ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Aug. 1983, p. 297-299
0066-4804/83/080297-03$02.00/0

Vol. 24, No. 2

In Vitro Activities of New β-Lactam Antibiotics Against *Acinetobacter* spp.

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Received 17 January 1983/Accepted 7 June 1983

The in vitro activities of new β-lactam antibiotics was studied and compared with those of other known agents against 51 clinical isolates of *Acinetobacter calcoaceticus* subsp. *anitratus* and 23 isolates of *A. calcoaceticus* subsp. *lwoffi*. Of the new β-lactam antibiotics, imipemide (*N*-formimidoyl thienamycin), ceftazidime, ceftizoxime, ceftriaxone, and piperacillin demonstrated good activities. The minimal inhibitory concentrations for *A. calcoaceticus* subsp. *lwoffi* were lower than those obtained for *A. calcoaceticus* subsp. *anitratus*.

Several β-lactam antibiotics, mostly semisynthetic in nature, have been developed in the last few years. These antibiotics have multiple advantages that include good distribution, minimal toxicity, broad spectra of activity, high achievable serum concentrations, resistance to degradation by β-lactamases, and prolonged half-lives (1–5, 8). Because of these properties, the majority of these antimicrobial agents can be evaluated in immunocompromised patients. *Acinetobacter calcoaceticus* has assumed significance in treating clinical infections and was isolated at our institution from the blood of 132 patients on 157 occasions over a period of 6 years. Of the 157 positive blood cultures, 107 (68%) were obtained from January 1981 through October 1982. These organisms have been shown to be resistant to a considerable number of antimicrobial agents (1–8). The susceptibilities of 51 isolates of *A. calcoaceticus* subsp. *anitratus* and 23 isolates of *A. calcoaceticus* subsp. *lwoffi* were tested against new β-lactams and semisynthetic penicillins as well as a variety of older antibiotics.

All of the organisms were obtained from blood cultures from cancer patients treated at the M. D. Anderson Hospital and Tumor Institute, Houston, Tex. Serial antibiotic concentrations were prepared manually in Mueller-Hinton broth and dispensed automatically with an MIC 2000 dispenser (Dynatech Laboratories, Inc., Alexandria, Va.). For the comparative studies of the antibiotics used, the plates were inoculated automatically. A Dynatech MIC 2000 inoculator delivered 0.0015 ml of inoculum containing 10^4 organisms into wells holding 0.1 ml of medium with various antibiotic dilutions. The minimal inhibitory concentration (MIC) was defined as the lowest concentration of drug that suppressed visible growth after incubation at 37°C for 18 h. The minimal bactericidal concentration (MBC) was determined by subculturing 0.01 ml of medium containing 10^3 organisms and defined as the lowest concentration of drug that resulted in ≥99.9% killing of the organism in the original inoculum after 18 h of incubation at 37°C.

The 25 antibiotics used were obtained from different pharmaceutical companies. Imipemide (*N*-formimidoyl thienamycin) was the most active drug of the new β-lactam antibiotics, inhibiting 50% of both subspecies tested at a concentration of 0.20 μg/ml (Tables 1 and 2). Both subspecies tested were found to be susceptible to ceftazidime, ceftriaxone, ceftizoxime, and piperacillin, although *A. calcoaceticus* subsp. *lwoffi* was found to have lower MICs. Piperacillin was the most active commercially available β-lactam compound tested, inhibiting 90% of *A. calcoaceticus* subsp. *anitratus* and *lwoffi* isolates at concentrations of 50 and 25 μg/ml, respectively. Ceftazidime inhibited 90% of *A. calcoaceticus* subsp. *anitratus* and *lwoffi* isolates at concentrations of 12.5 and 6.25 μg/ml, respectively. Ceftizoxime and ceftriaxone inhibited 90% of both subspecies at a concentration of 25 μg/ml. The aminoglycosides were extremely active against these organisms. Tobramycin and amikacin inhibited 90% of *A. calcoaceticus* subsp. *anitratus* and *lwoffi* at concentrations of 0.78 and 3.12 μg/ml, respectively. MBCs were almost identical to MICs for the aminoglycosides, imipemide, and ceftazidime. For the rest of the antibiotics tested, MBCs were equal to or 5 times greater than MICs. As previously described (5, 8), the new β-lactam antibiotics are as effective in vitro as are the aminoglycosides for the therapy of infections caused by *A. calcoaceticus*. A reasonable advantage will be the

