Acinetobacter baumannii at a Tertiary-Care Teaching Hospital in Jerusalem, Israel

A. SIMHON,1* G. RAHAV,1 G. SHAZBERG,2 C. BLOCK,1 H. BERCOVIER,1 AND M. SHAPIRO1

Department of Clinical Microbiology & Infectious Diseases, Hadassah-University Hospital,1 and
Department of Pediatrics, Bikur Holim General Hospital,2 Jerusalem, Israel

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In a retrospective 10-year analysis of 3,536 patient-unique isolates, Acinetobacter baumannii imipenem susceptibility declined from 98.1 (1990) to 64.1% (2000), and ciprofloxacin susceptibility decreased from 50.5 to 13.1%. Imipenem median zone diameters decreased from 27.7 (1997) to 18.8 mm (2000). No outbreaks were detected. Two clusters were identified for 41 strains genotyped by pulsed-field gel electrophoresis, but imipenem resistance was not clonal.


In a 650-bed, tertiary-care teaching hospital in Jerusalem, there were 3,536 patient-unique A. baumannii isolates from blood, pus, sputum, urine, and other specimens between January 1990 and April 2000. Susceptibility testing was performed by disk diffusion, according to NCCLS standard M2-A5, using Escherichia coli ATCC 25922 and Pseudomonas aeruginosa ATCC 27853 as controls. NCCLS interpretive criteria for Acinetobacter for the five antibiotics used here have remained unchanged over the 10-year study period. For each patient with multiple isolates, the five antibiotics were considered separately, and resistance rates were calculated with the WHONET program using the most resistant result (8). Imipenem susceptibilities were available for 3,471 isolates; amikacin susceptibilities for 3,182. In 1997, a Radius zone reader instrument was introduced (Mast Diagnostics, Bootle, United Kingdom) from which zone diameters were automatically uploaded to and retained on the main hospital computer. Not all antibiograms were read in the weekend (weekends, holidays, etc.), so that imipenem measurements were available for analysis for only 192 patient-unique isolates (84 in 1997 and 108 in 2000).

The molecular epidemiology of imipenem resistance was studied for 41 strains isolated between 1992 and 1998. First, all significant blood culture isolates, frozen routinely since 1992 and originating from neurosurgery and respiratory intensive care unit (ICU) patients, were selected (27 imipenem-susceptible isolates plus 3 imipenem-resistant isolates). Second, 11 imipenem-resistant isolates (6 from pus, 3 from blood, and 2 from sputum) were chosen from internal medicine, surgical, and burn patients. The latter were selected haphazardly and reflected the emergence of imipenem resistance during 1995 through 1998 in non-ICU patients. Imipenem MICs of these 41 strains were tested by the Etest (AB Biodisk, Solna, Sweden), using the breakpoints of the NCCLS standard M7-A3 for interpretation. E. coli ATCC 25922, Acinetobacter calcoaceticus NCTC 7844, and P. aeruginosa ATCC 27853 were used as controls.

For pulsed-field gel electrophoresis, the protocol of Gautom was used (3). ApaI macrorestriction fragments were resolved in a Bio-Rad CHEF DR-II apparatus. CHEF run conditions were as follows: 1.2% agarose, 15°C, 26 h, 200 V, 120° angle, and 5- to 35-s linear switch ramp. Combined gels were normalized against NotI-digested bands of E. coli MG 1655 and analyzed with a GelCompar 4.0 program (Applied Maths, Kortrijk, Belgium).

Figure 1 shows annual susceptibility rates using the most resistant result for each of five antibiotics. Imipenem susceptibility decreased from 98.1 (1990) to 64.1% (2000), while that of ciprofloxacin dropped from 50.5 to 13.1% (both tested by chi square; P < 0.001). Susceptibilities to minocycline, amikacin, and ceftazidime remained relatively unchanged. Over the 10-year period, imipenem-nonsusceptible patient-unique A. baumannii isolates totaled 194. Seventeen wards were involved (ICUs, 38%; general surgical, 30%; general medical 19%; other, 13%).

Zone sizes were analyzed with the Wilcoxon rank sum test (SAS statistical package version 6.12; SAS Institute, Cary, N.C.). The imipenem median zone diameter decreased from 27.7 (1997) to 18.8 mm (2000), with the distributions showing highly significant differences (P < 0.001). In 2000, the distribution was trimodal (Fig. 2), with 14% of isolates interpreted as intermediate, compared with 1% in 1997. Also in 2000, 20 (36%) of 75 fully susceptible isolates were in the 16- to 19-mm range, compared with 0% in 1997. The 16-mm NCCLS susceptible breakpoint for imipenem has remained unchanged in the last 10 years, and our data cast doubt upon the relevance of the breakpoint for this organism.

Two clusters containing both imipenem-susceptible and imipenem-nonsusceptible strains were evidenced (Fig. 3). Imi-
penem resistance was not ward associated. This is unlike the outbreaks described, among others (5, 6), by Tankovic (9), in which a distinct imipenem-resistant strain accounted for 21 of 22 cases, necessitating ICU closure. Despite intensified infection control measures at Hadassah for patients with imipenem-resistant *A. baumannii*, some degree of spreading of resistant subclones has occurred, as revealed by the increasing rate of imipenem resistance.

In summary, imipenem resistance in *A. baumannii* at Hadassah-University Hospital, Jerusalem, Israel, has become endemic. There is a highly significant decrease in imipenem zone sizes, confirming the worldwide trend of reduced susceptibility (Afzal-Shah and Livermore, Letter, J. Antimicrob. Chemother. 41:576–577, 1998). The trimodal distribution of inhibition zone diameters for imipenem, which developed with the advent of less-susceptible strains, places the relevance of current NCCLS breakpoints for this organism in serious doubt. Furthermore, no outbreaks were recorded and imipenem resistance was not

![FIG. 1. Antibiotic susceptibility of *A. baumannii* by year, calculated separately for each antibiotic using the most resistant result for each patient.](image)

![FIG. 2. WHONET histogram of distribution for imipenem zone diameters for 1998 and 2000. NCCLS breakpoints are shown by broken lines. R, resistant; I, intermediate; S, susceptible.](image)
associated with a particular pulsed-field gel electrophoresis clone or with a specific ward. The study of imipenem resistance in *Acinetobacter* species as a function of altered affinity of penicillin-binding proteins (4), porin deletion (2), or carbap- 

enemase expression (1) may shed more light on the epidemiology of this important nosocomial pathogen.

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REFERENCES


