

## In Vitro Activities of Ampicillin-Sulbactam and Amoxicillin-Clavulanic Acid against *Acinetobacter baumannii*

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Received 2 February 1998/Returned for modification 24 March 1998/Accepted 9 July 1998

**In vitro susceptibility patterns of newer  $\beta$ -lactamase-inhibiting antibiotics ampicillin-sulbactam (A/S) and amoxicillin-clavulanic acid (A/C) for 100 consecutive isolates of *Acinetobacter baumannii* obtained from various clinical samples were studied. The A/C MIC for 86% of the strains was more than 16/8  $\mu\text{g/ml}$ , whereas there was an A/S MIC of more than 16/8  $\mu\text{g/ml}$  for only 38% of the strains. This showed that A/S has significantly superior in vitro activity compared to A/C against *A. baumannii*, although, theoretically, both should have similar activities. The therapeutic superiority of A/S over A/C needs to be studied, or else the breakpoints for these agents in in vitro tests need to be redefined.**

*Acinetobacter baumannii* is emerging as a major cause of nosocomial infections, particularly in intensive care units, where antimicrobial use is greatest and the host is most susceptible (3). Besides they are frequently resistant to multiple antibiotics, including most of the  $\beta$ -lactams and aminoglycosides. Most of the resistance to  $\beta$ -lactams is due to production of  $\beta$ -lactamase enzyme (2). The newer  $\beta$ -lactamase-inhibiting antibiotics, such as ampicillin-sulbactam (A/S) and amoxicillin-clavulanic acid (A/C), are increasingly being used in the treatment of  $\beta$ -lactamase-producing strains involved in various infections in hospital patients. Theoretically they are considered to have almost identical spectra of activity (4). However, we noticed a lack of concordance of the antibiotic sensitivity results between A/S and A/C when tested against multidrug-resistant *A. baumannii* strains. We observed that 276 isolates of *A. baumannii* obtained from various samples in the Clinical Bacteriology Laboratory of the All India Institute of Medical Sciences, New Delhi, India, from January 1997 to August 1997 when tested against A/C and A/S by the disc diffusion test showed a discordance in susceptibility patterns. Sixteen percent of the isolates were susceptible to both combinations, and 13% were resistant to both. However, 71% of the isolates which were resistant to A/C were susceptible to A/S.

To determine the quantitative difference in the susceptibility of *A. baumannii* to A/S and A/C, the MICs of these agents were studied. Since ampicillin and amoxicillin are the antibacterial components of A/S and A/C, respectively, in these combinations, we tested the MICs of ampicillin and amoxicillin for these *A. baumannii* strains separately as well.

A total of 100 consecutive isolates of *A. baumannii* from various samples (54 from blood cultures, 38 from the respiratory tract, and 8 from urine cultures) obtained from different patients received in the Clinical Bacteriology Laboratory of the All India Institute of Medical Sciences from September to December 1997 were tested. The isolates were maintained at room temperature in nutrient agar slopes and were subcultured two times before testing. The agar dilution method was used to determine the MIC of A/S, A/C, ampicillin, and amoxicillin as per National Committee for Clinical Laboratory Standards guidelines (4). The breakpoints of resistance and suscep-

tibility were 16/8  $\mu\text{g/ml}$  for A/S and A/C and 16  $\mu\text{g/ml}$  for ampicillin and amoxicillin. *Escherichia coli* ATCC 25922 and *A. baumannii* ATCC 19606 standard strains were inoculated as quality controls each time the tests were performed. Statistical analysis of the results was done with McNemar's test to look for the significance of association and comparison of resistance of *A. baumannii* to A/S and A/C. The ranges of MICs and comparisons to those of A/S and A/C by agar dilution are shown in Table 1.

We observed that the A/C MIC for 86% of the strains was >16/8  $\mu\text{g/ml}$  (breakpoint, 16/8  $\mu\text{g/ml}$ ), whereas there was an A/S MIC of 16/8  $\mu\text{g/ml}$  (breakpoint, 16/8  $\mu\text{g/ml}$ ) for only 38% of the strains. Ampicillin also showed an advantage over amoxicillin in in vitro tests. A total of 93% of the strains were resistant to amoxicillin and 79% were resistant to ampicillin (MIC of > 32  $\mu\text{g/ml}$ ). This showed that A/S has a significantly superior activity against *A. baumannii* in in vitro tests compared to A/C ( $P < 0.001$ ). It has been reported that sulbactam is superior to and is a broader-spectrum  $\beta$ -lactamase inhibitor than clavulanic acid (1). It is still debatable if this in vitro activity of sulbactam is significant. Perhaps the difference between the combination of ampicillin in A/S and amoxicillin in A/C gives A/S some advantage over A/C. Recently O'Shaughnessy et al. (5) have also reported a discordance between the results of in vitro tests of sensitivity to A/S and A/C in *Escherichia coli* strains, in which they found A/C has a better in vitro activity than A/S.

In light of this finding, it is essential that a prospective study to determine the therapeutic superiority of A/S over A/C be done, or if in fact A/S and A/C are of equivalent clinical efficacies, then the in vitro susceptibility testing breakpoints for these agents need to be redefined.

TABLE 1. Susceptibility of *A. baumannii* to A/S and A/C based on MIC ranges by agar dilution

Antibiotic ( $n = 100$ )	No. (%) of isolates with susceptibility result		
	Sensitive <sup>a</sup>	Intermediate <sup>b</sup>	Resistant <sup>c</sup>
A/S	41 (41.0)	21 (21.0)	38 (38.0)
A/C	11 (11.0)	3 (3.0)	86 (86.0)

<sup>a</sup> MIC, <8/4  $\mu\text{g/ml}$ .

<sup>b</sup> MIC, 16/8  $\mu\text{g/ml}$ .

<sup>c</sup> MIC, >16/8  $\mu\text{g/ml}$ .

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