Original Article

Assessment of the Drug Utilization Pattern of Meropenem in a Tertiary Care Super Specialty Hospital, Telangana: An Observational Study

G Pradeep[1], P Yazna[2], N Sathish Raju[3], Pradeep Panigrahi[4], Pranuthi Mispah[5], Narendhar Devarakonda[1]

[1]Clinical Pharmacist, Department of Clinical Pharmacy, Sree Lakshmi Gayatri Hospitals Private Limited, Hyderabad, Telangana, India, [2]Pharm-D Intern, Department of Clinical Pharmacy, Sree Lakshmi Gayatri Hospitals Private Limited, Hyderabad, Telangana, India, [3]Former Assistant Medical Superintendent, Department of Hospital administration, Sree Lakshmi Gayatri Hospitals Private Limited, Hyderabad, Telangana, India, [4]Medical Director, Department of Hospital Administration, Sree Lakshmi Gayatri Hospitals Private Limited, Hyderabad, Telangana, India, [5]Consulatant Microbiologist, Department of Clinical Microbiology, Sree Lakshmi Gayatri Hospitals Private Limited, Hyderabad, Telangana, India

Abstract

Introduction: Drug utilization evaluation is a quality-improvement activity to ensure rational use of medications. High empirical prescription of meropenem in the hospitals may lead to the prevalence of resistance, rising the necessity for evaluation of its utilization pattern. Meropenem is a broad-spectrum β-lactam antibiotic of the carbapenem clan. This study aims to evaluate the appropriateness of meropenem utilization pattern in the hospital.

Purpose: The main objectives of this study are to assess prescribing pattern of the meropenem and to observe its efficacy among the study participants.

Methods: This is a single-centered, observational, and cross-sectional retrospective study done in a tertiary care super-specialty hospital. This study was conducted by reviewing the case files of the patients who received meropenem from April 2021 to September 2021.

Results: Meropenem was prescribed to a total of 104 patients including 78 males and 26 females in 6 months. It is observed that meropenem is used for an appropriate indication in 80.76% of the patients. Culture and sensitivity tests were conducted for 88.47%. Duration of antibiotic therapy for more than half of the patients in between 1 and 5 days. Continuation of the therapy is justifiable only in 53.8% of the total patients. About 87.5% of the patients met the therapeutic success.

Conclusion: Meropenem is used in appropriate indication for most patients but, considerable inappropriateness is noted in the continuation of meropenem therapy. An increase in adherence to standard treatment guidelines can maximize the rationality in antibiotic therapy and decrease antibiotic resistance.

Key words: Antimicrobial resistance, Drug utilization evaluation, Meropenem, Rational use of antibiotics

INTRODUCTION

According to the WHO, evaluation of drug utilization pattern is a continuous quality-improvement activity, defined as an ongoing, systematic program to ensure rational use of medications.[1] It is classified into three categories, that is, prospective, concurrent, and retrospective. Drug utilization evaluation is specific to a disease or a drug that will assess the pattern of prescription, dispensing, or administration of medications in the hospital.

Antibiotics are the most frequently and imprudently prescribed drugs in hospitals. Approximately 40% of hospitalized inpatients receive antibiotics either for prophylactic or empirical use.[2] Inappropriate use of antimicrobials may lead to resistance. Antimicrobial resistance is a widespread health issue accelerated by the excess use of antimicrobials worldwide. An increase in antimicrobial resistance can cause severe infections, complications, increased hospital stays, and mortality.[3] Rational use of antibiotics should include compliance with

Corresponding Author: P Yazna, Department of Clinical Pharmacy, Sree Lakshmi Gayatri Hospitals Private Limited, Hyderabad, Telangana, India.

the standard treatment guidelines for specific infections. As a broad-spectrum antibiotic of the carbapenem family, meropenem is mostly used to treat a wide variety of infections.

Spectrum and Mechanism of action of Carbapenems

Carbapenems are beta-lactam antibiotics having bactericidal activity. Amid hundreds of antimicrobials, they possess the broadest spectrum of activity against Gram-negative and Gram-positive aerobes and anaerobes. After the penetration into periplasm through outer membrane proteins, carbapenems bind with the penicillin-binding proteins and enzymes that are crucial for the formation of peptidoglycan chain in the bacterial cell wall. The reason for the efficacy of carbapenems is their ability to bind with multiple penicillin-binding proteins. They are often referred to as last-line agents as they are only used in sternly ill patients or if the suspected organism is multi-drug-resistant.[4] Meropenem therapy is highly efficient in the treatment of various infections in adults and children.[5] It is a key option for some serious bacterial infections as empirical treatment.

