Short Communication

Carbapenem sensitivity profile amongst bacterial isolates from clinical specimens in Kanpur city

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Abstract

Emerging antibiotic resistance against carbapenems is a serious issue and urgent measures are required to curb such development of resistance. There is paucity of data on the prevalence of carbapenem resistance in the Indian literature. This study involves a retrospective analysis of culture and sensitivity data on 174 clinical specimens obtained from different hospitals in Kanpur. Of the specimens, 15% grew bacilli which were resistant to at least one of the carbapenems. Of these bacilli 92% were resistant to Meropenem and sensitive to Imipenem. Only one specimen, that of urine grew *E-coli* which was resistant to Imipenem but sensitive to Meropenem. *Staphylococcus aureus* constituted majority (77%) of the resistant bacilli. *E-coli* were the second most common resistant bacilli to be isolated. *Pseudomonas aeruginosa* constituted 8% (2) of the resistant bacilli. Mengiococcus isolated once from a cerebrospinal fluid specimen was sensitive to Imipenem but resistant to Meropenem. Of the *E-coli* isolates 3% (3) were resistant. Results indicate alarming increase in the incidence of carbapenem resistance.

Key words: Carbapenem resistance, Kanpur

Introduction

Nosocomial infection is a serious challenge as it increases significantly the morbidity and mortality, besides, the high incidence of gram negative bacteria and development of multi-drug resistance still remains a serious problem. This has fueled the development and addition of newer antibiotics to the armamentarium and many guidelines for their use as well. Carbapenems first introduced in 1980 are now frequently used as a reserved drug in treating serious infection caused by multi-drug resistant gram negative bacilli. These antibiotics are stable to β-lactamases including the extended spectrum β-lactamases (ESBLs) and AmpC produced by gram negative bacilli. Unfortunately resistance to these antibiotics started emerging from 1990 and has been reported worldwide over the years with varying frequencies.[1] *Pseudomonas aeruginosa* and *Acinetobacter* spp. in particular are most often associated with carbapenem resistance. There is paucity of data on the prevalence of carbapenem resistance in the Indian literature, which is required for developing insight into management of serious nosocomial infections and measures for curbing the emergence of carbepenem resistance.[2,3] This study involves a retrospective analysis of the culture and sensitivity data on specimens obtained from various hospitals in Kanpur city in an attempt to answer key questions: 1) what is the incidence of various organisms 2) incidence of organisms with respect to the type of specimen 3) incidence of Imipenem and Meropenem resistance with respect to bacteria and type of specimen.

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Methodology

Culture and sensitivity data was obtained from a

diagnostic laboratory on specimens received over the past four months. Majority of specimens obtained were from private nursing homes and multi-specialty hospitals in and around Kanpur city. Many of these have intensive care set-up. Few specimens were also obtained from a large teaching hospital of the city. Samples with more than 24h of refrigeration were not processed. All specimens were inoculated on 5% sheep blood and MacConkey agar plates and incubated overnight at 37^{0}C aerobically (MacConkey agar) and in 5% carbon dioxide (blood agar). Bacterial pathogens were identified by conventional biochemical methods according to standard microbiological techniques.[4] A sample was included in the study only if it was positive for less than two types of bacteria. Antimicrobial sensitivity was performed on Mueller-Hinton agar (Hi-Media, India) against Imipenem (10 μg/disc) and Meropenem (10 μg/disc) by the standard disk diffusion method recommended by the National Committee for Clinical Laboratory Standards (NCCLS).[5] The diameter of the zone of inhibition of growth was recorded and interpreted as susceptible or resistant by the criteria of NCCLS.[5] Organisms with "intermediate" levels of resistance were included in the percentage of resistant organisms for final analysis. The variables recorded were the specimen source, bacteria grown and resistance to Imipenem and Meropenem. The data was analyzed using SPSS software (version 11, Chicago).

Results

174 specimens were surveyed over the past two month period, 120 samples in the first two months had to be excluded to prevent methodology bias, as culture plates and antibiotic discs being used, were of different make. Type of specimens included central line catheter tip (8%), endo-tracheal tube aspirate (3.4%), pus (25.8%), sputum (8%), urine (54%) and cerebrospinal fluid (CSF) (0.6%). Overall eight organisms were isolated namely Citrobacter (1.2 %), *E-coli* (50.6%), Enterobacter (0.6%), *Klebsiella pneumoniae* (6.9%), *Proteus mirabilis* (0.6%), *Pseudomonas aeruginosa* (8%), *Staphylococcus aureus* (31%) and Meningiococcus (0.6%).

