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ORIGINAL ARTICLE

Spectrum of Imipenem and Meropenem Susceptibilities amongst Gram Negative Rods

SADIA IKRAM[1], ANILA ERRUM[2], ASMA INAM[3], FARRUKH SARFARAZ[4], SADIA MAJEED[5], SAIMA PERVAIZ[6], SOHAILA MUSHTAQ[7]

[1]Associate Professor, [7]Professor, Department of Pathology, Azra Naheed Medical College, Superior University, Lahore
[2]Assistant Professor, Department of Pharmacology, Azra Naheed Dental College, Superior University, Lahore
[3]Associate Professor, Department of Pharmacology, Azra Naheed Medical College, Superior University, Lahore
[4]Assistant Professor, Department of Medical Education, Azra Naheed Medical College, Superior University, Lahore
[5]Assistant Professor, Department of Pharmacology, Continental Medical College, Lahore
[6]Assistant Professor, Department of Pathology, Azra Naheed Dental College, Superior University, Lahore
Correspondence to: Sadia Ikram, Cell: 0323-5315347, E-mail: dr_sadia.sajid@hotmail.com

ABSTRACT

Aim: To compare the resistance amongst Gram negative bacteria against imipenem and meropenem.
Study Design: Prospective, non-randomized, descriptive study.
Place and Duration of Study: Department of Microbiology, Mughal Laboratories, Lahore from 1st July 2019 to 31st December 2019.
Methodology: One hundred culture samples received, bacteria isolated and their susceptibilities to imipenem and meropenem were compared. Organisms were recognized by the microbiological techniques according to the current standards and susceptibility testing was done according to the guidelines of Clinical and Laboratory Standards Institute (CLSI) 2020by using Kirby Bauer Disc diffusion method.
Results: *Salmonella typhi, Citrobacter species and Proteus species* were 100% sensitive to imipenem. The rest of bacterial isolates had sensitivities to *E. coli 88%, Acinetobacter 80%, Klebsiella species 67% and Peudomonas species 64%.* The meropenem is highly resistant in all the bacteria as compared to imipenem.
Conclusion: Increasing the trend of carbapenem resistance amongst Gram negative bacteria excluding *Salmonella typhi* was recorded.
Key words: Gram negative rods, Resistance, Spectrum

INTRODUCTION

The antibiograms have a significantly vital place for carbapenems. Carbapenems possess the broadest range of activity and greatest potency against Gram-positive and Gram-negative bacteria amongst the different β-lactams. As a consequence, these are frequently used as "last-line agents" or "antibiotics of last resort" when patients with infections become fatally ill or are suspected of harbouring resistant bacteria.[1-3] Due to recent emergence of multidrug-resistant (MDR) pathogens, this class of life saving drugs in under serious threat.[4]As shown in several recent studies, resistance to carbapenems is increasing throughout the world.[5-7] Concerning their role with regard to β-lactamase inhibition, our understanding of how to best use these agents is undergoing a renaissance despite this alarming trend.

The carbapenems exhibit an overall broader antimicrobial spectrum*in vitro*as compared to penicillins, cephalosporins, and β-lactam/β-lactamase inhibitor combinations.[8] Generally against Gram-positive bacteria, imipenem, panipenem, and doripenem are more effective antibiotics [8,9] whereas meropenem, biapenem, ertapenem, and doripenemare somewhat more effectual against Gram-negative organisms.[8,10] There are certain significant considerations in this regard: (i) Ertapenemhas a more limited spectrum,[11]and is not as active as imipenem or meropenem against*P. aeruginosa*; (ii) Against *Acinetobacterbaumannii,* meropenem is not as potent as imipenem or doripenem[11]; (iii) Considering *P. Aeruginosa* and *A. baumannii*, doripenem has lower MICs than do imipenem and meropenem.[12]

MATERIALS AND METHODS

It was a prospective, non-randomized, descriptive study conducted at Microbiology Department of Mughal Laboratories, Lahore over a period of 6 months from 1st July 2019 to 31st December 2019. All the culture samples received during this period were analysed. According to the current standardsorganisms were recognized by the microbiological techniques and Kirby Bauer Disc diffusion procedure was used for susceptibility testing according to the guidelines of Clinical and Laboratory Standards Institute (CLSI) 2020**.** The identified isolates were subjected to antimicrobial susceptibility testing using Agar disc diffusion methods. Zone of inhibitions were measured and reported according to Clinical Laboratory Standard Institutes Criteria (CLSI 2020) and susceptibilities of isolated bacteria against imipenem and meropenem were compared. Data analysis of the present research was carried out and their graphical representation and statistical analysis was determined by using Microsoft Excel and SPSS version 23.

