Section, Veterans Administration Medical Center (113), Oklahoma City, Oklahoma 73104,[1] and Department of Microbiology and Immunology, Oklahoma University Health Sciences Center, Oklahoma City, Oklahoma 73190[2]*

Received for publication 27 June 1979

One hundred eight clinical isolates of *Proteus, Klebsiella, Serratia,* and *Pseudomonas* spp. were tested in vitro against LY127935, cefamandole, cefoxitin, ticarcillin, carbenicillin, gentamicin, tobramycin, and amikacin by broth microdilution. The activities of LY127935 were greater than or equal to those of the other antimicrobial agents against *Proteus vulgaris, Klebsiella pneumoniae,* and *Serratia marcescens.* Inhibitions were greatest, however, for ticarcillin and carbenicillin versus *Proteus morganii* and gentamicin versus *Pseudomonas aeruginosa.*

LY127935 is a new semisynthetic β-lactam antibiotic intended for parenteral use against a broad spectrum of microorganisms. This study compares LY127935 with seven commonly used antimicrobial agents against four bacterial genera which are potentially troublesome at the Veterans Administration Medical Center, Oklahoma City, Okla.

MATERIALS AND METHODS

Antimicrobial agents. Antimicrobial agents were supplied as follows: LY127935 powder and 30-μg disks, cefamandole powder, and tobramycin solution (Eli Lilly & Co.); ticarcillin and carbenicillin powders (Beecham Laboratories); cefoxitin powder (Merck Sharp & Dohme); gentamicin powder (Schering Laboratories); and amikacin powder (Bristol Laboratories).

Isolates. One hundred eight randomly selected clinical isolates of *Proteus* (indole positive), *Klebsiella, Serratia,* and *Pseudomonas* spp. were collected over a 3-month period from March through June 1979. Organisms were identified by conventional methods in the Clinical Microbiology Section of the Veterans Administration Medical Center. All isolates were lyophilized and then later subcultured onto Mueller-Hinton agar (Difco) before testing.

Susceptibility testing. Disk-agar diffusion testing (2) was performed on all isolates with 30-μg LY127935 disks. Minimum inhibitory concentrations (MICs) were determined by a broth microdilution method, using Mueller-Hinton broth (Difco). The inoculum consisted of 0.05 ml of a 1:700 dilution of a bacterial suspension (10^5 organisms/ml) with a turbidity equal to that of a 0.5 MacFarland standard (25 to 30 Klett-Summerson colorimeter units). The final volume in each microdilution plate well was 0.1 ml. Microdilution plates were incubated for 18 to 24 h at 35°C. The MIC was taken as the highest dilution of antimicrobial agent in which no growth appeared.

RESULTS

Table 1 shows MICs for the eight antimicrobial agents. Of significant note are the activities of LY127935 against the various species. None of the other drugs exhibited such a broad spectrum of activity as that of LY127935. The new drug was less impressive against *Pseudomonas aeruginosa* isolates, although its activity was better than those of the other β-lactams tested. There were five *Serratia marcescens* strains which were resistant to all antimicrobial agents tested except LY127935.

After storing the antimicrobial agent solutions (1,000 μg/ml) at 4 to 8°C for 4 days, four isolates were retested, and the MICs remained similar to the originals, indicating no significant loss in activity upon limited storage.

Disk-agar diffusion tests with 30-μg LY127935 disks showed the following MIC-zone size correlations: 11-mm zone size (125-μg/ml MIC), 13 mm (62 μg/ml), 17 mm (31 μg/ml), 21 mm (16 μg/ml), and 26 mm (8 μg/ml); zone sizes greater than 29 mm could not differentiate MICs between 4 and ≤ 0.5 μg/ml.

DISCUSSION

This study was done to determine if the new drug LY127935 was better than other currently used antimicrobial agents against six potential nosocomial pathogens. Indole-positive *Proteus* spp. and *S. marcescens* strains at the Veterans Administration Medical Center in Oklahoma City are more antibiotic resistant than those of other nearby institutions (5). *P. aeruginosa* isolates at this institution are also less likely to be inhibited synergistically by gentamicin-carbeni-