Urine was the most common specimen. Of the urine specimens, 84% grew *E-coli*, 8.5% grew *Klebsiella pneumoniae*, 2% grew *Pseudomonas aeruginosa* and *Staph aureus* and 1% grew Citrobacter, Enterobacter and *Proteus mirabilis*. The second most common specimen was pus, of which 75% grew *Staphylococcus aureus*, 9% grew *Pseudomonas aeruginosa*, 11% grew *E-coli* and 2% grew Citrobacter and *Klebsiella pneumoniae*. Half of the central line catheter tip specimens grew *Staphylococcus aureus*, 36% of these specimens grew *Pseudomonas aeruginosa* and 7% of the specimens grew *E-coli* and *Klebsiella pneumoniae.* Of the sputum samples, 71% grew *Staph aureus*, 21% grew *Pseudomonas aeruginosa* and 7% grew *E-coli*. Of the Endo-tracheal tube aspirate *E-coli, Klebsiella* and *Staphylococcus aureus* were grown with similar frequency (33%). There was only one specimen of CSF which grew Meningiococcus.

Carbapenem resistance profile of isolated organisms is shown in Table 1. Of the specimens, 15% grew Carbapenem resistant bacilli. Of these bacilli 92% were resistant to Meropenem and sensitive to Imipenem. Only one specimen, that of urine grew *E-coli* which was resistant to Imipenem but sensitive to Meropenem and just one specimen, that of sputum grew *Staphylococcus aureus* which was resistant to both Imipenem and Meropenem.

Staphylococcus aureus constituted majority (77%) of the resistant bacilli. Except one isolate which was resistant to both, all others were sensitive to Imipenem but resistant to Meropenem. Three fourths of these resistant Staph were isolated from pus, 10% from sputum

Table 1: Carbapenem resistance profile of isolated organisms

Organism	Number of isolates	Resistant to carbapenem	Resistant only to meropenem	Resistant only to Imipenem	Resistant to both
Citrobacter	2	0	0	0	0
E-coli	88	3	2	1	0
Enterobacter	1	0	0	0	0
Klebsiella pneumoniae	12	0	0	0	0
Proteus mirabilis	1	0	0	0	0
Pseudomonas aeruginosa	14	2	2	0	0
Staphylococcus aureus	55	20	19	0	1
Meningiococcus	1	1	1	0	0
Total	174	26	24	1	1

and urine and 5% from central line catheter tip.

E-coli were the second most common resistant bacilli to be isolated and constituted 12% (3) of the resistant bacilli. Two of these were sensitive to Imipenem but resistant to Meropenem and were isolated from pus, one isolate which was obtained from urine was resistant to Imipenem but sensitive to Meropenem.

Pseudomonas aeruginosa constituted 8% (2) of the resistant bacilli. Both of these were sensitive to Imipenem but resistant to Meropenem. One was isolated from central line catheter tip and other from urine.

Mengiococcus isolated once from a CSF specimen was sensitive to Imipenem but resistant to Meropenem.

Discussion

Carbapenems are one of the essential antibiotics in the armamentarium against serious nosocomial infections. Development of resistance against these is a cause of concern. Reasons behind such increase in the incidence of resistance against carbapenems could be several. Among physicians, fear of litigation and perception of patient's expectations contribute to antibiotic misuse and, therefore, bacterial resistance. It is possible that carbapenems are being used empirically.

It has been shown that inappropriate duration of antibiotic therapy also helps in development of resistance.[6] Subtherapeutic concentrations of the drug is another important cause of development of resistance.[7] Carbapenems are often used for critically-ill patients and it has been shown that the drug concentrations in tissues achieved in these patients are often subtherapeutic in spite of standard dosages administered.[8]

We found that incidence of resistance against Meropenem was more than Imipenem. Meropenem is well-tolerated and offers several potential advantages, including greater *in vitro* activity against Gram-negative pathogens and the option of bolus administration.[9] Besides these, problem of renal metabolism of Imipenem and risk of seizures and greater availability of Meropenem in the market might be the reasons behind possible greater use of Meropenem over Imipenem and hence the higher incidence of resistance.

The common form of resistance is mediated by lack of drug penetration (i.e., porin mutations and efflux pumps) and/or carbapenem-hydrolyzing - lactamses. Based on molecular studies, Carbapenem - hydrolyzing enzymes are classified into four groups A, B, C and D. The metallo betalactamases (MBLs) belong to group B and are enzymes requiring divalent cations as cofactors for enzyme activity, being inhibited by the action of a metal ion chelator.[10]

The prevalence of resistance among *Pseudomonas aeruginosa* (14%) was found to be similar to that reported in previous study in the Indian setup.[11] However evidence of resistance amongst *E. coli* was found to be alarming as a recent study on 353 *E. coli* specimens failed to reveal resistance.[12] The mechanism behind selective resistance against Meropenem needs to be investigated. Measures to reduce antibiotic resistance include evidence-based selection of antibiotics, shorter courses of appropriately selected antibiotics with adequate dosages, surveillance for resistance, prevention of spread of resistant organisms, cyclical use if new antibiotics become available, education of consumers and prescribers about use and misuse of antibiotics, development of new drugs to circumvent or block-resistance mechanisms and revival of susceptible bacteria through more appropriate antibiotic use or potential use of probiotics. Steps need to be taken to prevent antimicrobial resistance or else this emerging menace would erode the strength of life-saving antibiotics, leave them with the negligible effect of placebo and put all significant resources allocated to research and treatment to waste in an already resource poor country like ours.

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Source of Support: Nil, **Conflict of Interest:** None declared.