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Antimicrobial Susceptibilities of Clinical Isolates of *Acinetobacter baumannii* from Singapore

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The in vitro activities of 17 antimicrobial agents alone or in combination against 70 clinical isolates of *Acinetobacter baumannii* from Singapore were determined by broth microdilution. The MICs of amoxicillin, ampicillin, ceftazidime, ceftriaxone, gentamicin, and piperacillin for 90% of the strains were ≥128 μg/ml. Addition of sulbactam to ampicillin produced improved activity, whereas adding tazobactam to piperacillin did not. The MICs of amikacin, ciprofloxacin, and imipenem for 90% of the strains were 32, 32, and 16 μg/ml, respectively.

Acinetobacter baumannii (3) has emerged as an important nosocomial pathogen in intensive care units around the world. The organism is frequently multidrug resistant and difficult to treat, and it may produce serious infections such as bacteremia, pneumonia, and meningitis (2, 4, 5, 7). No previous study has reported the antimicrobial susceptibility of *A. baumannii* in Southeast Asia. The purpose of this study was to determine the susceptibility profile of clinical isolates of *A. baumannii* from Singapore.

Seventy clinical isolates of *A. baumannii* were collected at the National University Hospital, Singapore. The strains were from blood (30%), urine (17.1%), wounds (28.6%), and respiratory tracts (24.3%). The blood isolates were collected from January 1993 to February 1994; the others were isolated from August 1993 to February 1994. To avoid duplication of strains, only one isolate per patient from patients having multiple positive cultures was used. All strains were identified by using the ID 32 GN system (bioMérieux, Lyons, France) with the ATB instrument (bioMérieux), by motility testing, and by positive growth at 41 and 44°C.

The antimicrobial agents, in powder form, tested were as follows: amikacin (Bristol Laboratories); amoxicillin, clavulanic acid, amoxicillin-clavulanic acid, and ticarcillin (SmithKline Beecham, Surrey, United Kingdom); gentamicin (Fluka, Buchs, Switzerland); cefuroxime and ceftazidime (Glaxo, Middlesex, United Kingdom); ciprofloxacin (Bayer AG, Wuppertal, Germany); fleroxacin and ceftriaxone (Roche, Basel, Switzerland); imipenem (Merck, Sharp and Dohme, West Point, Va.); piperacillin and tazobactam (Lederle, Carolina, P.R.); ampicillin and sulbactam (Pfizer, Inc., New York, N.Y.); tobramycin (Eli Lilly, Inc., Carolina, P.R.); and polymyxin B (Sigma, St. Louis, Mo.). Amoxicillin-clavulanic acid in a 5:1 ratio was used.

MIC determinations were performed by the broth microdilution method. The recommendations of the National Committee for Clinical Laboratory Standards were followed (6). Briefly, a small number of colonies of a pure culture were suspended in 1.0 ml of Mueller-Hinton broth (cation adjusted) (BBL Microbiology Systems, Cockeysville, Md.) and incubated at 37°C for 3 to 4 h until a turbidity of McFarland 0.5 was achieved. Suspensions were further diluted in Mueller-Hinton broth to obtain a final inoculum concentration of 5×10^5 CFU/ml. Microtiter plates with twofold dilutions of the respective antimicrobial agents were inoculated and then incubated at 37°C for 16 to 18 h prior to determination of the MICs. *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853 served as quality control strains and were tested in each run. β-Lactamase production was assessed by using cefinase discs (BBL Microbiology Systems).

