

# Comparative in Vitro Activity of Arbekacin and Amikacin against Gram-Negative Bacilli Isolated from Patients with Hospital-Acquired Infections at Siriraj Hospital, Thailand

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## ABSTRACT

*In vitro* activity of arbekacin and amikacin against 36 isolates of *Pseudomonas aeruginosa*, 36 isolates of *Acinetobacter baumannii*, 36 isolates of extended-spectrum beta-lactamase (ESBL)-producing *Klebsiella pneumoniae*, and 30 isolates of ESBL-producing *Escherichia coli* isolated from different patients with hospital-acquired infections at Siriraj Hospital, Bangkok, Thailand was determined by Kirby-Bauer disk diffusion method. The resistance rates of *P. aeruginosa* to arbekacin and amikacin were 5.5 and 13.9 percent, respectively. The resistance rates of *A. baumannii* to arbekacin and amikacin were 27.8 and 33.3 percent, respectively. All isolates of ESBL-producing *K. pneumoniae* and *E. coli* were susceptible to both arbekacin and amikacin. In vitro activity of arbekacin against *P. aeruginosa*, *A. baumannii*, and ESBL-producing *K. pneumoniae* and *E. coli* was at least comparable to amikacin. (*J Infect Dis Antimicrob Agents* 2009;26:7-10.)

## INTRODUCTION

The prevalence of hospital-acquired infections (HAIs) in Thailand in 2006 was 6.5 percent.<sup>1</sup> The prevalence of HAIs was higher in tertiary care hospitals particularly in intensive care units. The common types of HAIs include pneumonia, urinary tract infection, surgical site infection and blood-stream infection.

Seventy percent of HAIs were caused by Gram-negative bacteria including *Pseudomonas aeruginosa*, *Acinetobacter* spp., and extended-spectrum-beta-lactamase (ESBL)-producing *Klebsiella pneumoniae* and *Escherichia coli*. Aminoglycosides, especially amikacin, have been commonly used for the therapy of HAIs. Arbekacin is a derivative of dideoxykanamycin

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B (dibekacin) with activities against both Gram-positive and Gram-negative bacteria.<sup>2</sup> Arbekacin is stable in the presence of aminoglycoside-modifying enzymes produced by methicillin-resistant *Staphylococcus aureus* (MRSA), hence it is an effective aminoglycoside antibiotic against MRSA.<sup>3-5</sup> Arbekacin will be available in Thailand shortly.

The objective of our study was to determine the in vitro activity of arbekacin against Gram-negative bacilli isolated from patients with HAIs at Siriraj Hospital, a medical school, Bangkok, Thailand.

### MATERIALS AND METHODS

Thirty-six isolates of *P. aeruginosa*, 36 isolates of *Acinetobacter baumannii*, 36 isolates of ESBL-producing *K. pneumoniae*, and 30 isolates of ESBL-producing *E. coli* isolated from different hospitalized patients with HAIs from 2006 to 2008 were included. The activity of arbekacin and amikacin against the studied organisms was determined by Kirby-Bauer disk diffusion method. The arbekacin disk (30 µg, Eiken Chemical Co. Ltd., Japan) and amikacin disk (30 µg, Oxoid Co. Ltd., UK.) were used. A quality control (QC) strain was performed by testing the susceptibility of *E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853. The methodology for susceptibility testing was performed as recommended by the Clinical Laboratory Standards Institute (CLSI).<sup>6</sup> The test isolate was grown overnight onto blood agar plate at 35°C, and then 3-5

colonies were picked up and immersed in tryptic soy broth. The broth was incubated at 35°C for 3-6 hours, and then diluted with saline until equivalent to a 0.5 McFarland standard. The suspension was used to inoculate onto Mueller-Hinton agar plate, and the disks were placed onto the surface of the inoculated agar plate. The agar plates were incubated at 35°C for 16-18 hours before the inhibition zone diameters were measured. The interpretative criteria for susceptibility of *P. aeruginosa*, *A. baumannii*, and ESBL-producing *K. pneumoniae* and *E. coli* to arbekacin and amikacin are shown in Table 1. The interpretative criteria of arbekacin are from the package insert of arbekacin disks made by Eiken Chemical Co. Ltd., Japan and the interpretative criteria of amikacin are from the CLSI.<sup>6</sup>

