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Original Article

The Susceptibility Evaluation of Multiresistant Gram-Negative Bacilli to Meropenem and Imipenem

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Abstract

Introduction: Nosocomial infections are responsible for the much of the morbidity and mortality found in hospitals. The present study was conducted on 70 bacterial strains isolated from hospitalized patients in various medical units of Baqiyatallah Hospital in Tehran, Iran during a period of 12 months from; March to February 2009.

Methods: The bacterial sensitivity for meropenem and imipenem was evaluated using the E-test and explanations of the MIC values. All patients were included in this study that had been hospitalized with no signs and symptoms of infection within the first 48 hours of hospitalization and began presenting signs and symptoms of infection after 48 hours of hospitalization.

Results: Resistance to meropenem and imipenem was confirmed with E-test (AB Biodisk, Sweden) and disc diffusion methods. Meropenem and imipenem were active against 61 (64.2%) and 62(65.2%) strains, respectively, of the 95 ESBL positive strains.

Conclusion: The activity of meropenem or imipenem against gram negative ESBL-positive bacilli is decreasing rapidly but even so these antibiotics are effective against nosocomial multiresistant organisms.

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Introduction

Secondary infections due to Gram-negative bacilli continue to be one of the leading causes of mortality and morbidity. Resistance to beta-lactam antibiotics has increased remarkably in the last two decades and has been documented in both community and hospital settings [1-3]. During the past decade, Gram-negative bacteria have extended resistance too many antibiotics, including quinolones, aminoglycosides and β-lactams. Some gram negative rods, such as: some strains of Proteus mirabilis, Escherichia coli and Klebsiella spp. are known to make extended spectrum β-lactamases (ESBLs) or stably derepressed AmpC Beta -lactamases (AmpC) resulting in their wide resistance to the monobactams and third generation cephalosporins [4,5].

Meropenem and Imipenem are widely used against Beta-lactamase positive bacteria. They are active against most clinically important gram-positive and gram-negative bacteria, including anaerobic and aerobic forms. Nevertheless, reckless use of these antimicrobials has increased Carbapenem resistance among nosocomial pathogens [6]. Antimicrobial therapy of strains producing extended-spectrum β-lactamases and inducible β-lactamases (IBL) has become restricted and the progression of resistance to carbapenems makes the problem more acute [7,8]. The aim of this investigation was to assess the in vitro activity of meropenem and imipenem against Gram-negative bacilli isolated from hospitalized patients in various medical units of Baqiyatallah hospital in Tehran, Iran over 1 year, and resistance to meropenem and imipenem was confirmed with disc diffusion and E-test (AB Biodisk, Sweden) methods.

Methods

1. Strain collection

The study was performed during a period of 12 months from March to February 2009 Baqiyatallah hospital in Tehran, Iran. All patients with no symptoms and signs of infection before the first 48 hours of hospitalization and presenting signs and symptoms of infection after 48 hours of hospitalization (nosocomial infection) were included. Finally, 350 specimens were collected via blood samples from peripheral veins.

2. The determination of ESBL

The testing protocols were ratified in accordance to the guidelines of the National Committee for Clinical Laboratory Standards.[9] The ESBL study used two different E test strips on Mueller Hinton Agar (MHA): cefotaxime/cefotaxime with clavulanic acid or ceftazidime/ceftazidime with clavulanate.[10] The recommendations of the January 2003 NCCLS guide was used as the criterion for ESBL-positivity [9]. The specimens were concluded to be ESBL-positive if the addition of clavulanic acid diminished the MIC of either of the β-lactam agents by three-fold or more. E. coli ATCC 25922, P. aeruginosa ATCC 27853 and K. pneumoniae BCC 1395 were used as control strains.

Table 1. Imipenem and meropenem susceptibility of ESBL

	Total	ESBL positive			
		Imipenem		Meropenem	
Susceptibility		S	R	S	R
Strains		n	n	n	n
A. baumannii	45	26	19	28	17
P. aeruginosa	28	16	12	11	17
Klebsiella spp	13	11	2	13	0
E. coli	4	4	0	4	0
Enterobacter spp.	5	5	0	5	0
Total	95	62	33	61	34

S, susceptible_4 mg/l; R, Resistant_16 mg

3. In vitro assessment of ESBL strains for meropenem and imipenem

The susceptibilities to meropenem and imipenem of the 95 ESBL positive specimens were definite using the E-test and explanations of the MIC values in mg/l were made from the NCCLS document [9]. The limit values of MIC were regarded as: more than 16 mg/l; resistant, 8 mg/l; intermediate and less than 4 mg/l; unsusceptible. Resistance to meropenem and imipenem was confirmed with disc diffusion and E-test (AB Biodisk, Sweden) methods.

