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An assessment study of using Meropenem Injection in Iraqi Hospitals

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Abstract
Antibiotics are being used irrationally all over the world. Meropenem, which is a new and expensive antibiotic, is also being used irrationally which lead to the emergence of resistant strains and consequently failure of therapy and high costs of morbidity. Data regarding this issue in Iraq is deficient. This observational study showed the pattern of meropenem injection using in Iraqi public hospitals. A total of (9736) records of in-patients in the years 2015-2016 were studied from secondary and tertiary hospitals in different governorates in Iraq. The upmost indication were it was used was septicemia in about 46% of the cases, after which came skin and soft tissue infections in about 16% of the cases. There were about 5% of the cases which composed not approved indications. Culture and sensitivity was done in about 9% of cases only; causes of which should be investigated separately Ministerial regulations for the use of carbapenems in general were set to be followed, however, these regulations should be updated according to data in this study.

Keywords: meropenem injection, Iraqi hospitals

Introduction
Antibiotics are one of the drug groups that made dramatic changes in disease treatment and improved prognosis of patients with bacterial infections. Their use in hospitals has been a major concern in the last years for several reasons. About 60% of hospitalized patients in the United States receive an antibacterial drug during hospitalization and about 50% of this use is unnecessary and the cost involved is therefore correspondingly high [1], and up to 40% of a total hospital's drug expenditure may be devoted to the purchase of antibiotics [2]. Widely used antibiotics such as tetracycline, erythromycin and vancomycin unfortunately got resistance to the microorganisms and hence lost much of their therapeutic effectiveness over the years [3]. Different types of antibiotic misuse, such as failure to complete therapy, skipping doses, reuse of leftover antibiotics, inappropriate choice of antibiotics, inappropriate combination, inappropriate dose regimen and too long duration of drug usage expose patients to suboptimal doses of antibiotic therapy. Such antibiotic taking behavior can result in insufficient antibiotic exposure for eradicating infectious bacteria and potentially create an environment that promotes antibiotic resistance [4] and therapy failure which imposes pressure on physicians who tend to prescribe newer broad spectrum agents for excessive periods of time [5]. It has been observed that inappropriate use of antibiotics has become a common practice in health care setting [6] and their irrational use in hospitalized patients has been reported to be about 9–64% [7]. This irrational utilization of antibiotics lead to emergence of resistant strains which lead to unwanted clinical outcomes and increased medical cost in both mortality and morbidity as well as hospitalization costs [8-11]. Rational antimicrobial use is essential for effectiveness of drugs, prevention of emergence of resistant strains, reducing unwanted effects and lowering high costs [12]. Nowadays, the antimicrobial resistance in general, is considered as a world-wide medical and public health problem [13].
The last lines of antibiotics, like carbapenems, started to be used to reach therapeutic effectiveness with patients. In 2012, carbapenem-resistant infections were identified in US hospitals. The antimicrobial resistance surveillance data in Thailand reported that the rate of carbapenem resistance against Acinetobacter baumannii (CR-AB) infection increased from 2.1% in 2000 to 46.7% in 2005 [14].
Strict policies have been developed by regulatory bodies in different countries for meropenem use in hospitals [15]. In Iraq the drug regulatory authority, which is the pharmacy department, set a policy in which carbapenems in general (imipenem and meropenem) should be considered for sepsis, severe life threatening infections.
Being such an increasing health care problem, several studies have been designed in different countries to measure the magnitude of the problem in terms of frequency, doses, intervals, and routes of administration and the appropriateness of the choice of antibiotics [16-17].

Methods
All health directorates of health were asked to report the use of meropenem injection in their hospitals. There are 21 directorates of health in Iraq. Three of them are in the region of Kurdistan which have their own regulatory authorities, other three were under the role of ISIS during the period of this research, and another directorate of health namely the directorate of public clinics are not allowed to use meropenem, so the remaining directorates would be 14. They contain 152 hospitals out of 260 hospitals in the whole country. Reports from these 14 directorates of health were

collected for two years from 1/1/2015 till 31/12/2016 according to a standardized sheet by clinical pharmacists in the hospitals.