Indications of Meropenem

Meropenem is mostly prescribed as an empirical therapy prior the identification of causative organisms or after the identification of causative organisms for the treatment of a disease. It is approved for indication in complicated intra-abdominal infections, complicated skin infections, complicated urinary tract infections, respiratory tract infections, pneumonias, septicaemia, febrile neutropenia, bacterial meningitis, obstetric and gynecological infections, and also in cystic fibrosis.[6]

As stated by Salehifar *et al.* in an evaluation study on meropenem therapy, high evident empirical prescriptions of meropenem in the hospitals may increase the resistance of meropenem, rising the necessity for evaluation of its utilization pattern.[7]

To maximize benefits from meropenem therapy, its utilization in the hospitals must fully comply with the standard guidelines. This study aims to study and analyze the appropriateness of the utilization pattern of meropenem in the hospital and suggest recommendations if necessary.

STUDY METHODOLOGY

Idea Conceptualization

The idea of evaluating the utilization pattern of an antibiotic in our hospital originated due to the observation of high empirical prescription of antibiotics without de-escalation by the clinical pharmacist during the regular prescription audits.

Study Setting

Tertiary care super-specialty hospital located in Hyderabad city, South India. The study was started after the approval of the hospital management with vide acknowledgement number SLGH/CLAD/CPI/002/2021-22

Study Type

This is a retrospective observational study.

Study Tool

An annexure was designed to collect the data. The collected data include demographics of the patient, medical and medication history, current diagnosis, duration and dosing of meropenem, clinical outcomes, microbial culture and sensitivity reports, and the type of infection.

Study Population and Source of Data

All the hospital in-patients who received meropenem during 6 months, that is, from April 2021 to September 2021 were included in the study. A total of 104 files were gathered. All files including the clinical case records, laboratory values, culture, and sensitivity test reports of the hospitalized patients prescribed with meropenem.

Statistical Analysis

The data which have been collected are compiled in a Microsoft Excel spreadsheet after coding and sorting, the results are exported in the form of frequency and percentages and represented in the form of tables and graphs.

RESULTS

A total of 104 files of the patients under meropenem therapy during the study period were analyzed. The ratio of male and female patients is observed as 3:1 with 75% male and 25% females. Table 1 shows the distribution of the study population based on age and gender. The total number of patients was divided into five age groups. In the age group of 21–40 year, the number of male and female patients was equal. The age group of 41–60 year contains the highest number of patients in which 16 are female and 32 are male patients. The age group above 80 year has the least numbers of two male patients.

Table 1: Distribution of the patients in accordance to age and gender

Age Group (in years)	Gender		Grand Total (*n*=104)
	Female	Male	
<20	0	0	0
21–40	8	8	16
41–60	16	32	48
61–80	2	36	38
>80	0	2	2
Total	26	78	104

Table 2 presents the comorbid illness that was observed in 60% of total patients. The remaining 40% of the patients had no comorbid illness. Hypertension and diabetes mellitus were most commonly observed in the study participants. Ten of them are post-COVID pneumonia patients.

Graph 1 shows the antibiotic used before meropenem. About 50% of the patients were on a combination of Cefoperazone and Sulbactam before changing to meropenem and 40.4% of patients were started directly with meropenem, respectively. Table 3 presents the final diagnosis of the patients prescribed with meropenem. COVID viral pneumonia is the most common diagnosis among the study population. Septic shock with multiple organ dysfunction syndrome (MODS) is seen in 12 patients.

Evaluation of Meropenem Therapy

Initially, all the patients received meropenem as empirical treatment. 84 (80.76%) cases were deemed appropriate for indication and 20 (19.24%) were inappropriate. COVID viral pneumonia and urosepsis were the most common indications for meropenem therapy in the present study.

