Journal of Pharmaceutical Care
jpc.tums.ac.ir

Drug Utilization Evaluation of Carbapenems in a Teaching Hospital in Tabriz-Iran

Taher Entezari-Maleki[1], Nooshin Ebrahimi[1], Zhinous Bayatmakoo[2,3], Haleh Rezaee[1,2*]

[1]Department of Clinical Pharmacy, Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran.
[2] Infectious and Tropical Diseases Research Center, Tabriz University of Medical Sciences, Tabriz, Iran.
[3]Department of Infectious Diseases, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.
Received: 2018-05-02, Revised: 2018-05-15, Accept: 2018-05-17, Published: 2018-08-01.

ARTICLE INFO

Article type:
Original article

Keywords:
Drug Utilization Review;
Carbapenems;
Hospital

ABSTRACT

Background: Carbapenems are beta-lactam antibiotics with broad-spectrum activity for Gram-positive, Gram-negative and anaerobic bacteria and have become the antibiotics of last resort for many serious bacterial infections. The irrational use of carbapenems (imipenem or meropenm) has increased the risk of multi-drug resistant pathogens. The aim of this study was to evaluate the pattern of carbapenem utilization within 9 months and measure compliance with references in Imam Reza Hospital, Tabriz, Iran.
Methods: During 9 months, 100 patients who received carbapenems randomly get selected under the supervision of the attending physician in Imam Reza Hospital affiliated to the Tabriz university of Medical sciences. After coordination with supervisor of each ward, the necessary information was extracted and American Hospital Formulary System (AHFS) and UpToDate 21.3 references were used to assess appropriate indication and accurate dosage of carbapenems.
Results:: The most common cause of prescribing was lower respiratory tract infection (29%). Carbapenems were prescribed for 64% of patients as an appropriate indication. The dose of carbapenems was correct in 74% of patients and duration of carbapenems therapy was correct in 84% of cases. Dose readjustment was necessary for 28 patients, although for 25 of whom it was performed. Only 19 patients had positive culture results.
***Conclusion*:** Despite the global guidelines, carbapenem consumption in health care systems is incorrect. So, comprehensive programs for rational drug use in all medical centers conducted by a clinical pharmacist seems necessary to be employed.

J Pharm Care 2018; 6(1-2): 9-12.

► Please cite this paper as:
Entezari-Maleki T, Ebrahimi N, Bayatmakoo Z, Rezaee H. Drug Utilization Evaluation of Carbapenems in a Teaching Hospital in Tabriz-Iran. J Pharm Care 2018; 6(1-2): 9-12.

Introduction

Drug Utilization Evaluation (DUE) studies are designed to evaluate drug usage appropriateness (1,2). DUE is a structured process to analyse the pattern of drug administration in various practice settings, including hospitals in relation to guidelines or predetermined standards. Considerable therapeutic effects of antibiotics and the emergence of resistance make antibiotics very valuable worldwide drugs so appropriate use of them is necessary (2, 3).

Carbapenems are beta-lactam type antibiotics with broad spectrum of activity and coverage of Gram-positive and Gram-negative aerobic and anaerobic bacteria.

* *Corresponding Author:* Dr Haleh Rezaee
Address: Department of Clinical Pharmacy (Pharmacotherapy), Faculty of Pharmacy, Tabriz University of Medical Sciences, Daneshgah St., Tabriz, Iran, P.O. Box: 51664-14766.Tel: +984113344798/Fax:+984113341315.
Email: rezaeeha@tbzmed.ac.ir

Table 1. Demographic and clinical characteristics of the patients (N=100).

Gender	Male	59%
	Female	41%
Age* (years)		58.2±19.5
Length of stay* (days)		17.7±19
Diagnosis	Lower respiratory tract infections	29%
	Urinary tract infections	26%
	Intra-abdominal infection	24%
	Skin infections	6%
	Neutropenic fever	5%
	Septicemia	4%
	Meningitis	2%
	Other	4%

*: Values are presented based on mean ± standard deviation (SD).

Like other broad spectrum antibiotics, carbapenems are prescribed as a part of empiric therapy in most serious nosocomial infections. Imipenem is a semisynthetic carbapenem co-administrated with cilastatin, to prevent renal metabolism of imipenem by dehydropeptidase I (DHP I). In contrast, this co-administration with the renal dehydropeptidase inhibitor, cilastatin is not necessary with meropenem, because this agent is not hydrolyzed by DHP I. The incidence of imipenem and meropenem resistance is increasing among Gram-negative pathogens, especially Acinetobacter spp. (4).

Due to lack of information about Carbapenems prescription in Imam Reza hospital, as a referral educational hospital, this study was designed to evaluate the rational use of Carbapenems in this center. Considering the importance of the Carbapenems in treatment of infectious diseases and the consequences of irrational use, the present DUE study can help identify defects related to the drug use and then, to develop rational antimicrobial implementation protocols to prevent development of resistance.

