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Comparison of Imipenem Prescription Model in Imam Khomeini and Taleghani Educational Center of Urmia

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Abstract
Introduction: Drug utilization evaluation (DUE) studies are designed to evaluate the rational use of drugs. Our purpose in this study is to evaluate the pattern of Imipenem, a broad-spectrum antibiotic used in different parts of Imam Khomeini and Taleghani Educational Center of Urmia.
Method and material: This is a cross-sectional and retrospective study. The study was conducted by reviewing medical records of 200 admitted patients who received Imipenem during March 2016 to 2017.
Results: In the study Imipenem was prescribed most frequently for intra-abdominal infection in 71 cases (35.5%), 41cases (20.5%) respiratory infection, 31 cases (15.5%) urinary tract infection, 25 cases (12.5%) skin infection, 15 (7.5%) cases septicemia infection, 7 (3.5%) cases bone and neutropenic infection, endocarditis infection were reported in 3 cases (1.5%). The highest incidence was related to intra-abdominal infections. 61% of Talehgsni hospital patients and 46% of Imam Khomeini hospital patients received Imipenem less than a week. The used dose in all patients was between one to four grams per day and the frequency of use was not correct in 7% of Taleghani hospital patients and 23% of patients in Imam Khomeini hospital.
Conclusion: Some AB combination was proved to be inappropriate to the guidline consedering the indication or the microorganism to be covered. It is necessary to take action to improve prescribing habit in order to reduce the unnecessary usage of antibiotic thus enhance rational antibiotic use.
Keywords: Imipenem; Drug resistance; Antibiotics

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Introduction

Antibiotic treatment is one of the important components of the treatment of many hospitalized patients. Today, antibiotics around the world are growing and increasing as a result of their overuse in the community as well as in hospitals. Antibiotics should be administered in such a way as not only to improve patients and to produce the desired outcome, but also to minimize the incidence and prevalence of antibiotic resistance.

Imipenem is a broad-spectrum antibiotic that is used to treat serious and life-threatening infections by multi-drug resistant microorganisms when not in use, and also to prevent its kidney breakdown with Silastatin is used. Imipenem is a highly effective antibiotic for aerobic and anaerobic bacteria that is a gram positive and a gram-negative agent of human disease (1-4). This wide-ranging ability to treat a single drug in a neutropenic fever (5). The degree of drug resistance to Imipenem is increasing among gram negative bacteria, especially Pseudomonas aeruginosa and Acinetobacter spp (6).

Resistance to imipenem among Pseudomonas occurs between low concentrations (MIC 8-32 mg / L), which is due to decreased permeability due to the loss of outer membrane protein (OmpD2) and constant expression of beta-lactamase chromosome (10-9). Resistance to imipenem among pseudomonas at high concentrations (MIC> 32 mg / L) is not common, but can be due to the presence of plasmoid metal β-lactamase (11). Although this resistance mechanism is rare, it has a potential for rapid onset (12). Imipenem resistance in the acinetobacter is due to the loss of the outer membrane protein or changes in the penicillin-binding proteins (19-20).

Imipenem is a sterile, non-febrile, broad-spectrum, antibacterial carbapenem for intravenous infusion. the chemical formula is, (5R,6S)-6-[(1R)-1-hydroxyethyl]-3-({2-[(iminomethyl)amino]ethyl}thio)-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid. The empirical formula is C12H17N3O4S and its molecular weight is 299.347 g / mol. The structural formula is equal to Figure 1.

Because where imipenem is consumed alone, it is rapidly decomposed and inactive by an enzyme called dipeptidase or dehidroropeptidase 1, which should be used in conjunction with the same amount of cilastatin to prevent imipenem from being inactive. Cilastatin itself does not have antibacterial activity and does not affect the immunogenic activity of imipenem, but by inhibiting renal enzyme, it prevents the imipenem from being inactivated and provides its efficacy. Imipenem is not absorbed by the oral route; therefore, it should be taken by injection (IM or IV). The absorption of imipenem from the intramuscular route is 60-75% and the absorption of cilastatin is 95% to 100%. The half-life of imipenem / cilastatin components is 60 minutes and its prolonged with kidney damage. In table 1, the plasma concentrations of imipenem after injection of 500 and 750 mg of intravenous formulation (imipenem / cilastatin sodium) and intramuscular formulation (imipenem / cilastatin) containing 2- and 3-ml lidocaine 1% respectively, has been brought (29,28-25). See Table 1.

