

Full Length Research Paper

Comparison of *in vitro* activity of imipenem productions on bacterial isolates from Hashemi Nezhad Tehran hospitalized patients

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Carbapenams are one of the β -lactamase antibiotic resistances to penicillin that were introduced in 1980 to the medical world. Imipenem- a semi-synthetic derivative of thienamycin- is one of the most important broad spectrum β -lactamase in carbapenems. The irregular usage of drugs, especially in these types of gram-negative bacteria will lead to a serious problem in the treatment of pathogenic bacteria. Comparison of *in vitro* activity of imipenem productions is the aim of this study. 135 strains of various gram positive and gram negative bacteria collected from Hashemi Nejad Hospital in Tehran were studied. Initially strains were identified by phenotypic methods; then Disk Diffusion and MIC methods based on instructions of Forum France Microbiology were used. From 135 samples, urine samples (36%) were the most and trachea (4%) was the lowest. Among gram-negative bacteria isolated, both *E. coli* and *Pseudomonas* (37%) had most common and *Enterobacter* (1%) was the lowest. By disk diffusion method, Supranem, Taynam and Mast pharmaceutical products, showed similar result, but the results related to internal company disks were different. 20% of the total bacteria studied had MIC over 8 mg (resistant). Due to results of this study using standard disks and antibiotic powder (Imipenem/Cilastatin sodium) (Supranem) or (Tienam) is recommended.

Key words: β -lactamase, antibiogram, imipenem.

INTRODUCTION

Carbapenems were introduced in 1980 and now are commonly applied as the last choice in treating crucial infections caused by multidrug-resistant strains of gram negative bacilli. These antibiotics are stable to β -lactamase generated by gram-negative bacilli. The carbapenems are a class of β -lactamase antibiotics different from the penicillins by the replacement of a carbon to sulfur atom and by the addition of a double bond to the five member rings of the penicillin nucleus. Carbapenems block the elongation and cross linking function of the peptidoglycan cell wall by binding to

bacterial peptidases (Pastel, 1986; Bonfiglio et al., 2002; Barza, 1985; Barry et al., 1985). Imipenem were one of the most important broad spectrum β -lactamase in Carbapenems. Imipenem, also referred to as N-formimidoyl thienamycin monohydrate, is a semi-synthetic derivative of thienamycin, the parent compound produced by the filamentous bacterium *Streptomyces cattleya*. Cilastatin is a competitive, reversible and specialized inhibitor of dehydropeptidase-I enzyme, the renal enzyme which metabolizes and inactivates imipenem (Bonfiglio et al., 2002; Barza, 1985; Barry et al., 1985). It has no intrinsic antibacterial activity and does not affect the antibacterial activity of imipenem. Combination of imipenem/cilastatin against an infrequently wide spectrum of pathogens makes it mainly

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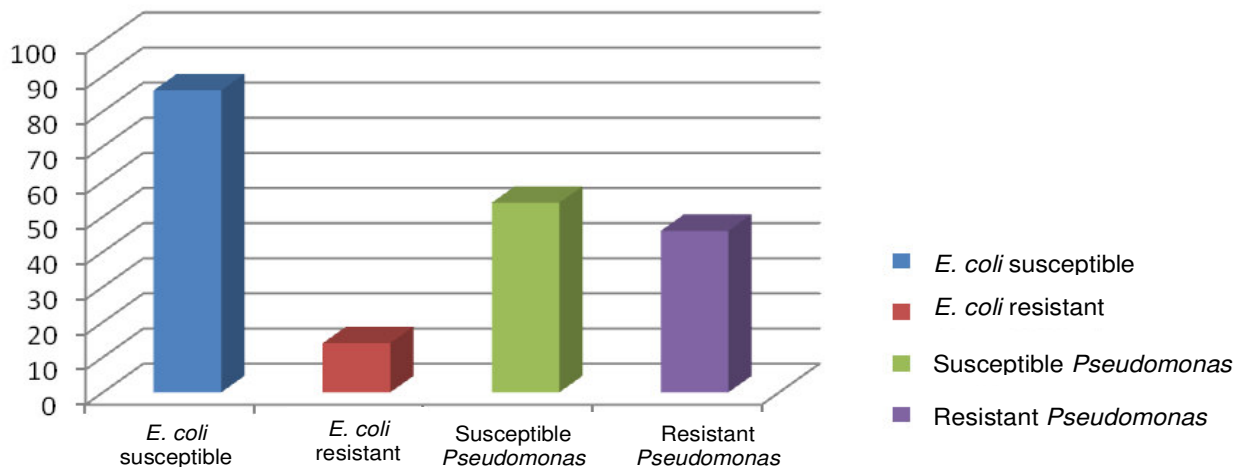


Figure 1. *E. coli* and *Pseudomonas* antimicrobial susceptibility test by supranem powder.