The activities of the various antimicrobial agents against the *A. baumannii* strains are presented in Table 1. The cephalosporins tested showed little activity (MICs for 90% of the strains [MIC_{90}s] of ≥128 μg/ml). Gentamicin was the least active aminoglycoside, less active than amikacin and tobramycin. The MIC_{50} of tobramycin was 8 and 32 times lower than those of amikacin and gentamicin, respectively. The quinolones ciprofloxacin and fleroxacin showed only moderate activity (MIC_{90}s of 32 and 16 μg/ml, respectively). Three β-lactamase inhibitors were included in this study: sulbactam, tazobactam, and clavulanic acid. Ampicillin in combination with sulbactam showed improved activity compared with ampicillin alone, but no advantage for combination at a 2:1 ratio over combination at a 1:1 ratio was apparent. Improved activity was not observed when clavulanic acid was combined with amoxicillin, and the same lack of improvement was observed for tazobactam when combined with piperacillin. We observed a large number of β-lactamase producers, with 78.6% of the strains being β-lactamase positive. For a significant number of the *A. baumannii* strains (12.9%) MICs of imipenem were ≥16 μg/ml; none of these strains were isolated from blood. We do not have evidence as to whether these strains are derived from a single clone. Checkerboard microdilution tests of imipenem with sulbactam and imipenem with tazobactam were performed on these strains. Results indicated that there was no additive or synergistic effect (data not shown).

The results of this study clearly indicate that the various antimicrobial agents tested had either moderate or little activity against the strains of *A. baumannii* from Singapore. The broad-spectrum cephalosporins had MIC_{90}s of ≥32 μg/ml for more than 40% of the strains. This might be attributed to the wide usage of broad-spectrum antibiotics in Singapore.

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TABLE 1. Activities of antimicrobial agents against 70 isolates of *A. baumannii*

Drug or drug combination (ratio)	MIC (μg/ml)[a]		
	Range	50%	90%
Amikacin	0.25–128	2	32
Amoxicillin	2–≥128	8	≥128
Amoxicillin-clavulanic acid	2–≥128	8	≥128
Ampicillin	2–≥128	32	≥128
Ampicillin-sulbactam (1:1)	1-1–64-64	2-2	16-16
Ampicillin-sulbactam (2:1)	1-0.5–128-64	4-2	32-16
Cefuroxime	16–≥128	64	≥128
Ceftazidime	2–≥128	8	128
Ceftriaxone	2–≥128	32	≥128
Ciprofloxacin	≤0.125–64	0.25	32
Clavulanic acid	8–≥128	64	≥128
Fleroxacin	≤0.125–32	0.5	16
Gentamicin	0.25–≥128	8	≥128
Imipenem	≤0.125–64	0.25	16
Piperacillin	32–≥128	64	≥128
Piperacillin-tazobactam (8:1)	16-2–≥256-32	32-4	128-16
Piperacillin-tazobactam[b]	4–≥128	64	≥128
Polymyxin B	8–32[c]	16[c]	16[c]
Sulbactam	1–64	4	16
Tazobactam	2–≥128	8	64
Ticarcillin	4–≥128	16	≥128
Tobramycin	≤0.125–16	0.25	16

[a] 50% and 90%, MIC_{50} and MIC_{90}, respectively.
[b] Tazobactam added at a fixed amount of 4 μg/ml.
[c] Units per milliliter.

Ampicillin in combination with sulbactam showed better activity than ampicillin alone against *A. baumannii*, a finding in agreement with the data of Vila et al. (10). The increased activity of ampicillin-sulbactam compared with those of amoxicillin-clavulanate and piperacillin-tazobactam was due to the intrinsic activity of sulbactam alone. In contrast to the findings of a recent study (1), in the present study tazobactam did not improve the activity of piperacillin.

Perhaps the most interesting and alarming finding of this study is the presence of a significant number of *A. baumannii* strains for which the MICs of imipenem were high. Previous reports from Europe have indicated that there is 5% resistance to imipenem in France (2), whereas no resistant strains were detected in surveys done in Spain (10), Chile (12), and Germany (8, 9). In the United States, an outbreak due to imipenem-resistant strains of *A. baumannii* has recently been reported (11). In our hospital, imipenem has increasingly been used to treat multidrug-resistant *A. baumannii* infections. Imipenem must be kept as a last resource in our armamentarium to treat *A. baumannii* infections, or otherwise we should expect a higher percentage of resistance to this drug in the near future, which may have potentially catastrophic consequences. Obviously, there is a need for new drugs or combinations of drugs to treat infections produced by these multidrug-resistant strains of *A. baumannii*.

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