### RESULTS

The tested and range of inhibition zone diameters of arbekacin as well as amikacin against QC strains *E. coli* ATCC 25922 were 24 and 25 as well as 23-25 and 19-26 mm, and those of arbekacin as well as amikacin against *P. aeruginosa* ATCC 27853 were 23 and 25 as well as 22-24 and 18-26 mm, respectively. The distributions of susceptibility of *P. aeruginosa*, *A. baumannii*, and ESBL-producing *K. pneumoniae* and *E. coli* to arbekacin and amikacin are shown in Table 2. The resistance rates of *P. aeruginosa* to arbekacin and amikacin were 5.5 and 13.9 percent, respectively. The resistance rates of *A. baumannii* to arbekacin and

**Table 1. Interpretative criteria for susceptibility of *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae* and *Escherichia coli* to arbekacin and amikacin.**

Antibacterial	Disk content	Resistant	Intermediate	Susceptible
Arbekacin	30 mg	<13 mm	14-17 mm	>18 mm
Amikacin	30 mg	<14 mm	15-16 mm	>17 mm

**Table 2. Distribution of susceptibility of *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae* and *Escherichia coli* to arbekacin and amikacin.**

Organism (number of isolates)	Antibacterial	Susceptible		Intermediate		Resistant	
		Number	Percentage	Number	Percentage	Number	Percentage
<i>P. aeruginosa</i> (36)	Arbekacin	31	86.1	3	8.3	2	5.5
	Amikacin	29	80.5	2	5.5	5	13.9
<i>A. baumannii</i> (36)	Arbekacin	17	47.2	9	25	10	27.8
	Amikacin	23	63.9	1	2.8	12	33.3
ESBL-producing <i>K. pneumoniae</i> (36)	Arbekacin	33	91.7	3	8.3	0	0
	Amikacin	32	88.9	4	11.1	0	0
ESBL-producing <i>E. coli</i> (30)	Arbekacin	30	100	0	0	0	0
	Amikacin	30	100	0	0	0	0

amikacin were 27.8 and 33.3 percent, respectively. All isolates of ESBL-producing *K. pneumoniae* and *E. coli* were susceptible to both arbekacin and amikacin.

## DISCUSSION

Even though arbekacin was much more active than amikacin against MRSA,<sup>4</sup> the in vitro activity profiles of it for common Gram-negative bacilli causing HAIs at Siriraj Hospital observed from our study was comparable to that of amikacin. Our observations were similar to the previous report that showed that the in vitro activity of arbekacin against aerobic Gram-negative bacilli was comparable to that of other aminoglycosides.<sup>7</sup> Arbekacin has been shown to be effective in therapy of MRSA infections<sup>8-18</sup>, and it has been widely used in Japan for therapy of MRSA infections. The recommended dosage of arbekacin is 3-4 mg/kg per day. Arbekacin showed a strong bactericidal activity and an inhibition of regrowth against a mixture of *P. aeruginosa* and MRSA, and arbekacin

was evidently more effective than gentamicin and netilmicin in mice infected with MRSA and *P. aeruginosa*.<sup>19</sup> Therefore, if arbekacin is empirically given to the patient with HAI, it could inhibit both MRSA and aerobic Gram-negative bacilli, which is similar to a combination of vancomycin and amikacin. Arbekacin has a potential for nephrotoxicity similar to other aminoglycosides, and it was shown to be less nephrotoxic than vancomycin in rats.<sup>20</sup>

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