Introduction about DUE

DUE (Drug utilization evaluation) is a continuous evaluation system that ensures optimal drug use. In fact, it is a way to get information to resolve drug-related issues. In a DUE program, all efforts are made to modify the drug therapy process. In a way that not only improves the quality of treatment but also reduces the cost of treatment in health centers (30). As defined by the World Health Organization (WHO), DUE studies include the distribution, prescribing and use of drugs in the community, with emphasis on medical, social and economic outcomes (30). Successful implementation of a DUE study will ensure the proper, safe and effective use of drugs (31).

Methods

This study was retrospective and conducted in different parts of Imam Khomeini Hospital and Taleghani Hospital. In the retrospective phase, the demographic and clinical data related to the number of patients who were treated with imipenem in the first 6 months of the year of 1396 were collected based on a checklist according to the recommendations for prescribing and rational use of the drug.

The criteria for entering the study were: All patients receiving imipenem and exclusion criteria: Patients with illegible or incomplete cases. Data were extracted from files stored in patients and section information was recorded separately. The degree of compliance of imipenem with the recommendations mentioned in the UpToDate source was determined.

Results

The number of patients admitted to Imipenem in the first 6 months of the year 96 was 126 patients in Taleqani Hospital and 359 patients in Imam Khomeini Hospital who were randomly assigned to 100 patients from each of the centers. The subjects were randomly selected and Based on a random number table. The frequency distribution of patients according to their gender shows that 54% of patients in

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Taleghani hospital are male and 46% of them are women. 51% of Imam Hospital patients are male and 49% of them are women. See Diagram 1. The mean age of patients in Taleghani Hospital was 60/90 and the mean age of patients in Imam Khomeini Hospital was 50/54. The mean hospitalization time in Taleghani Hospital was 8.49 ± 4.8, The mean hospitalization time was 13/10 ± 6/77 in Imam Khomeini Hospital. See Diagram 2.

Frequency distribution of patients according to their recovery status shows that complete recovery due to the reason for initial hospitalization in Taleghani Hospital was zero and relative improvement of 89 cases and death of 11 cases. Also, complete recovery in Imam Khomeini Hospital was zero for a relative improvement of 81 cases and died of 19 cases. Relative improvement in Taleghani Hospital was higher than Imam Khomeini Hospital and the proportion of deaths in Taleghani Hospital was lower than that of Imam Khomeini Hospital. See: Table 2.

Frequency testing was based on antibiotic start showed that 84% of patients in Taleghani hospital were on first day and 12% on the second day and 4% on other days and also in Imam Khomeini hospital 81% of the patients were on first day of admission and 11% of the day Second and 8% Antibiotics were started on other days. See Diagram 3.

Possible cause of imipenem administration to patients Duration of taking imipenem in patients. See Table 3 and 4.

In the frequency of drug injection, Taleghani Hospital had 61 cases (half an hour infusion) and 39 cases (one hour infusion) and also had 24 cases (half hour infusion) and 76 cases (one hour infusion) in Imam Khomeini Hospital. See Table 5.

Taking other medications

The most important drug interactions are imipenem with Probenecid, valproic acid and gancyclovir drugs. In this study, 1 case of gancyclovir, 3 cases of valproic acid and none of the probenecid were reported in Taleghani Hospital. No case of gancyclovir was reported in Imam Khomeini Hospital. 5 cases of valproic acid and no reported cases of probenecid were reported.

Discussion and conclusion

Imipenem is one of the most common and commonly used antibiotics in the hospital. Due to the lack of use of many antibiotics and expanding the resistance of antibiotics, it seems that in order to achieve the desired status of antibiotics, having a perspective on the current state of their consumption in educational centers that cover the majority of patients is necessary and therefore the aim of this study is to report on the status of use of antibiotic imipenem in educational centers of Imam Khomeini and Taleghani.