Methods

This descriptive and retrospective study was conducted at the infectious disease, neurology, surgery, intensive care units (ICU), internal medicine wards (nephrology, pulmonary and gastroenterology), orthopedics, thoracic, endocrinology and rheumatology, urology and trauma wards in Imam Reza teaching hospital, in Tabriz, Iran. The medical records of admitted patients who received carbapenems during March to November 2015 were reviewed and entered data collection forms. Demographic data, diagnosis, antimicrobial therapy received (agents, doses, dose intervals, routes of administration, number of doses, initiation times, and durations of administration) and also details about carbapenems including initiation time, doses, doses intervals, route of administration, dosage adjustments in renal failure, durations of administration, other prescribed antimicrobials, drug-prescriber specialty, sample sites and results of culturing and susceptibility test were collected from the patient's medical records. Compliance with the recommendations and defined standards was assessed by the UpToDate and American Hospital Formulary System (AHFS). All the data were coded and SPSS version 22.0 was used for the statistical analysis.

Results

One-hundred patients were included in this study. Mean age of patients was 58.23±19.5 years (Range 17-93 years). Lower respiratory tract infections, urinary tract infections and intra-abdominal infection were the most frequent infections, accounting for 29%, 26% and 24% of the diagnosis respectively. Carbapenems was prescribed most frequently in infectious disease (16%), nephrology (14%) and pulmonary (14%) wards. Demographic and clinical data are shown in Table 1.

Average time elapsed between the patient admissions and receiving the first dose of antimicrobials or the first dose of carbapenems were 1.58 and 3.62 days, respectively.

The mean duration of carbapenem therapy was 10.52±0.78 days and also the mean duration of antimicrobial therapy (including carbapenems or other

Table 2. Antibiotic prescribing data.

	All patients	Min	Max
Time of starting antibiotic (days)	1.58±0.17	1	15
Time of starting carbapenems (days)	3.62±0.48	1	30
Duration of antibiotic therapy(days)	16.07±1.8	2	43
Duration of carbapenems therapy(days)	10.52±0.78	1	35
Dose of meropenem (mg)	1150±136.9	0	6000
Dose of imipenem(mg)	967±108.9	0	4000
Serum creatinine level (mg/dl)	1.96±0.1	0.48	11.8

Values are presented based on mean ± standard error (SE).

antimicrobials) was 16.07±1.83 days. Data associated with antibiotic prescription with an emphasis on carbapenems are presented in Table 2 .

The most frequently prescribed antimicrobials concomitant with carbapenems were Ciprofloxacin (39%), Vancomycin (26%), Metronidazole (13%), Clindamycin (6%), Teicopelanin (4%), Amikacin (3%), Ceftazidim (3%), Azithromycin (1%) and Co-trimoxazole (1%) respectively.

All the patients received carbapenems as an empiric therapy. Whit regard to the indication 64% was appropriate. 81 (81%) patients received appropriate doses, comply with the recommendations and guidelines whereas doses in 19 (19%) cases was inappropriate. Treatment duration with carbapenems was 84% appropriate in accordance with the recommendations. From 26 individuals with improper duration of treatment, 14 patients received carbapenems longer than the periods justified by guidelines and recommendations. Twenty eight patients needed a dosage adjustment due to low weight or renal failure and 25 patients received the correct doses. Overall, 70% of hospitalized patients of this center received the correct dose of carbapenems for the proper duration (Table 3).

The most significant reported complication was seizure which occurred in two patients. Clinicians requested cultures Seventy eight patients (78%). Samples were collected from urine, blood, sputum, wound, and cerebro-spinal fluid, stool, plural and tracheal.

However culture results were positive in only 19 samples and the others were negative. E.coli and Enterobacter aerogenes were isolated from 9 and 6 patients with positive cultures.

Discussion

Infectious diseases are one of the most important causes of morbidity and mortality throughout the world (5). However, the high level of availability and consumption of antibiotics, for the management of infectious diseases, have led to higher incidence of irrational use and greater incidence of resistance to antibiotics (6).

The goal of this study was to evaluate the appropriateness of Carbapenems as a broad-spectrum antibiotics in a teaching hospital of Tabriz-Iran.

Results of this study show that all the patients received Carbapenems as an empiric treatment and Carbapenems was mainly used for the treatment of lower respiratory tract infections; in 81% of patients the dose of drug and

Table 3. Appropriateness of Carbapenems Use.

Variable (N=100)	Appropriate (%)	Inappropriate (%)
Indication	64	36
Dose	81	19
Duration of therapy	84	26
Dose + Duration	70	30
Dosage adjustment If needed	89	11

in 84%, duration of treatment was appropriate. Similar to our findings, in another study in Tehran, Javadi et al., show that empiric therapy was justified in most cases (78%), but continuation of treatment according to the culture result in several cases was unjustified (47%) (4) Another study in another city of Iran, Sakhaiyan et al., indicated that in 51.6% of patients undergoing bone marrow transplantation, duration of antimicrobial therapy with duration of antimicrobial therapy with imipenem was inappropriate; however all patients received appropriate dose of imipenem (7).

