

## Imipenem Resistance among Gram-Negative and Gram-Positive Bacteria in Hospitalized Patients

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(Received 17 Nov 2009; accepted 11 Jun 2010)

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### Abstract

**Background:** Recent analyses of hospital outbreaks have documented the spread of resistance to imipenem, which is currently a major problem among gram positive and gram-negative bacteria. The aim of this study was to describe the rate of gram-positive and gram-negative isolates resistance to imipenem as an antibiotic.

**Methods:** Recorded files of 242 hospitalized patients with at least one sample of positive culture specimens in one of the two general hospitals of Shahid Beheshti and Naghavi in Kashan, Iran in 2005 were randomly selected and reviewed. All strains were tested for antibiotic susceptibility by Disk Diffusion and were designated for imipenem.

**Results:** *Escherichia coli* (21.9%), *Kelebsiella* (19.8%) and coagulase-negative *Staphylococci* (17.8%) were the most common isolated organisms. Imipenem had coverage against 96.2% of *Escherichia coli*, 58.4% of *Kelebsiella*, 79.1% of coagulase-negative *Staphylococci*, 81.8% of *Pseudomonas aeruginosa*, and 85.7% of *Entrococci* isolates. *Proteus* and *Salmonella* isolates susceptibility to imipenem was 100%.

**Conclusion:** Susceptibility of *Escherichia coli*, *Salmonella* and *Proteus* to imipenem is satisfactory; however, the susceptibility of *Pseudomonas aeruginosa* to this antibiotic was dramatically lower in our region. Because of the major health problems caused by imipenem resistance, attempts have been made to organize a national surveillance program in our country.

**Keywords:** *Bacteria resistance, Imipenem, Antibiotic, Pseudomonas*

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### Introduction

Resistance patterns among bacterial pathogens are one of the most important problems in hospitals that may vary widely from country to country and its-related mortality and morbidity remain extremely high (1). Rate of bacterial resistance are markedly higher in many developing countries, probably because of a lack of supervision, poor infection prevention practices, inappropriate use of limited resources, and overcrowding of hospitals (2, 3). It seems that the overuse of effective antibiotics is also a potent cause of bacterial resistance especially in these counties. Imipenem has retained in vitro activities that are superior to those of other antimicrobials, and in many centers, it has been selected as a first choice for patients with infections caused by various types of gram-positive and gram-negative bacteria (4-9). Imipenem remains the most active drug; indeed, until recently,

Imipenem retained activity against 100% of strains, and in some previous reports, the only active drug was Imipenem (10). However, recent analyses of hospital outbreaks have documented the spread of resistance to this antibiotic and it is currently a major problem among gram positive and gram negative bacteria.

In the present study, we tried to describe the rate of gram-positive and gram-negative isolates resistance to Imipenem as an antibiotic that is widely used in our country.

### Materials and Methods

In a retrospective case series study, recorded files of 242 hospitalized patients in one of the two general hospitals of Shahid Beheshti and Naghavi in Kashan, Iran in 2005 were randomly selected and reviewed. All patients had at least one sample of positive culture and patients without any positive culture specimens were excluded. The pa-

tients consisted of 132 females and 110 males, with a mean age of 62.4±2.6 yr. The clinical isolates in this study had been isolated from urine (n= 60), blood (n= 47), wound (n= 35), sputum (37), tracheal tube secretion (n= 43), and cerebrospinal fluid (n= 20). All strains were tested for antibiotic susceptibility by Disk Diffusion and were designated for Imipenem as susceptible if the inhibition zone diameter was ≥ 16 mm, intermediate if the inhibition zone diameter was 13-16 mm, and resistant if the inhibition zone diameter was ≤ 13 mm, as recommended by the American Society of Microbiology (11). Results were expressed as the mean±standard deviation (SD) for quantitative variables and percentages for categorical variables.

## Results

In total, 242 various organisms were isolated from 242 patients. The isolated organisms and their

specimens are given in Table 1. *Escherichia coli* (21.9%), *Kelebsiella* (19.8%) and *Coagulase-negative Staphylococci* (17.8) were the most common isolated organisms. Isolated organisms were frequently isolated from urine sample (24.8%) and blood sample (19.4), respectively.

Based on the results from susceptibility testing, imipenem had coverage against 51 (96.2%) of 53 *Escherichia coli* tested isolates. *Proteus* and *Salmonella* species had complete susceptibility to imipenem. However, 20.9% of *Coagulase-negative Staphylococci* and 18.2% of *Pseudomonas aeruginosa* were resistant to this antibiotic.

