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Short Communication

Evaluation of Antimicrobial Resistance of *Acinetobacter baumannii* to Imipenem, Ciporofloxacin and Ceftazidime using E Test

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Abstract

Background: Resistance patterns among nosocomial bacterial pathogens in hospitals may vary widely from country to country at any given point and within the same country over time. *Acinetobacter baumannii* is one of the most important bacterium causes hospital acquired infections. Therefore, surveillance of antibiotic resistance of *A. baumannii* is necessary, especially in our country which there is no have much data in this field.

Methods: In a prospective study, strain comprised of a total of 191 recent clinical isolates selected consecutively from clinical infections of separate patients from three University hospitals in Tehran. Minimum inhibitory concentration (MIC) of these organisms for imipenem, ciprofloxacin and ceftazidime was determined using E test method according to CLSI guideline. Also, MIC_{50} and MIC_{90} percent was calculated for each of these antibiotics.

Results: The percentages of *Acinetobacter baumannii* isolates susceptible to ciprofloxacin and ceftazidime by E test were 55.5% and 44.5%, respectively. The percentage of bacterium susceptible to imipenem by E test was 72.8%. MIC_{50} and MIC_{90} of imipenem in E test were 1.5 and >32, respectively.

Conclusion: High antimicrobial resistance against *A. baumannii* species has been seen in Iran; therefore, it is necessary to implement some approaches for prevention of bacterial spread.

Keyword: Acinetobacter, *Antimicrobial susceptibility, E test, Imipenem, Ciprofloxacin, Ceftazidim*e

Introduction

Microorganisms causing health care-associated infections are making major problems for the patients and clinicians regarding their mortality and morbidity especially due to their antibiotic resistance (1). In many countries, nosocomial infection rates are high because of a lack of supervision, poor infection prevention practices, inappropriate use of limited resources, and overcrowding of hospitals (2). Among these bacteria, *Acinetobacter baumannii* is an important nosocomial pathogen, with a rising prevalence. About 89.2% of *A. baumannii* recovered were from hospitalized patients. The infection caused by *A. baumannii* is difficult to control due to multi-drug resistance, which limits therapeutic options in critically ill and debilitating patients especially from intensive care units, where their prevalence is most noted (3). Unfortunately, recent analyses of hospital outbreaks have documented the spread of imipenem-resistant isolates. This emergence of imipenem- resistant *A. baumannii* (IRA) has become a worldwide problem and a troublesome development that threatens the continued successful treatment of *A. baumannii* species infections (4).

In the present study, we tested the antimicrobial resistance of *A. baumannii* to imipenem and compared with ciprofloxacin and ceftazidime with E test.

Material and Methods

In a prospective study, strain comprised of a total of 191 recent *A. baumannii* isolates selected consecutively from clinical infections of separate patients from the Emam Khomeini and Shariati hospitals and Tehran Heart Center with more than 400 beds in each one. *A. baumannii* isolates were provisionally identified using biochemical tests (typical reaction of *A. baumanni* to glucose is posi-

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tive and to oxidase, mannitol, maltose, Esculin, Indole, and H_2S are negative). *A. baumannii* has also ALK/ALK reaction on Triple sugar iron (TSI) agar (5). Mueller-Hinton plates were inoculated with a 0.5 Mc Farland standard of suspension harvested from plates. Etest strips (AB Biodisk, Solna, Sweden) were placed on each. After overnight incubation in incubator at 35º C, the MIC was read as intersect where the ellipse of growth inhibition intersects the strip. It was used a cut-off point of ≥16 μg/ml to define imipenem resistance and a cut-off point of ≤ 4 μg/ml to define imipenem susceptibility. Also, the cut-off points of ≥32 μg/ml and ≤4 μg/ml for ceftazidime and ≥4 μg/ml and ≤1 μg/ml for ciprofloxacin were defined. Furthermore, it was defined the cut-off points of results were expressed as the mean±standard error (SE) for quantitative variables and percentages for categorical variables.

A stepwise logistic regression was used for evaluation of relation between bacterial susceptibility as dependent variable and type of antibiotic and test as independent variables. Categorical variables were evaluated with odds ratios (OR), 95% confidence intervals, and the chi-square test. Means of MICs values were compared using paired *t* test. *P* values of <0.05 were considered significant.