The frequency and dosing duration were analyzed in Table 4. Dosing frequency of meropenem in 53.8% of the total patients was 8th hourly, 42.30% of patients was 12th hourly, and 3.9% patients was 24 hourly. The dosing duration analysis of the total study population is as follows. One day was considered as minimum time duration and 14 days as maximum time duration. The duration of

meropenem therapy for most of the patients, that is, 63.46% was in between 1 and 5 days.

A clear analysis of sensitivity patterns among the study population is summarized in Table 5. Meropenem indication in all the patients was empirical. Out of 104 study subjects, 11.53% of the patients were not ordered for culture and sensitivity tests. In the remaining 88.47%, it is observed that the study drug was sensitive against the particular organism in 44.23% population and 9.63% of the patients were continued with the drug despite its resistance.

A total of 56 patients were isolated with microorganisms. Out of the identified organisms for which meropenem was used, Klebsiella pneumoniae is most prevalent and was isolated in 18 patients through culture and sensitivity tests [Table 6]. Continuation of the therapy was evaluated in all the 104 patients. It is observed that 53.8% of the cases were justified for the continuation of antibiotic [Flowchart 1].

Among the total study population, 87.5% of them were well recovered after using this antibiotic [Table 7].

DISCUSSION

The rational use of antibiotics is a key element for preventing resistance to antimicrobials. This evaluation was attempted

Table 2: Distribution of the patients on basis of comorbid illness

Comorbid illness	Number of Patients
Chronic kidney disease	14
Hypertension	40
Diabetes Mellitus	42
Cerebral vascular accident	2
Post-COVID pneumonia	10
Coronary artery disease	12

Table 3: Frequency of patients based on the diagnosis

Diagnosis	Number of patients
COVID viral pneumonia	18
Septic Arthritis	2
Urosepsis	16
Septic Shock with MODS	12
Intra-abdominal Infections	8
Skin Infections	14
Dengue Shock Syndrome	6
ENT Infections	8
Melioidosis	2
Cancer of Buccal Mucosa	4
Others	14

MODS: Multiple organ dysfunction syndrome, ENT: Ear, nose, and throat
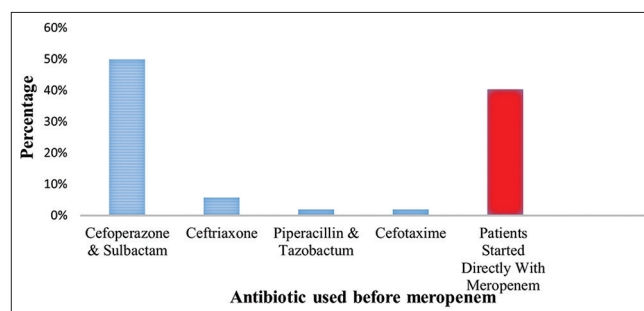
Graph 1: The distribution of patients based on the antibiotic used before meropenem

Table 4: Dosing frequency of meropenem in the patients

Dosing frequency	Number of Patients (*n*=104)	Percentage
8th hourly	56	53.8
24 hourly	4	3.9
12th hourly	44	42.30
Duration of meropenem in the patients		
Duration of Antibiotic	Number of Patients (*n*=104)	Percentage
1–5 days	66	63.46
6–10 days	30	28.84
11–15 days	8	7.7
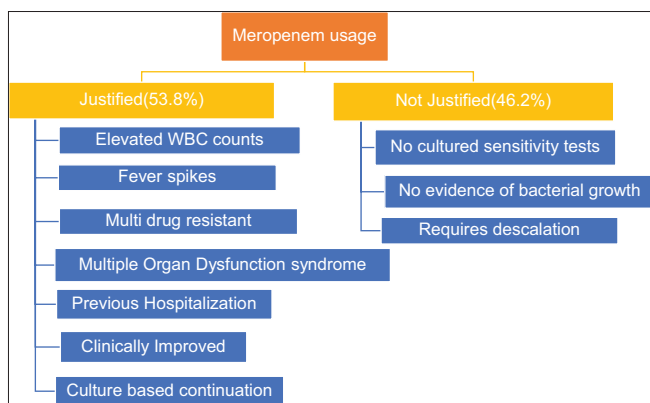
Flowchart 1: Flowchart representing evaluation for continuation of meropenem therapy