*Escherichia coli* isolates from urine and tracheal tube secretion samples had the highest susceptibility to imipenem. Totally, bacteria isolated from urine and cerebrospinal fluid had the highest susceptibility for Imipenem (96.7% and 95.0%, respectively), whereas isolates from wound had the lowest susceptibility for Imipenem (85.7%).

**Table 1:** Susceptibility results of various bacteria isolated from different specimens

Organisms	Total No. of susceptible isolates (%)	Number of susceptible isolates from each sample (susceptible/total isolates)					
		Blood	Urine	Wound	Sputum	TTS	CSF
<i>Escherichia Coli</i>	51 (96.2)	3/4	31/31	7/8	-/-	9/9	1/1
<i>Kelebsiella</i>	41 (58.4)	-/-	7/8	6/7	12/15	13/15	3/3
<i>C-N Staphylococci</i>	30 (79.1)	16/21	2/2	6/7	5/7	2/3	3/3
<i>Enterococci</i>	34 (85.7)	8/11	5/5	3/3	3/3	6/8	5/5
<i>Pseudomonas</i>	27 (81.8)	4/5	5/6	5/7	4/4	5/6	4/5
<i>Proteus</i>	16 (100)	5/5	7/7	3/3	1/1	-/-	-/-
<i>Salmonella</i>	14 (100)	1/1	1/1	-/-	7/7	2/2	3/3
<b>Total</b>	213 (88.0)	37/47	58/60	30/35	32/37	37/43	19/20

TTS: Tracheal Tube Secretion

CSF: Cerebrospinal Fluid

C-N: Coagulase-negative

## Discussion

Resistance to antibiotic drug therapy is an increasing public health problem in all populations. In the recent years, through the abuse and misuse of antibiotics, many bacteria have developed resistance to the variety of antibiotics. This pattern of resistance can be different in various populations and therefore, each of them needs to special program for reduction of resistance to

antibiotics especially those are most commonly used for treatment. In the present study, we considered and measured the resistance of some gram-positive and gram-negative bacteria to Imipenem in a region of our country and found a bacterial susceptibility of 71.9% (for *Coagulase-negative Staphylococci*) to 100% (for *Proteus and Salmonella*) to Imipenem. Also, the susceptibility of *Pseudomonas* to imipenem was low and estimated as

81.8%. In a study, the percentage of *Pseudomonas* susceptibility to imipenem by Disk Diffusion was 94.4% (4). The percentage of *Pseudomonas* susceptibility was 92% (6) and the rate of *enterococcuse* resistance to imipenem was 4% (7). In a report, the percentage of *Escherichia coli* susceptibility was 100% (8) and the rate of *Kelebsiella pneumonia* susceptibility was 100% (9). Review of reports in other countries showed a higher susceptibility of *Pseudomonas* to imipenem in the range of 91.7% to 86% (12-16). In nine educational hospitals in France, resistance of anaerobic gram-negative bacilli to imipenem was extremely low and was measured as 1% (17). In Saudi Arabia, it was shown that the resistance of *Escherichia coli* isolates to imipenem was 99.7% (18), whereas the resistance of this bacterium to imipenem in our study was 96.2%. Comparison of the results of our study and other similar studies in different regions in Iran and even other countries shows that the susceptibility of some bacteria such as *E. coli*, *Salmonella*, and *Proteus* to imipenem is satisfactory; however, the susceptibility of *Pseudomonas* to this antibiotic was dramatically lower in our region in comparison with other regions. Previous studies have demonstrated that imipenem is a broad-spectrum Carbapenem antibiotic with activity against *Pseudomonas aeruginosa* and this antimicrobial agent is effective in the treatment of infections caused by *Pseudomonas aeruginosa* isolates that are resistant to the antipseudomonal Cephalosporins (19). Furthermore, it has been shown that treatment with imipenem, but not with other beta lactam drugs, is a major risk factor for the development of imipenem-resistant *Pseudomonas* in hospitalized patients (20). It was also reported a three-fold rise in the consumption of imipenem worldwide. Given this substantial use of antibiotic, it is not surprising to note the change in the microbial ecology, with predominance of multi-resistant strains of *Pseudomonas*. It is also well documented that the indiscriminate use of imipenem can lead to the selection and dissemination of antibiotic-resistant organism (21).

In conclusion, it seems that the infection control measures to limit the emergence of Imipenem resistance are important issues in all population especially in developing countries. Because of the major health problems caused by antibiotic resistance in the last few years, attempts have been made to organize a national surveillance program in these countries.

### Ethical Consideration

All Ethical issues (such as informed consent, conflict of interest, plagiarism, misconduct, co-authorship, double submission, etc) have been considered carefully.

### Acknowledgements

This research project has been supported by Kashan University of Medical Sciences, Iran. The authors would like to thank the interviewers who collected the information and all participants who gave up their time for the study.

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