beneficial in the treatment of polymicrobial mixed aerobic/anaerobic infections (Queenan and Bush, 2007; Zhanel et al., 2007; Oteo et al., 2008; Kohler et al., 1999). Resistance to carbapenems emerged from 1990 and has been reported in gram negative bacilli. Multi-drug resistance (including carbapenem) in gram-negative bacteria established a crucial problem as a result of the lack of therapeutic choices and the capability transfer of antibiotic resistance to other virulent pathogens. Offered carbapenems in Islamic Republic of Iran are meropenem and imipenem. Combination of imipenem/cilastatin is used in the treatment of the following infections due to susceptible organisms: Intra-abdominal infections, lower respiratory tract infections, gynecological infections, septicemia, genitourinary tract infections, bone and joint infections, skin and soft tissue infections and endocarditis. Also, the mentioned compound is used in the treatment of mixed infections caused by susceptible strains of aerobic and anaerobic bacteria (Queenan and Bush, 2007; Zhanel et al., 2007; Oteo et al., 2008; Kohler et al., 1999; Jones et al., 2005).

MATERIALS AND METHODS

135 clinical isolates of various strains of gram positive and gram negative bacteria (*E. coli*, *Pseudomonas*, *Streptococci*, *Staphylococci*, *Enterococci*, *Proteus*, *Klebsiella pneumonia*, *Enterobacter*) from hospitalized patients in Hashemi Nezhad Hospital of Tehran from April 2008 to November 2009 were studied. The identification of the bacteria was determined by using routine bacteriology methods. Therefore antimicrobial susceptibility patterns of clinical isolates were determined by standard NCCLS methods.

Antibiogram method

The antimicrobial susceptibility test was performed by

disk diffusion method as recommended by France Microbiology Institute protocol, 2007. The antibiotics used were trimethoprim sulfamethoxazole (SXT), ciprofloxacin (CIP), amikacin (AN), ofloxacin (OFX), nalidixic acid (NA), cefotaxime (CTX), vancomycin (VA), amoxicillin (AMX), nitrofurantoin (FD), ampicillin (AM), ceftizoxime (ZOX), ceftriaxon (CRO) provided from Pad tan Teb Co, Iran. Then all strains were examined for *in vitro* imipenem susceptibility test by using the following disks which were made from supranem, tineam and Pad tan Teb Co powders; each of these disks were compared with the others.

Determination of MIC

The MICs for all isolates were determined by Agar dilution method according to standard NCCLS by using supranem powder from Exir Co and tienam powder from Merck Co (van Ogtrop et al., 1998; Castanheira et al., 2009; NCCLS, 2003, 2001; Clinical and Standards Institute (CLSI), 2007).

RESULTS

In total, during the study period 135 gram positive and gram-negative bacterial infections were isolated from 242 patients. Gram positive and gram-negative bacteria were most frequently recovered from urine (36%), followed by surgical-site cultures (32%), blood (28%) and (4%) trachea. The most percentage of clinical isolates, which includes *E. coli* and *Pseudomonas* were predominant among clinical strain, while *Enterobacter* has minimum percentage. Among gram-negative bacteria isolated, both *E. coli* and *Pseudomonas* had most common (37%) and *Enterobacter* was the lowest (1%) by disk diffusion method. Supranem, Taynam and Mast pharmaceutical products, showed the same result (Figures 1 and 2); however, the results related to internal company disks

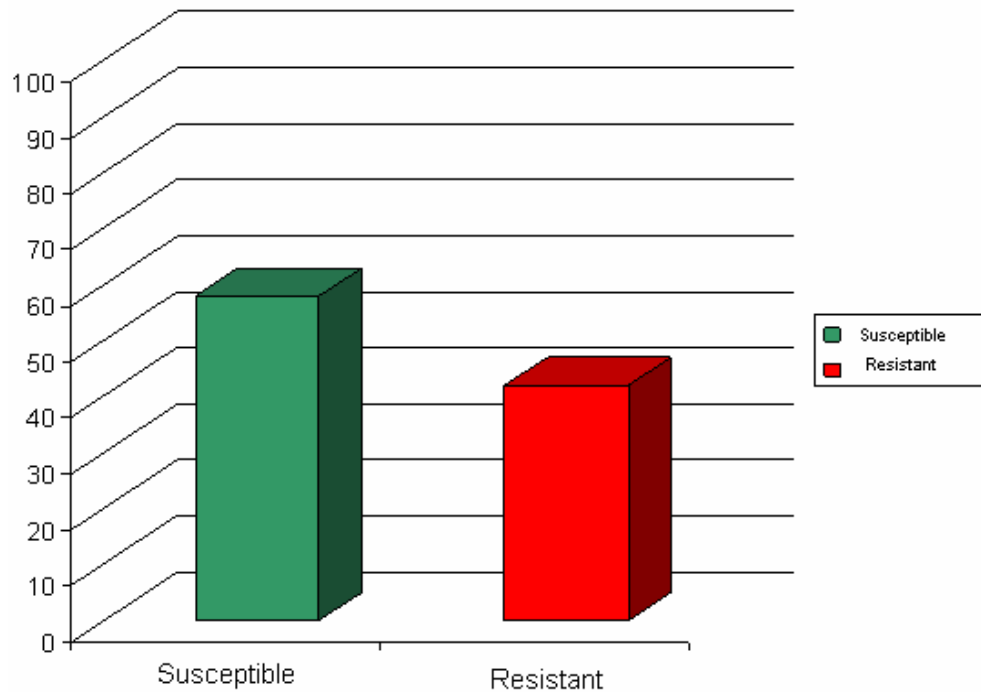


Figure 2. *Pseudomonas* antimicrobial susceptibility test by tienam powder.