Table 5: Assessment of the sensitivity pattern

Condition	Number of patients (*n*=104)	Percentage
No microbial growth	36	34.61
Sensitive to meropenem	46	44.23
Multidrug Resistant cases	10	9.63
Empirical therapy	12	11.53

Table 6: List of organisms isolated in the culture and sensitivity tests

Name of the Organism	No of Patients
Burkholderia pseudomonas	2
Pseudomonas aeruginosa	6
Burkholderia cepacia	2
Candida Species	2
Escheleria coli	8
Enterobacter cloacae	2
Enterobacter aerogens	2
Klebsiella pneumoniae	18
Proteus mirabilis	2
Providencia rettgeri	2
Staphylococcus aureus	2
Staphylococcus hemolyticus	4
Stenotrophomonas maltophilia	4

Table 7: Clinical outcome of the patients

Condition	Number of Patients (*n*=104)	Percentage
Improved	91	87.5
Left against medical advice	4	3.85
Death	9	8.65

to gather basic data for the examination of antibiotic usage in our hospital. This study includes the data of patients administered with meropenem admitted to intensive care unit, surgical, and medical wards in the hospital.

A total of 104 case files were evaluated during the study period, similar to the evaluation carried out in Kolkata by Bera *et al.* on 173 patients, prospectively.[8] As presented in Table 1, the patients who received meropenem were above 20 years and there is no pediatric population in the study. Among the study participants, 75% are males due to the high admission of male patients in the hospital during the study period. Meropenem utilization in 80.76% of the cases was deemed as appropriate for indication and 19.24% were inappropriate. The results are relatively higher in our center compared to results of a similar drug utilization study conducted by Foroughinia *et al.* having 64.8% appropriateness indication, respectively.[9]

In a retrospective evaluation by Farzad *et al.*, 41.9% of meropenem prescriptions were inappropriate.[10] Culture and sensitivity tests results have a key role in the optimization of the antibiotic regimens and detection of antibiotic resistance among isolated organisms. While assessing the data, it is observed that 88.45% of patients were ordered for microbial culture and sensitivity tests similar to the observations of Mahini *et al.* in which 89.7% were tested for microbial culture.[11] Out of the identified organisms, Klebsiella pneumoniae is most prevalent which was similar to the study conducted by Bera *et al.*[8] Gram-negative bacteria were the predominant isolates and most of them were sensitive to cephalosporins, penicillin's, and aminoglycosides.

The dosing duration analysis shows that 53.8% of the patients were given meropenem thrice daily. More than half of the patients, that is, 63.46% received meropenem therapy in the duration of 1–5 days which was in correlation to Bera *et al.* where 63% had the duration of 1–4 days.[8] During this observational study, we found that the continuation of meropenem therapy is justifiable in 53.8% of patients. A study conducted by Al-Hadithi *et al.* in Oman retrospectively has a justification of 55% for the continuation of therapy.[12]

Appropriateness of antibiotic use includes termination or de-escalation of antimicrobial treatment when required. About 46.2% of inappropriateness in meropenem utilization is observed when the drug was used as an empirical therapy without any evidence of culture and sensitivity tests was constant to the study conducted by Sanhoury *et al.*[13] Overall meropenem therapy was initiated without evidence of culture tests depending on the knowledge and experience of the prescribers.

Meropenem was administered to patients with septic shock and MODS among which 8.65% were deceased. About 87.5% of the total study population were well recovered after meropenem therapy while in Sanhoury *et al.,* 20% of patients died and 65.2% were well controlled. Most of the deaths are due to COVID viral pneumonia.[13]

A high clinical outcome of 87.5% was observed after meropenem administration. Our study has higher results

compared to the results reported by Sanhoury *et al.*, where 65.2% met the therapeutic success after meropenem therapy.[13]

Our study highlights that about 80% of patients were prescribed with meropenem for appropriate indication and continuation of meropenem therapy was justifiable in more than half of them. We also present deviation from the standard guidelines in meropenem prescription including a high rate of empirical use, inadequate culture and sensitivity tests for some patients, and lack of de-escalation of antibiotic regimen in some cases. The appropriateness can be maximized by the implementation of standard guidelines for the usage of antibiotics.