There was no significant difference in age between patients in both hospitals. The results indicate an increase in the use of imipenem in older people. The data of these two hospitals indicate an increase in the length of hospitalization of patients receiving imipenem in Imam Khomeini Hospital. Since Imam Khomeini Hospital is a General Hospital, this seems to be a significant difference in the number of hospital days due to hospitalization of the patients. Frequency distribution of patients according to their recovery status shows that, the increase in mortality rate was related to the amount of hospitalization period and probably due to the fact that the patients were hospitalized at Imam Hospital. The prevalence of probable causes of imipenem administration in Taleghani hospital showed that, the most likely causes of imipenem administration in the urinary tract infections are skin and abdominal infections, accounting for more than 60% of the reason for the administration of the drug in this hospital. Frequency of the days of imipenem administration showed that, 61% of the patients admitted to Taleghani Hospital and 46% of the patients admitted to Imam Hospital received Imipenem less than one week of treatment, which seems to be short and unreasonable and increase the resistance to imipenem.

Conflict of interest

The author declares that there is no conflict of interests.

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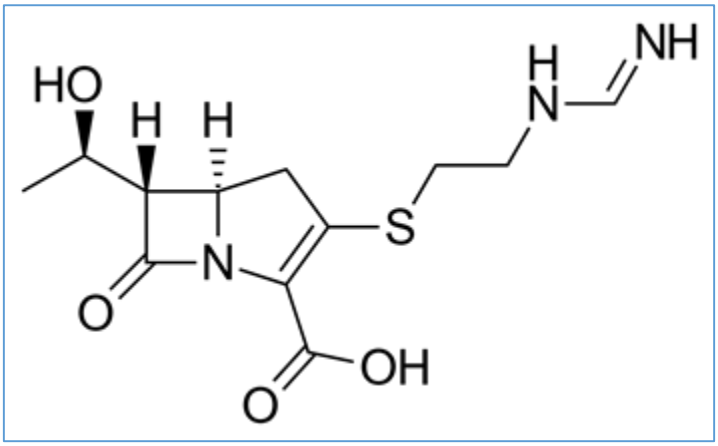

Figure 1. Chemical structure of imipenem

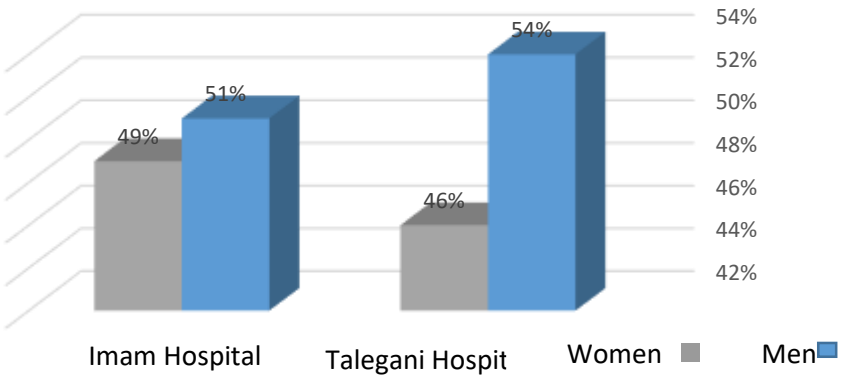

Diagram2. Describes the frequency of gender of patients by hospital

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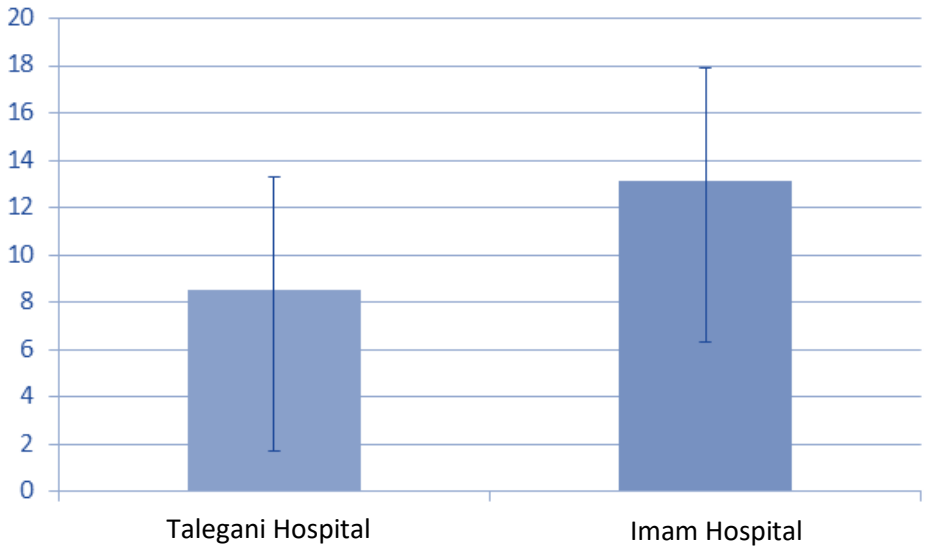