TABLE 1. In vitro activities of new β-lactam antibiotics against 51 isolates of *A. calcoaceticus* subsp. *anitratus*

Drug	MIC (μg/ml)[a]		
	Range	50%	90%
Cephalothin	1.56–>100	50	>100
Cefoxitin	6.25–>100	100	>100
Cefamandole	3.12–>100	100	>100
Cefuroxime	3.12–>100	25	50
Moxalactam	1.56–100	50	100
Ceftizoxime	0.39–25	6.25	25
Ceftriaxone	0.39–>100	12.5	25
Cefoperazone	6.25–>100	100	>100
Ceftazidime	1.56–25	6.25	12.5
Cefsulodin	3.12–100	50	100
Aztreonam	6.25–>100	100	>100
Temocillin	12.5–>100	>100	>100
Piperacillin	3.12–>100	12.5	50
Mezlocillin	3.12–>100	25	100
Azlocillin	3.12–>100	50	>100
Ticarcillin	1.56–>100	25	50
Imipemide	0.05–12.5	0.20	0.39
Ampicillin	0.78–>100	12.5	50
Erythromycin	12.5–>100	>100	>100
Tetracycline	0.78–>100	25	100
Chloramphenicol	1.56–>50	50	>50
Gentamicin	0.10–50	0.39	3.12
Amikacin	0.20–12.5	1.56	3.12
Tobramycin	0.10–3.12	0.39	0.78
TMP-SMZ[b]	0.06-1.18–>16-304	2-38	8-152

[a] 50% and 90%, MIC inhibiting 50 and 90% of the isolates, respectively.
[b] TMP-SMZ, Trimethoprim-sulfamethoxazole (1:19).

TABLE 2. In vitro activities of new β-lactam antibiotics against 23 isolates of *A. calcoaceticus* subsp. *lwoffi*

Drug	MIC (μg/ml)[a]		
	Range	50%	90%
Cephalothin	1.56–>100	50	>100
Cefoxitin	1.56–100	12.5	100
Cefamandole	0.39–100	12.5	50
Cefuroxime	0.20–>100	6.25	50
Moxalactam	0.39–>100	12.5	100
Ceftizoxime	0.10–12.5	1.56	12.5
Ceftriaxone	0.39–12.5	3.12	12.5
Cefoperazone	1.56–100	50	100
Ceftazidime	0.39–12.5	3.12	6.25
Cefsulodin	1.56–>100	25	100
Aztreonam	6.25–>100	100	>100
Temocillin	3.12–>100	>100	>100
Piperacillin	1.58–100	6.25	25
Mezlocillin	3.12–100	12.5	100
Azlocillin	3.12–>100	50	>100
Ticarcillin	0.10–>100	6.25	50
Imipemide	0.05–0.78	0.20	0.39
Ampicillin	0.10–>100	6.25	50
Erythromycin	0.39–>100	>100	>100
Tetracycline	0.78–>100	12.5	100
Chloramphenicol	1.56–>100	25	50
Gentamicin	0.05–0.78	0.20	0.39
Amikacin	0.05–>50	0.78	3.12
Tobramycin	0.05–50	0.20	0.78
TMP-SMZ[b]	0.06-1.18–>16-304	1-19	8-152

[a] 50% and 90%, MIC inhibiting 50 and 90% of the isolates, respectively.
[b] TMP-SMZ, Trimethoprim-sulfamethoxazole (1:19).

avoidance of aminoglycoside nephrotoxicity. This study showed that some of the new β-lactam antibiotics tested might be effective in the treatment of infections caused by this organism.

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