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In Vitro Antibacterial Activity of Aztreonam Against Gram-Negative Bacilli Isolated in 1985

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ABSTRACT

The antibacterial activity of aztreonam (AZT), a newly developed monobactam, against a total of 637 gram-negative bacilli was investigated using clinical isolates from patients with surgical, respiratory and urological diseases in 1985. Against *Pseudomonas aeruginosa*, AZT exhibited favorable activity similar to that of cefsulodin. AZT also had high antibacterial activity against *Klebsiella pneumoniae*, *Escherichia coli*, *Serratia marcescens* and *Haemophilus influenzae*, but not against *Enterobacter aerogenes*.

Key words: *Aztreonam, Clinical isolates, Gram-negative bacilli*

Aztreonam (AZT), the first clinically available monobactam, is known to possess potent antimicrobial activity against aerobic gram-negative bacilli, especially *Enterobacteriaceae* and *Pseudomonas aeruginosa*[2]. We examined the antibacterial activity of aztreonam against gram-negative bacilli isolated from patients with surgical, urological and respiratory diseases. We employed clinical strains isolated before the commercial distribution of AZT began in 1986.

MATERIALS AND METHODS

Antibiotics. Aztreonam (AZT) was supplied by Eizai Co., Ltd., Tokyo, Japan. Gentamicin (GM) (Essex Japan, Osaka, Japan), cefsulodin (CFS) (Takeda Chemical Industries, Ltd., Osaka, Japan) and latamoxef (LMOX) (Shionogi & Co., Ltd., Osaka, Japan) were also used.

Bacteria. Bacteria were isolated and identified by the surgical and urological wards, Hiroshima University Hospital, and the respiratory ward, Hiroshima Prefectural Hospital. To examine the susceptibility of the isolates prior to the clinical use of AZT, we used strains isolated mainly in 1985. *Pseudomonas aeruginosa, Klebsiella pneumoniae, Enterobacter aerogenes, Escherichia coli, Serratia marcescens* and *Haemophilus influenzae* were examined in the present study.

Antibacterial activity. Antibacterial activity was determined by an agar dilution method with Mueller-Hinton agar. Briefly, a bacterial suspension (10^6/ml) was inoculated onto agar plates containing two-fold serial dilutions of antibiotics and incubated at 37°C for 24 hr. Minimal inhibitory concentration (MIC) was defined as the lowest concentration at which no bacterial colony appeared.

RESULTS AND DISCUSSION

Table 1 summarizes MICs of AZT against 637 clinical isolates. As for *P. aeruginosa*, 42.8, 33.3 and 52.4% of isolates from the respiratory, urological and surgical wards, respectively, were resistant to AZT (MIC greater than 12.5 μg/ml). The antibacterial activity of AZT was almost similar to those of GM and CFS. MIC_{50} and MIC_{90} obtained in this study were equivalent to those in the studies of Neu and Labthavikul[3] and Thompson et al[6], but far higher than those obtained in other studies[4,5].

AZT was highly active against *K. pneumoniae*. Although one strain from the surgical ward exhibited MIC greater than 12.5 μg/ml, MIC_{50} and MIC_{90} were similar to those of previous studies[1,3]. AZT showed the lowest MIC among four agents used against *E. coli*. Three strains (2.6%) from the surgical ward exhibited MIC greater than 12.5 μg/ml,

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Table 1. Comparative *in vitro* activities of aztreonam and other agents against gram-negative bacilli isolated from respiratory, urological and surgical wards.

Bacteria / Antibiotics	Ward where the bacteria were isolated — Minimal Inhibitory Concentration (μg/ml)								
	Respiratory			Urological			Surgical		
	Range	MIC_{50}	MIC_{90}	Range	MIC_{50}	MIC_{90}	Range	MIC_{50}	MIC_{90}
P.aeruginosa	n=28			n=33			n=164		
AZT	0.39— 100	6.25	50	1.56—>100	6.25	50	0.78—>100	12.5	50
GM	0.2 —>100	3.13	12.5	<0.1 —>100	0.39	>100	0.39—>100	3.13	25
CFS	0.78— 100	3.13	50	0.78—>100	3.13	>100	0.78—>100	6.25	>100
LMOX	3.13—>100	50	100	6.25—>100	25	50	6.25—>100	50	>100
K.pneumoniae	n=29			n=15			n=59		
AZT	0.1 —0.1	0.1	0.1	<0.1 —0.39	<0.1	<0.1	<0.1 — 100	<0.1	<0.39
GM	0.2 —0.78	0.39	0.78	0.2 —0.78	0.39	0.39	0.2 — 25	0.39	12.5
LMOX	0.1 —0.39	0.2	0.39	<0.1 —0.39	<0.1	0.2	<0.1 —>100	0.2	0.78
E.aerogenes	n=28						n=21		
AZT	0.1 —100	0.1	50				<0.1 —>100	12.5	100
GM	0.39—100	0.39	1.56				0.39—>100	0.78	1.56
LMOX	0.1 — 12.5	0.2	12.5				<0.1 —>100	3.13	100
E.coli				n=53			n=116		
AZT				<0.1 —0.78	<0.1	<0.1	<0.1 —>100	0.1	0.2
GM				0.2 —3.13	0.78	1.56	0.2 — 6.25	0.78	1.56
LMOX				<0.1 —1.56	<0.1	0.2	<0.1 — 100	0.1	0.39
CZX				<0.1 —3.13	<0.1	<0.1			
S.marcescens				n=28			n=9		
AZT				<0.1 —>100	0.78	1.56	0.1 — 6.25	1.56	6.25
GM				0.2 —>100	12.5	100	0.39—>100	25	>100
LMOX				0.2 —>100	25	>100	0.39—>100	100	>100
H.influenzae	n=54								
AZT	0.1 —100	0.1	0.39						
GM	0.1 — 1.56	0.39	1.56						
LMOX	0.1 — 3.13	0.1	0.1						
CFS	1.56—100	25	50						

whereas all strains from the urological ward were sensitive to AZT. AZT exhibited highest antibacterial activity among three drugs used against *S. marcescens*. None of the strains of *S. marcescens* from the surgical ward were resistant to AZT (MIC greater than 12.5 μg/ml). Only one strain of 28 from the urological ward was resistant to AZT. Clinical isolates of *S. marcescens* resistant to AZT have been reported by Neu et al[2] and van Landuyt et al[1]. Seventeen and 16 strains from the urological ward were resistant to LMOX and GM, respectively. AZT demonstrated rather low MIC_{50} and MIC_{90}, similar to LMOX, against *H. influenzae*. However, two strains were resistant to AZT (12.5 and 100 μg/ml), whereas none were resistant to LMOX. Van Landuyt et al[1] reported the *in vitro* activity of AZT against 20 clinical isolates of which no strain exhibited MIC greater than 1 μg/ml.

AZT had rather weak antibacterial activity against *E. aerogenes* with MIC_{90} of 50 and 100 μg/ml for isolates from the respiratory ward and the surgical ward, respectively. Three and two of four resistant strains from the respiratory ward were resistant to LMOX and GM, respectively.

AZT is the first clinically available monobactam which is highly active against aerobic gram-negative bacilli. Gram-negative bacilli are often isolated from respiratory, urological, post-operative and opportunistic infection. The satisfactory MICs obtained in this study suggest that AZT is an excellent antibiotic for antimicrobial chemotherapy. Sensitivity testing after the start of clinical use is required.

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