Diagram 3. Frequency distribution chart for hospitalization (day) of patients

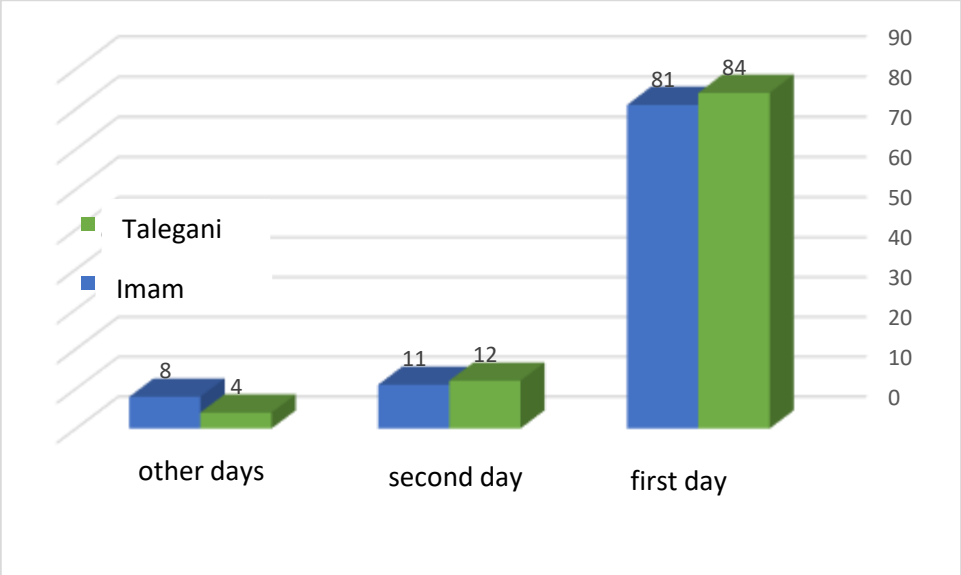

Diagram 4. Frequency distribution chart for the start of antibiotics on the day of hospitalization of patients by hospital

500 mg	750mg			
TIME	I.V.	I.M.	I.V.	I.M.
25 min	45.1	6.0	57.0	6.7
1 hr	21.6	9.4	28.1	10.0
2 hr	10.0	9.9	12.0	11.4
4 hr	2.6	5.6	3.4	7.3
6 hr	0.6	2.5	1.1	3.8
12 hr	ND*	0.5	ND*	0.8

Table 1. Comparison of Imipenem Plasma Concentration after Injection of IM and IV µg/ml
ND: Not Detectable (<0.3 µg/ml)

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	Imam Hospital	Talegani Hospital
complete recovery	0	0
relative improvement	81	89
death	19	11
Number	100	100

Table 2. Frequency distribution table for patient recovery status by hospital

	Imam Hoslital		Talegani Hospital	
	Percent	Number	Percent	Number
Bone and joint infections	6	6	1	1
Skin infection	4	4	21	21
Urinary tract infection	7	7	24	24
Intra-abdominal infection	49	49	20	20
Respiratory infection	20	20	18	18
Pseudomonas infection (VAP)	0	0	3	3
Neutropenic fever	2	2	5	5
Liver abscess	0	0	2	2
Endocarditis	2	2	1	1
septicemia	10	10	4	4
shok	0	0	1	1
Total	100%	100	100%	100

Table 3. Frequency distribution table the probable cause of administering amenopenum to patients by hospital

	Imam Hospital	Talegani Hospital
1 to 7 days	46%	61%
8 to 14 days	45%	23%
15 to 21 days	8%	14%
21 onwards	1%	2%
Total	100%	100%

Table 4. Percentage of frequency distribution of amenopenomy patients by hospital

	Imam Hospital	Talegani Hospital
half an hour infusion	24	61
one hour infusion	76	39
Total	100	100

Table5. Frequency distribution table for how to inject a drug into a hospital

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