Results

Ninety five of 350 strains were confirmed to be resistant to β-lactam antibiotics. The frequency of microbial agents in this investigation was stated as; Escherichia coli 4(4.2%), Klebsiella pneumoniae 13(13.6%), Enterobacter spp. 5(5.2%), Pseudomonas aeruginosa 28 (29%), Acinetobacter baumannii 45 (47%).

In our study, meropenem and imipenem were active against 61 (64.2%) and 62(65.2%) strains, respectively, of the 95 ESBL positive strains. In Acinetobacter baumannii, where there was the highest incidence of ESBL production, imipenem and meropenem were effective against 84.6% and 100% of strains, respectively. Activity of imipenem against P. aeruginosa and Klebsiella spp. strains was 57.1% and 84.6% but meropenem activity against these strains was 39.2 and 100% respectively. Imipenem and meropenem were completely active against E. coli and Enterobacter spp. Other results are shown in Table 1.

Discussion

In this study, meropenem and imipenem were active against 61 (64.2%) and 62(65.2%) strains of the ESBL positive strains, respectively. Imipenem was minutely more effective against all ESBL positive strains than meropenem. In the investigations conducted by Garau [7] and Colardyn [8], imipenem and meropenem were effective against 74.3, 74 and 81.7, 75%, respectively [7,8].

The effectiveness of both carbapenems in intra-abdominal surgical patients in three studies on ICU strains was more than 94% but this is in disagreement with our findings [11-13]. The rate of resistance to imipenem was 8% in a Polish study and 13% in a Belgian study, and this is in disagreement with our results [14-15]. In a similar study, Zanetti et al., found meropenem and imipenem to be 87.1% and 92% effective [16]. However, in a study in Turkey, resistance to imipenem (8.4–33.4%) was lower than that of our investigation [17]. Two studies results showed carbapenems (imipenem and meropenem) to be more potent in vitro than any other drug against the Enterobacteriaceae [18-19]. Similar studies have explained the efficacy of meropenem and imipenem to be 100 and 95.4 % for ESBL producing strains and 94.9 and 96.9 % for strains producing undefined-lactamases [20-21]. In Iaconis study, 13% of strains were resistant to imipenem and 4% to meropenem [22]. Imipenem resistance was found in two strains of K. pneumoniae, but meropenem resistance was found in none due to ESBLs. Meropenem and Imipenem are absolutely resistant to β-lactamase enzymes of Gram-negative bacteria and acquired resistances due to carbapenemases are scarce in these bacteria [23–25]. The difference of our study with other similar studies is that we screen tested to select ESBL strains of specimens and then a susceptibility test was performed.

Durmaz et al. In a lesser but similar study found no meropenem resistance in 22 Gram-negative strains with ESBL positivity and imipenem resistance existed only in one K. pneumoniae strain [20]. In Iran, Hadadi et al described the resistance pattern of Gram-negative bacteria (but no ESBL) to imipenem. Except E.Coli, imipenem resistance was increased in our study versus the Hadadi study [26]. Hawser's study demonstrated that the most active agents against ESBL-positive K. pneumoniae were imipenem, with susceptibility percentages of 89.5% .[27] In Iran, as a developing country, multidrug resistance isolates are commonly reportedly due to antibiotics abuse [28]. The results explain carbapenems (imipenem and meropenem) being more effective in vitro than any other drug against Gram-negative bacilli.

Conclusion

The prevalence of antibiotic resistance in Gram-negative rods is high in Asia. The activity of meropenem or imipenem against gram negative ESBL-positive bacilli is decreasing rapidly but these antibiotics are continuing to show effectiveness against nosocomial multiresistant organisms. This study's results can be used in preparing evidence-based guidelines for antibiotic therapy, especially empirical treatment of nosocomial bacterial infections.

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