Table 1: The number of *Acinetobacter baumannii* isolates susceptible, intermediate, and resistance to Ciprofloxacin, Ceftazidime, and Imipenem by E test

Susceptibility	E test n=191 n (%)
Ciprofloxacin	
Resistance	102 (53.4)
Intermediate	4 (2.1)
Susceptible	85 (44.5)
Ceftazidime	
Resistance	79 (41.4)
Intermediate	6 (3.1)
Susceptible	106 (55.5)
Imipenem	
Resistance	47 (24.6)
Intermediate	5 (2.6)
Susceptible	139 (72.8)

Results

The number of *A. baumannii* isolates susceptible, intermediate, and resistance to ciprofloxacin and ceftazidime by E test was shown in Table 1. The percentages of *A. baumannii* isolates susceptible to ciprofloxacin and ceftazidime by E test were 55.5% and 44.5%, respectively. The percentage of bacterium susceptible to imipenem by E test was 72.8%. Fifty percentile of MICs (MIC_{50}) of imipenem, ciprofloxacin, and ceftazidime in Etest were 1.5, 0.5, and >256, whereas 90 percentile of MICs (MIC_{90}) of these antibiotics were >32, >32, and > 256, respectively. There was significant relation between susceptibility of *A. baumannii* and type of antibiotic in Etest was seen (imipenem, 72.8%; ciprofloxacin, 55.5%; ceftazidime, 44.5%; $P < 0.0001$).

Discussion

Resistance patterns among nosocomial bacterial pathogens may vary widely from country to country at any given point and within the same country over time. Previous studies have shown that the first line therapy for *A. baumannii* infections includes amikacin, imipenem, ceftazidime, or a quinolone (6). This study has assessed the use of E test for determining imipenem, ciprofloxacin and ceftazidime MICs. For some relatively new antibiotics, such as broad-spectrum cephalosporins (cefotaxime, ceftazidime), imipenem, and fluoroquinolones, partial susceptibility remains, but the MICs of these antibiotics for *A. baumannii* isolates have increased substantially in the last decade. imipenem remains the most active drug; indeed, until recently, imipenem retained activity against 100% of strains (7, 8) and in some reports the only active drug was imipenem. The most recent extensive analyses of hospital outbreaks have documented the spread of imipenem-resistant strains (9, 10). Most resistance to imipenem has been observed in strains identified as *A. baumannii*, while the MIC of carbapenems for non- *A. baumannii* strains has remained below 0.3 mg/liter, but the widespread emergence and/or spread of resistance to imipenem is likely to pose a serious threat in the near

future. Differences in antibiotic susceptibility have been observed between countries, probably as a result of environmental factors and different patterns of antimicrobial usage (11).

In the present study, the resistance of *A. baumannii* isolates to imipenem was 24.6%. In a similar study in three university hospitals in Tehran, it was found that all *A. baumannii* isolates were resistant to multiple antibiotics including ceftazidime and meropenem and it was emphasized the presence and spread of multi-drug resistant *Acinetobacter* spp. in the hospitals of Iran (12). Simhon et al. study showed that 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 ceftazidime remained relatively unchanged (30-35%) (13). In a study in England, Wales and Northern Ireland, it is showed that resistance among *A. baumannii* varied according to the species, antimicrobial agent, and geographic location. Ciprofloxacin susceptibility ascertainment ranged from 6% to 51% in English regions with resistance levels varying from 4% to 50%. Ceftazidime susceptibility ascertainment ranged from12% to 85% in English regions with resistance levels varying from 40% to 69%, whereas imipenem susceptibility ascertainment 93% in English regions (14). Totally, it seems that the resistance of *A. baumanniii* is constantly changing and the consideration of this change is necessary in various countries. It seems that a surveillance of nosocomial pathogens for resistograms is needed for every country and/or even for every hospital in order to guide appropriate selection for empiric therapy.

In summary, 90 percentile of MICs of imipenem, ciprofloxacin, and ceftazidime for assessment susceptibility of *A. baumannii* in E test were >32, >32, and >256, respectively. The susceptibility of *A. baumannii* to imipenem was higher than ciprofloxacin and ceftazidime in this test.

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The authors declare that there is no conflict of interests.

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