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In vitro activities of ampicillin, sulbactam and a combination of ampicillin and sulbactam against isolates of *Acinetobacter calcoaceticus–Acinetobacter baumannii* complex isolated in Chile between 1990 and 1998

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Helia Bello[a]*, Mariana Domínguez[a], Gerardo González[a], Raúl Zemelman[a,b], Sergio Mella[a,c], Hilary-Kay Young[d] and Sebastian G. B. Amyes[e]

[a]*Departamento de Microbiologia, Facultad de Ciencias Biológicas, Universidad de Concepción;* [b]*Facultad de Medicina, Universidad San Sebastián,* [c]*Departamento de Medicina Interna, Facultad de Medicina, Universidad de Concepción, Concepción, Chile;* [d]*Department of Biological Sciences, University of Dundee, Dundee DD1 4HN;* [e]*Department of Medical Microbiology, School of Medicine, University of Edinburgh, Edinburgh EH8 9AG, UK*

*Corresponding author. Tel: +56-41-203237; Fax: +56-41-24975; E-mail: hbello@udec.cl

Sir,

Isolates belonging to the *Acinetobacter calcoaceticus–Acinetobacter baumannii* (Acb) complex are being isolated increasingly from hospitalized patients with serious infections.[1] These organisms tend to exhibit resistance to multiple antibiotics, including β-lactams, aminoglycosides and quinolones.[2] However, a considerable percentage of isolates remain susceptible to the combination of ampicillin and sulbactam.[3] Recently, Corbella *et al.*[4] evaluated the efficacy of sulbactam alone as treatment for patients with non-life-threatening infections caused by isolates of *A. baumannii* and concluded that this compound accounted for the *in vitro* activity of the combination. They also warned that extensive use of sulbactam in this setting would lead to an increase in the incidence of resistance to it. The aim of the present study was to determine the susceptibilities of 280 isolates belonging to the Acb complex obtained from patients in Chilean hospitals during four time periods between 1990 and 1998.

The organisms studied were 280 non-replicate clinical isolates recovered from patients in hospitals in Chile during the periods 1990–1992 (group A; $n = 75$), 1993–1994 (group B; $n = 59$), 1995–1996 (group C; $n = 72$) and 1997–1998 (group D; $n = 74$). The isolates were identified as described previously[5] and maintained in glycerol trypticase broth at –70°C. MICs were determined by an agar dilution method

Table. *In vitro* activities of ampicillin, sulbactam and the ampicillin/sulbactam combination against 280 Acb clinical isolates

Antibiotic	Time period	MIC (mg/L)			Resistant isolates (%)[a]
		MIC_{50}	MIC_{90}	range	
Ampicillin	A	>512	>512	32–>512	100
	B	>512	>512	32–>512	97.4
	C	>512	>512	32–>512	95.6
	D	>512	>512	32–>512	98.4
Sulbactam	A	8	16	1–128	30.8
	B	16	32	2–128	40.1
	C	16	32	2–128	51.5
	D	16	64	2–128	54.7
Ampicillin/ sulbactam	A	8/4	16/8	1/0.5–16/8	0
	B	16/8	16/8	4/2–32/16	10.3
	C	16/8	32/16	4/2–128/64	36.8
	D	32/16	128/64	4/2–256/128	56.3

[a]According to the following MIC breakpoints for resistance recommended by the NCCLS:[6] ampicillin ≥32 mg/L; ampicillin/sulbactam ≥32/≥16 mg/L. As a breakpoint for sulbactam alone has not been recommended, the concentration recommended for the sulbactam in the combination, i.e. ≥16 mg/L, has been adopted.

recommended by the NCCLS;[6] the ratio of ampicillin and sulbactam in the formulation was 2:1.

The susceptibilities of the 280 isolates are summarized in the Table. Ampicillin exhibited either negligible or no activity against the isolates, with percentages of resistant isolates during the four time periods ranging from 95.6 to 100%. Although the activity of sulbactam was greater than that of ampicillin, it declined during the study periods, the MIC_{90}s increasing four-fold from 16 to 64 mg/L and the percentage of resistant isolates increasing from 30.8 to 54.7%. The activity of the ampicillin/sulbactam combination was greater than that of sulbactam alone, at least during the earlier time periods. Indeed, all of the isolates isolated during 1990–1992 were susceptible to the formulation. However, both the MIC_{90}s and percentage of resistant isolates increased thereafter, to the extent that the figures for 1997–1998 were comparable to those for sulbactam alone during the same time period. For isolates belonging to groups A, B and C, the percentages of isolates resistant to the combination were lower than the corresponding percentages of isolates resistant to either of the constituents. The implication of this finding is that ampicillin and sulbactam were acting synergically. In contrast, analysis of the MICs of ampicillin alone, sulbactam alone and the ampicillin/sulbactam formulation for individual isolates revealed that, in approximately one-third of cases, inhibition was attributable to the intrinsic activity of sulbactam (data not shown), an observation that has also been made by Corbella *et al*.[4]

The results of this study are in accord with earlier concerns that excessive use of the ampicllin/sulbactam combination to treat patients with infections caused by isolates belonging to the Acb complex will be associated with further increases in the incidence of resistance to the formulation among these organisms and suggest the need to monitor *in vitro* susceptibilities to this antibiotic combination.

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