RESULTS

The division of bacteria isolated were*: E.coli 41%, Psedomonas species 25%, Klebsiella species 12%, Salmonella typhi 11%, Acinetobacter species 5%, Proteus species 4%, Citrobacter species 2%*. It was established that the most common bacteria isolated was *E.coli* followed by *Pseudomonas* and so on (Fig. 1).

The individual susceptibilities of isolated bacteria against imipenem (Table 1). *Salmonella typhi, Citrobacter species and Proteus species* were 100 % sensitive to imipenem. The rest of bacterial isolates had sensitivities as

under; *E. coli 88%, Acinetobacter 80%, Klebsiella species 67% and Peudomonas species 64% (Table 1).*

The individual susceptibilities of isolated bacteria against meropenem are shown in table 2. *Salmonella typhi was 100 % sensitive and acinetobacter* was completely resistant to meropenem. The rest of bacterial isolates had sensitivities as under; *Citrobacter 50%, E. coli 49%, Pseudomonas species 29%, Proteus species 25% and Klebsiella species 17% (Table 2).*

The comparison of susceptibilities to imipenem and meropenem in all the bacterial isolates enrolled in the study. The graph clearly shows that meropenem is highly resistant in all the bacteria enrolled in the study as compared to imipenem (Fig. 2). Percentage resistance to meropenemagainst different isolates were; *Acinetobacter 100%, Proteus species 75%, Pseudomonas species 68%, Klebsiella species 67%, E. coli 51% and Citrobacter 50%*. There was no resistance observed in *Salmonella typhi* against both drugs and p value was highly significant (0.0001).

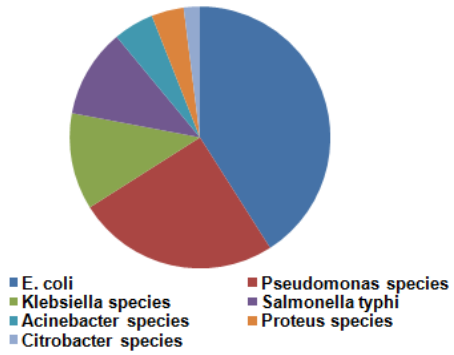


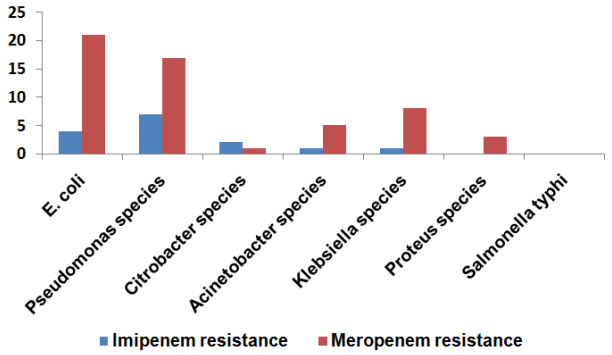
Fig 1: Frequency of Gram negative bacteria

Table 1: Susceptibility profile of Gram negative bacteria against Imipenem on disc diffusion (n=100)

Bacterial Isolate	Imipenem		
	Resistant N (%)	Intermediate N (%)	Sensitive N (%)
E. coli (41)	4 (10%)	1 (2%)	36 (88%)
Pseudomonas species (25)	7 (28%)	2 (8%)	16 (64%)
Citrobacter species (2)	-	-	2 (100%)
Acinetobacter species (5)	1 (20%)	-	4 (80%)
Klebsiella species (12)	1 (8%)	3 (25%)	8 (67%)
Proteus species (4)	-	-	4 (100%)
Salmonella typhi (11)	-	-	11 (100%)

Table 2: Susceptibility profile of Gram negative bacteria against Meropenem on disc diffusion (n=100)