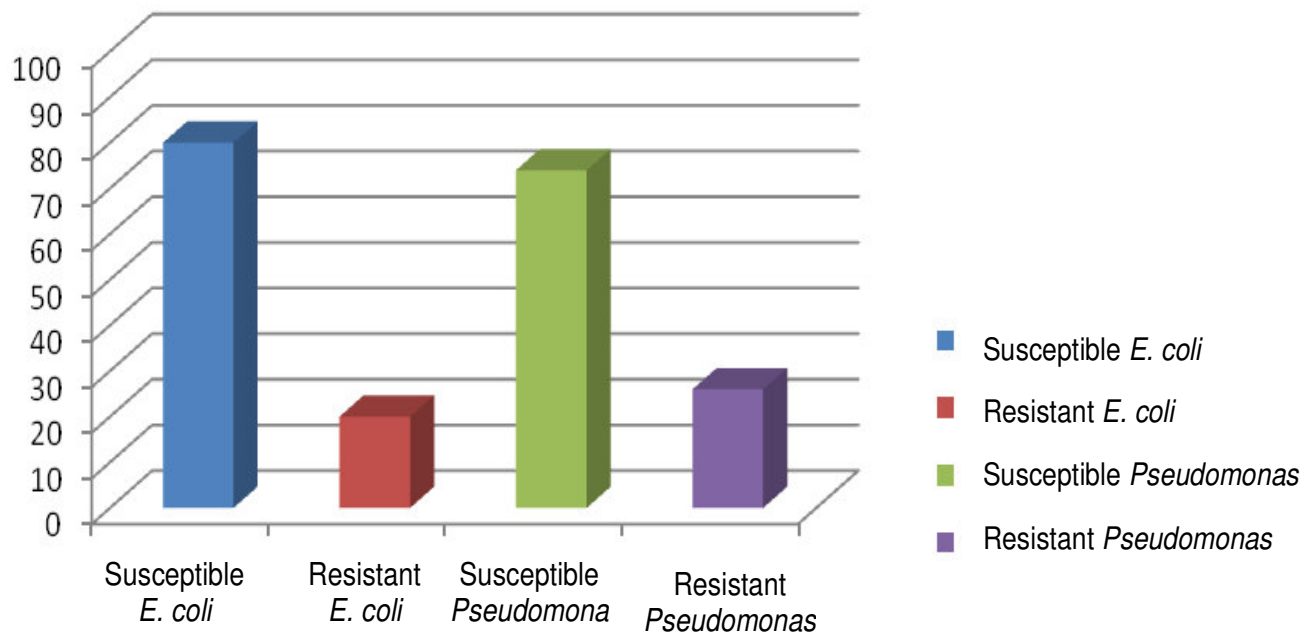


Figure 3. MIC results of *E. coli* and of *Pseudomonas* by using supranem powder (S<8 mg/l) (R>8 mg/l).

were different. 20% of the total bacteria studied had MIC over 8 mg (resistant) (Figure 3).

The antimicrobial susceptibility test result from disk diffusion.

DISCUSSION

Resistance to antibiotic drug therapy is an increasing public health problem in all populations. In 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 be specially programmed for reduction of resistance to antibiotics especially those most commonly used for treatment. Most studies show that imipenem is the most effective agents against gram-negative bacteria especially enterobacteriaceae and pseudomonas (Kohler et al., 1999). 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. The results of our study demonstrated that more than 80% of *E. coli* was sensitive to antimicrobial susceptibility test by disk diffusion made from supranem and tienam. The result of antimicrobial susceptibility test for gram-positive bacteria for both supranem and tienam powder were the same. Therefore antimicrobial susceptibility for all isolates was performed by Mast Co disk provided, and similar results were obtained. Our studies show supranem and tienam have the same effective spectrums; however, both native disks showed completely different results. On the other hand, determination of imipenem antimicrobial activity with both powder by MIC method shows that only 20% of strains have MIC>8. As a matter of fact supranem and tienam had a similar effect on studied strains, hence avoiding the use of non standard disks is recommended. These antibiotics are frequently used to treat infections caused by multi drugs-resistant strains of gram negative bacteria especially *P. aeruginosa* and *E. coli*.

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.

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