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Susceptibility of Gram-Negative Aerobic Bacilli Resistant to Carbenicillin in a General Hospital to Piperacillin and Ticarcillin

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During an 8-month period, 858 gram-negative aerobic rods resistant to carbenicillin (minimum inhibitory concentration, ≥128 μg/ml) were isolated. Susceptibility testing of 233 of these suggested that piperacillin might be active against more of these organisms than would carbenicillin or ticarcillin.

Piperacillin (T-1220, Lederle) is a new carbenicillin analog for which initial in vitro clinical studies indicate greater activity per milligram than that with carbenicillin and ticarcillin against *Pseudomonas aeruginosa,* indole-positive *Proteus* sp., *Klebsiella* sp., *Enterobacter* sp., *Shigella* types, *Salmonella* types, *Citrobacter freundii, Streptococcus faecalis,* and *Bacteroides* sp. and comparable activity against *Escherichia coli, Serratia* sp., *Acinetobacter* sp., and many gram-positive organisms (4, 5, 7-9). However, the benefit of such increased relative potency depends, in part, upon both the frequency with which carbenicillin-resistant organisms are encountered in a specific patient population and the level of resistance in these organisms. This study was designed to measure these two factors.

From 1 December 1976 through 31 July 1977, 858 aerobic gram-negative rods isolated in the Clinical Microbiology Laboratory from cultures of inpatients at Grady Memorial Hospital, a 1,076-bed municipal hospital, were shown by agar diffusion disk testing (3) to be resistant to carbenicillin (Table 1). When multiple cultures from the same patient were obtained during a single episode of infection (determined by review of the clinical record), only the initial isolates were included.

We tested 245 strains of these gram-negative aerobic bacilli isolated from 224 patients during the 8-month period. For these organisms, we determined minimum inhibitory concentrations (MICs) of disodium carbenicillin, ticarcillin disodium, and piperacillin sodium (kindly supplied by Beecham Laboratories and Lederle Laboratories) by a microtiter dilution technique (2), using an inoculum of 10^5 organisms per ml (as monitored by surface plate counts) and an incubation period of 18 h at 35°C. Twelve strains with a carbenicillin MIC of ≤64 μg/ml were excluded from further testing.

When MICs of ticarcillin disodium and piperacillin sodium were determined and compared with MICs of carbenicillin, the median MIC for piperacillin was lower than that for the other two drugs against *Citrobacter, E. coli, Enterobacter, Proteus, Pseudomonas,* and *Serratia* (Table 2).

Had a carbenicillin-like drug been considered necessary for the patients from whom these strains were isolated, our in vitro data suggest that piperacillin sodium would have been suitable therapy for many of the patients from whose specimens carbenicillin-resistant orga-

TABLE 1. *In vitro susceptibility[a] to carbenicillin of gram-negative aerobic bacilli[b] isolated from inpatients from December 1976 to 31 July 1977 at Grady Memorial Hospital*

Organism	Susceptibility results (no.)		
	Susceptible	Intermediate	Resistant
Acinetobacter sp.	103	10	6
Citrobacter sp.	15	2	30
E. coli	881	9	274
Enterobacter sp.	132	8	117
Klebsiella sp.	23	20	291
Proteus mirabilis	364	1	7
Other *Proteus* sp.	67	5	27
P. aeruginosa	255	26	47
Other *Pseudomonas* sp.	5	0	18
Serratia sp.	71	3	25
Others[c]	16	1	16

[a] Agar diffusion method.

[b] Only first of multiple isolates from same patient included.

[c] *Alcaligenes,* 6; *Providencia,* 6; *Salmonella,* 9; *Aeromonas,* 4; *Flavobacterium,* 6; *Moraxella,* 2.

TABLE 2. *Susceptibility to carbenicillin (Carb), ticarcillin (Ticar), and piperacillin (Piper) of selected carbenicillin-resistant[a] gram-negative aerobic bacilli at Grady Memorial Hospital*

Organism	Drug	No. susceptible at MIC (μg/ml) of:									
		>512	256	128	64	32	16	8	4	2	≤1
Citrobacter sp. (7)[b]	Carb	3	3	1							
	Ticar	2	1	4							
	Piper	1		1	1			1	3		
E. coli (91)	Carb	83	3	5							
	Ticar	82	3	4				1			1
	Piper	35	11	8	15	12	3	2	4		1
Enterobacter[c] (25)	Carb	19	3	3							
	Ticar	17	2	4							2
	Piper	12		1	7	4			1		
Klebsiella sp. (16)	Carb	16									
	Ticar	16									
	Piper	9	3		2	1			1		
Proteus[d] (10)	Carb	7	1	2							
	Ticar	7		1	2						
	Piper	5		1			1	1		1	1
Pseudomonas[e] (53)	Carb	30	11	12							
	Ticar	21	4	11	6	5	3		2		1
	Piper	7	1	2	4	7	13	8	11		
Serratia sp. (27)	Carb	26		1							
	Ticar	26			1						
	Piper	10	2	3	5	2	1	1	3		
Others[f] (4)	Carb	2		2							
	Ticar	2		1		1					
	Piper	1		1	1	1					

[a] MIC > 64 μg/ml.
[b] Numbers within parentheses indicate numbers of organisms.
[c] *E. aerogenes*, 2; *E. agglomerans*, 7; *E. cloacae*, 16.
[d] *P. mirabilis*, 2; *P. morganii*, 1; *P. rettgeri*, 4; *P. vulgaris*, 3.
[e] *P. aeruginosa*, 49; other species, 4.
[f] *Alcaligenes*, 2; *Providencia*, 1; *Acinetobacter*, 1.

nisms had been isolated. This consideration takes into account not only the relative activity of these antimicrobial agents against specific groups of organisms (Table 2), but also the relative frequency with which we recovered organisms resistant to carbenicillin in our patient population (Table 1). However, susceptibility to antimicrobial agents is relatively difficult to define objectively and depends upon many factors other than in vitro determination of relative potency per milligram of agents against microorganisms (1, 4, 6). Thus, whether piperacillin sodium will be as useful or more useful than carbenicillin to clinicians will depend upon clinical evaluation of effectiveness and likelihood of toxicity. Even if findings on these considerations are favorable, final determination of the value of piperacillin may depend upon a judgment of whether the relative cost of the agent is justified by the benefits of decreased sodium load (9) and the enhanced spectrum of activity indicated by these in vitro studies.

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