De With *et al*. stated that implementation of standard treatment guidelines for usage of antimicrobials enhances their rational use and prevents antimicrobial resistance which maximizes clinical outcomes of the patients.[14] Data analysis by a single observer to reduce the inter-observer variation is the major strength of the study. As this study is retrospective, it has a few limitations. The data were collected from the available inpatient medical records and the proper reasons for the continuation of meropenem therapy after the culture and sensitivity reports cannot be completely investigated in some of the patients.

CONCLUSION

Meropenem is used for appropriate indication as per the guidelines in most patients. Considerable inappropriateness is noted in the continuation of meropenem therapy. An increase in adherence to standard treatment guidelines maximizes the rationality in antibiotic therapy and decreases antibiotic resistance.

RECOMMENDATIONS

Based on results obtained by the above study, the following recommendations are proposed
- Functional pharmacy and therapeutic committee programs could aid in achieving rationality in antimicrobial use
- To revise and implement the treatment guidelines to reduce inappropriate use of antimicrobials
- Regular studies on utilization patterns of antibiotics by clinical pharmacists to obtain definitive outcomes
- To implement antibiotic stewardship forms for monitoring the use of antibiotics

- To decrease the rate of empiric prescriptions and increase the advice of microbial culture and sensitivity tests for the patients
- Conducting awareness programs for the healthcare professionals regarding antibiotic resistance to promote rational use of antibiotics
- To conduct cost-effective studies on various antibiotics for further evaluation.

ACKNOWLEDGMENT

REFERENCES

1. World Health Organization. Drug and Therapeutics Committee Training Course: Session. Geneva: World Health Organization; 2007. p. 227-40.
2. Erbay A, Colpan A, Bodur H, Cevik MA, Samore MH, Ergonul O. Evaluation of antibiotic use in a hospital with an antibiotic restriction policy. Int J Antimicrob Agents 2002;21:308-12.
3. Llor C, Bjerrum L. Antimicrobial resistance: Risk associated with antibiotic overuse and initiatives to reduce the problem. Ther Adv Drug Saf 2014;5:229-41.
4. Papp-Wallace KM, Endimiani A, Taracila MA, Bonomo RA. Carbapenems: Past, present, and future. Antimicrob Agents Chemother 2011;55:4943-60.
5. Blumer JL. Meropenem: Evaluation of a new generation carbapenem. Int J Antimicrob Agents 1997;8:73-92.
6. Baldwin CM, Lyseng-Williamson KA, Keam SJ. Meropenem: A review of its use in the treatment of serious bacterial infections. Drugs 2008;68:803-38.
7. Salehifar E, Shiva A, Moshayedi M, Kashi TS, Chabra A. Drug use evaluation of Meropenem at a tertiary care university hospital: A report from Northern Iran. J Res Pharm Pract 2015;4:222-5.
8. Bera U, Chakraborty K, Acharya D, Roy AD, Ganguly S. A prospective study on concurrent drug utilization review of meropenem in tertiary care teaching hospital in Kolkata. Int J Pharm Sci Rev Res 2019;54:73-6.
9. Foroughinia F, Hashemian S, Fahimi F. Drug utilization evaluation of meropenem: An important broad-spectrum antibiotic for the treatment of serious bacterial infections in hospitalized patients. Trends Pharm Sci 2017;3:25-30.
10. Mahini S, Hayatshahi A, Torkamandi H, Gholami K, Javadi MR. Carbapenem utilization in critically ill patients. J Pharm Care 2013;1:141-4.
11. Farzad BF, Hadavand N, Salehi H, Shekari M. Carbapenems, linezolid, teicoplanin utilization evaluation in a large teaching-based hospital (Shahid Rajaie heart center, Tehran): A quality improvement study. Biomed Pharmacol J 2016;9:525-32.
12. Al-Hadithia D, Al-Zakwania I, Balkhairb A, Al Suleimania YM. Evaluation of the appropriateness of meropenem prescribing at a tertiary care hospital: A retrospective study in Oman. Int J Infect Dis 2020;96:180-6.
13. Sanhoury OM, Eldalo AS. Evaluation of Meropenem utilization in intensive care unit in Sudan. Int J Clin Pharmacol Pharmacother 2016;1:106.
14. De With K, Allerberger F, Amann S, Apfalter P, Brodt HR, Eckmanns T, *et al*. Strategies to enhance rational use of antibiotics in hospital: A guideline by the German society for infectious diseases. Infection 2016;44:395-439.