TABLE 1. *Comparison of MICs for eight antimicrobial agents against six species*

Species (no. of isolates tested)	Antimicrobial agent	MIC (μg/ml)		
		MIC_{50}[a]	MIC_{90}[b]	Range
Proteus morganii (9)	LY127935	4	8	≤0.5–31
	Cefamandole	1	16	≤0.5–16
	Cefoxitin	8	8	1.0–16
	Ticarcillin	1	4	≤0.5–8
	Carbenicillin	≤0.5	4	≤0.5–8
	Gentamicin	6.25	12.5	0.37–12.5
	Tobramycin	12.5	25	1.5–25
	Amikacin	25	50	6.25–50
Proteus rettgeri (10)	LY127935	2	16	≤0.5–500
	Cefamandole	8	250	1.0–250
	Cefoxitin	4	16	4–125
	Ticarcillin	250	>500	4–>500
	Carbenicillin	500	>500	4–>500
	Gentamicin	50	100	0.37–100
	Tobramycin	50	100	1.5–>100
	Amikacin	12.5	50	0.18
Proteus vulgaris (7)	LY127935	4	8	≤0.5–8
	Cefamandole	250	500	1.0–500
	Cefoxitin	4	8	2–8
	Ticarcillin	31	62	2–62
	Carbenicillin	125	125	1–125
	Gentamicin	1.5	12.5	0.18–12.5
	Tobramycin	12.5	50	0.37–50
	Amikacin	12.5	50	1.5–50
Klebsiella pneumoniae (27)	LY127935	2	8	≤0.5–16
	Cefamandole	≤0.5	8	≤0.5–16
	Cefoxitin	2	8	≤0.5–62
	Ticarcillin	250	>500	31–>500
	Carbenicillin	500	>500	125–>500
	Gentamicin	0.37	12.5	≤0.09–50
	Tobramycin	12.5	25	≤0.09–50
	Amikacin	6.25	50	0.18–50
Serratia marcescens (27)	LY127935	8	16	≤0.5–250
	Cefamandole	>500	>500	8–>500
	Cefoxitin	62	250	8–250
	Ticarcillin	>500	>500	2–>500
	Carbenicillin	>500	>500	4–>500
	Gentamicin	50	100	≤0.09–>100
	Tobramycin	50	100	3.12–>100
	Amikacin	50	50	1.5–100
Pseudomonas aeruginosa (28)	LY127935	16	125	4–500
	Cefamandole	>500	>500	62–>500
	Cefoxitin	>500	>500	62–>500
	Ticarcillin	31	125	2–250
	Carbenicillin	62	250	1.0–500
	Gentamicin	1.5	12.5	≤0.09–>100
	Tobramycin	6.25	25	≤0.09–>100
	Amikacin	12.5	50	≤0.09–100

[a] MIC_{50}, Concentration required for inhibition of 50% of strains.
[b] MIC_{90}, Concentration required for inhibition of 90% of strains.

cillin combinations than are those at other Oklahoma City institutions (4). Therefore, the isolates tested provide a significant challenge for new drugs.

Several new β-lactam antibiotics (e.g., cefamandole and cefoxitin) having extended spectrums (1, 3, 6, 7) have recently been marketed. Upon comparison, LY127935 activities were significantly greater than those of cefamandole and cefoxitin against *S. marcescens* and *P. aeruginosa* isolates. In addition, it produced a broader spectrum of inhibition than did any of the cur-

rently used drugs, and it may be useful for multiple-antibiotic-resistant strains of *S. marcescens*.

ACKNOWLEDGMENT

This work was supported by Clinical Grant no. 8352D from the Lilly Research Laboratories.

LITERATURE CITED

1. **Adams, H. G., G. A. Stilwell, and M. Turck.** 1976. In vitro evaluation of cefoxitin and cefamandole. Antimicrob. Agents Chemother. **9**:1019–1024.
2. **Bauer, A. W., W. M. Kirby, J. C. Sherris, and M. Turck.** 1966. Antibiotic susceptibility testing by a standardized single disc method. A. J. Clin. Pathol. **45**:493–496.
3. **Chow, A. W., and D. Bednorz.** 1978. Comparative in vitro activity of newer cephalosporins against anaerobic bacteria. Antimicrob. Agents Chemother. **13**:668–671.
4. **Flournoy, D. J., K. M. Cunningham, and E. R. Rhoades.** 1979. Variation in response of *Pseudomonas aeruginosa* to combinations of gentamicin and carbenicillin. J. Okla. State Med. Assoc. **72**:145–149.
5. **Flournoy, D. J., N. S. Parker, and W. R. Sackett.** 1979. Variations in antimicrobial susceptibility patterns among three hospitals. Lab. Med. 10:39–41.
6. **Jones, R. N., and P. C. Fuchs.** 1976. Comparison of in vitro antimicrobial activity of cefamandole with cephalothin against over 8,000 clinical bacterial isolates. Antimicrob. Agents Chemother. **9**:1066–1069.
7. **Rylander, M., J. E. Brorson, J. Johnsson, and R. Norrby.** 1979. Comparison between agar and broth minimum inhibitory concentrations of cefamandole, cefoxitin, and cefuroxime. Antimicrob. Agents Chemother. **15**:572–579.