Another study in the Amir teaching hospital-Medical University of Zabol also has shown that despite correct dose administration in 96%, duration of therapy was appropriate only in 8% (8).

In a retrospective observational study conducted by Salehifar et al., in surgical/medical wards of tertiary referral hospital in north of Iran, use of meropenem was evaluated. Their study showed that meropenem was prescribed most frequently in intensive care unit (22%), and pneumonia was the most common diagnosis (35%). The third-generation cephalosporins were the most frequently prescribed antimicrobials after meropenem (53%) and in 21% of the patients, imipenem was changed to meropenem. In their study most of the inappropriate uses were seen in terms of frequency of meropenem use (34%), followed by duration of meropenem therapy (28%) (9).

In a prospective DUE study of three broad spectrum antimicrobials, cefepime, piperacillin-tazobactam and meropenem, the appropriateness rates of antimicrobials was increased after the intervention of pharmacist. Similar to our study, the majority of their broad spectrum antibiotic regimen was initiated empirically. Also, the rate of appropriateness was significantly lower for empirically selected treatment than for that tailored based on relevant microbiology results. With heavy use of broad spectrum agents, the risk of multi-drug resistant organisms ‘emergence would be increased (10). In our study, seventy eight patients (78%) were ordered for microbiology culture, but only 19% patients had positive culture results, and the others were negative. The results showed that in nine of the Patients, microorganism was resistance in imipenem.

Inadequate initial antimicrobial therapy in nosocomial infections is associated with developing of antimicrobial-resistance, increased morbidity and mortality rate (11). For this reason selection of correct antimicrobial with appropriate dose and duration of treatment plays an important role not only in improvement of patient outcomes, but also in the effectiveness of antimicrobials in future infections (12).

In summary, our findings highlight the carbapenems prescription defects in Imam Reza hospital, including high rate of empiric prescription, inadequate dosing in considerable percentage of patients and initiation of antimicrobial therapy from the first day of hospitalization in high percentage of patients. Sharing and discussing study results with drug and therapeutics committees of hospital, antibiotic stewardship programs, consulting with a clinical pharmacist, informing the physician from the results of study, paying more attention to sampling, culturing and sensitivity tests and also considering specific protocols for carbapenem’s prescribing are strategies that can be used in order to help to improve rational use of antibiotics and outcome of antimicrobial therapy in the patients.

References

1. Fahimi F, Baniasadi SH, Behzadnia N, Varahram F, Ghazi Tabatabaie L. Enoxaparin Utilization Evaluation: An Observational Prospective Study in Medical Inpatients. Iranian J Pharm Res 2008;7:77-82
2. Hamishehka H, Ebrahimi D, Mahmoodpoor A, Mashayekh S, Asgharian P, Rezaee H. Drug Utilization Evaluation of Vancomycin in a Teaching Hospital in Tabriz-Iran. Pharm Sci 2015;21(1):25-29
3. Stolar M. Drug use review: operational defenitions. Am J Hosp Pharm 1978;33:225-230.
4. Javadi M, Gholami K, Torkmandi H. Carbapenem Utilization in Critically Ill patients. J Pharm Care 2013;1(4):141-144.
5. Murray CJ, Lopez AD. Mortality by cause for eight regions of the world: Global Burden of Disease Study. Lancet 1997; 349(9061):1269-76.
6. Al-Niemat SI, Bloukh DT, Al-Harasis MD, Al-Fanek AF, Salah RK. Drug use evaluation of antibiotics prescribed in a Jordanian hospital outpatient and emergency clinics using WHO prescribing indicators. Saudi Med J 2008;29(5):743-8.
7. Sakhaiyan E, Hadjibabaie M, Gholami Kh, et al. Drug utilization evaluation of imipenem in patients undergoing bone marrow transplantation. IJHOSCR 2009;3:10-13.
8. Mousavi S, Behi M, Taghavi M, Ahmadvand A, ZiaieSh, MandanaMoradi. Drug utilization evaluation of imipenem and intravenous ciprofloxacin in a teaching hospital. Iran J Pharm Res 2013;2:161-7.
9. Salehifar E, Shiva A, Moshayedi M, Samiei Kashi T, Chabra A. Drug use evaluation of Meropenem at a tertiary care university hospital: A report from Northern Iran. J Res Pharm Pract 2015;4(4): 222-5.
10. Raveh D, Muallem-Zilcha E, Greenbergn A. Prospective drug utilization evaluation of three broad-spectrum antimicrobials: cefepime,piperacillin -tazobactam and meropenem .Q J Med 2006;99:397-406.
11. Kollef, Marin H. Inadequate antimicrobial treatment: an important determinant of outcome for hospitalized patients. Clin Infect Dis 2000;31:131-8.
12. Meakins MD, Jonathan L, Byron J, Masterson R. Prevention of postoperative infection. ACS Surgery: Principles and Practice 2004: 26-35.