Bacterial Isolate	Meropenem		
	Resistant N (%)	Intermediate N (%)	Sensitive N (%)
E. coli (41)	21 (51%)	-	20 (49%)
Pseudomonas species (25)	17 (67%)	1 (4%)	7 (29%)
Citrobacter species (2)	1 (50%)	-	1 (50%)
Acinetobacter species (5)	5 (100%)	-	-
Klebsiella species (12)	8 (67%)	2 (16%)	2 (17%)
Proteus species (4)	3 (75%)	-	1 (25%)
Salmonella typhi (11)	-	-	11 (100%)



Graph 2: Resistance in Gram negative bacteria against Imipenem and Meropenemby disc diffusion (n=100)

DISCUSSION

Increasing drug resistance has been a peril and threat to society and a persistently growing global problem. Carbapenem (meropenem, imipenem) have been the most active broad-spectrum antimicrobial class amongst the beta lactam drugs, but because of rapidly growing drug resistance, this class of antibiotics is also under serious threat. In the current study, we analyzed and compared the susceptibilities of Gram negative bacteria against imipenem and meropenem. Each of them needs to be catered by special programs for reduction of resistance to antibiotics especially those which are most commonly used for treatment, as the pattern of resistance can be different in various populations.

During the study period, the most commonly isolated bacteria from different culture samples were *E. coli* followed by pseudomonas. Considering Imipenem individually, *Salmonella typhi* were 100 % sensitive to imipenem. As carbapenems are the main stay of treatment due to rising resistance, the findings in our study were comparable to the XDR strains of Salmonella typhi earlier reported from Pakistan which were also found susceptible to carbapenems. In a study from Pakistanalmost 90% of patients with *Salmonella typhi* were sensitive to imipenem and meropenem.[13]

In the present study, *E. coli was 88%, Acinetobacter 80%, Klebsiella species 67% and Peudomonas species 64%* sensitive to imipenem, which was comparable to various studies conducted globally.[14]

The percentage of *E. coli* susceptiblity was 100% and the rate of *Kelebsiella pneumonia* susceptibility was 100% in another report.[15] Higher susceptibility of *Pseudomonas* to imipenem in the range of 91.7% to 86% was observed from review of reports in other countries.[16] Resistance of anaerobic gram-negative bacilli to imipenem was extremely low and was measured as 1% in a study from nine educational hospitals in France.[17] The resistance of *E. coli* isolates to imipenem was 99.7%[18], in Saudi Arabia, whereas the resistance of this bacterium to imipenem in our study was 64%. 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, when comparison of the results of our study and other similar studies in different regions in Iran and even other countries was done.Previous

studies have demonstrated that anti-pseudomonal cephalosporins fail for the treatment of infections caused by *Pseudomonas aeruginosa* isolates, whereas imipenem proved to be a broad-spectrum carbapenem antibiotic with better activity against *Pseudomonas aeruginosa.*[19] Furthermore, it has been observed that because of excessive use of this class of antibiotic and no other beta lactam drugs, there is emergence of imipenem-resistant *Pseudomonas* in hospitalized patients.[20] A three-fold rise in the consumption of imipenem worldwide was also reported by certain studies.In this study, susceptibilities against meropenem, it was observed to be less sensitive as compared to imipenem other than Salmonella typhi which was 100% sensitive.[13]

The rest of bacterial isolates had sensitivities as under*; Citrobacter 50%, E.coli 49%, Pseudomonas species 29%, Proteus species 25% and Klebsiella species 17%.Acinetobacter* was completely resistant to meropenem. This is comparable to a study conducted in a tertiary care hospital in Iran.[21]

Although generally, meropenem is 2 to 16 fold more active than imipenem against Gram-negative aerobes[22,23] and 4 to 16 fold more active against Enterobacteriaceae, but when we compared the study drugs, it was observed that percentage resistance to meropenem against the study isolates was more as compared to imipenem

CONCLUSION

Increasing the trend of carbapenem resistance amongst Gram negative bacteria, excluding *Salmonella typhi* was highlighted. Furthermore the curve was more inclined toward resistance to meropenem as compared to imipenem that is a different trend and new aspect. In order to improve the quality of empiric antimicrobial prescribing or guiding development of antimicrobial policies for such precious class of antibiotics, antimicrobial susceptibility surveillance programs represent one of the main recommendations to control resistant organisms.

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