Reports included the following data: patient's name, age, diagnosis, days of meropenem use, frequency of dosing, culture and sensitivity, as well as other detailed information. Data were entered into excel sheet and analyzed. Investigation included comparison with standard indications, doses, compliance with regulatory policies. Indications for meropenem injection were considered those mentioned in the British National Formulary 70 which included severe hospital-acquired infections, polymicrobial infections including septicemia, hospital acquired pneumonia, intra-abdominal infections, skin and soft tissue infections, complicated UTIs, exacerbations of chronic lower respiratory-tract infection in cystic fibrosis, meningitis, and endocarditis.

Results

The study included 9736 patients on meropenem injection therapy during the years 2015-2016 in hospitals that responded to study. Their distribution was as shown in table 1 showing that 48.91% of them were in 2015. Their age range was from 1 day till 100 years as in table 2. Duration of meropenem use in hospitals was (1-42) days, as is shown in table 3 were the highest was two days followed by one day and then three days. There were cases in which patients received the drug 42 days. Only 9.15% of cases had culture and sensitivity testing as shown in table 4. Table 5 shows the number of doses per day given to patients. Septicemia was the highest indication where meropenem was used for, which formed about 46% of the cases, whereas about 6% of cases were indications not recommended. Table 6 shows the indicated vs not indicated use of meropenem. The average cost per patient, regardless of age, indication and duration was calculated to be about $74.52.

Table 1: Patient distribution between years

Year	No. of patients	%
2015	4762	48.91
2016	4974	51.09
Total	9736	100

Table 2: Age distribution of patients

Age	Number	%
0-90 days	377	3.87
90 days-1 year	1251	12.85
1-18 years	1981	20.35
18 - 50years	2894	29.72
Over 50 years	1721	17.68
not mentioned	1512	15.53
	9736	100

Table 3: Duration of meropenem use

Duration in days	No. of patients	%
1	1365	14.02
2	1498	15.39
3	1271	13.05
4	1085	11.14
5	989	10.16
6	621	6.38
7	753	7.73
8	460	4.72
9	320	3.29
10	433	4.45
11	153	1.57
12	130	1.34
13	123	1.26
14	160	1.64
15	128	1.31
16	38	0.39
17	17	0.17
18	26	0.27
19	17	0.17
20	40	0.41
21	38	0.39
22	10	0.10
23	10	0.10
24	11	0.11
25	8	0.08
26	3	0.03
27	8	0.08
28	4	0.04
30	5	0.05
31	2	0.02
32	2	0.02
33	2	0.02
34	1	0.01
36	2	0.02
37	1	0.01
40	1	0.01
42	1	0.01
	9736	100

Table 4: Cases in which there was culture and sensitivity testing

Culture and sensitivity	No. of patients	%
No	8845	90.84
Yes	891	9.15

Table 5: Number of doses per day

Doses per day	No. of patients	%
One	165	1.69
Two	3024	31.06
Three	5054	51.91
Four	1491	15.31
Six	2	0.02

Table 6: Indicated vs not indicated use.

Indication	No. of patients	%
Indicated cases	9138	93.85
Not indicated cases	598	6.15
Total	9736	100

Discussion

Assessment of drug use could be of different levels including indications, dose, route, duration, and drug interactions. The study design would be according to parameters needed to be assessed. This study was a starting study to set general information about the appropriateness of meropenem injection use in Iraqi hospitals. Such a study is essential for obtaining information to improve rational use of this drug.

Our results showed that the distribution between the two years of the study was nearly the same (48.91 and 51.09%). This can be an indicator that the availability of the drug in hospitals was nearly the same in the two years and there was no change in the attitude of physicians in prescribing it.

The age distribution showed that the age in about 15.53% of the cases was not mentioned. This could be due to the data collectors who did not fill in the cells of the age in the collection form, however, the percent of this category should not affect the overall picture of the rest of results. The highest percent was seen in the adult group (18-50 years) after which comes the pediatric and teenager group (1-18 years) and this could be due the size of this population. The geriatric and pediatric group were less, the cause could be the size of this population and the special care that should be taken when giving meropenem in these two groups in terms of dosing and monitoring, especially the kidney functions.

The duration of treatment depends on factors that were not documented or mentioned in this study. However, causes could be due discharge of the patient, changing the drug due to unavailability or due to culture and sensitivity results. Studying the causes of changing was beyond the scope of our study, nevertheless it should be the subject for further research. It can be obvious that the least duration for meropenem use was for one day in 14% of cases, a duration that could not be rational in all measures.

Prescribing according to culture and sensitivity results is an issue of great debate. In this study only about 9% of prescribing was according to culture and sensitivity results. Causes could be due urgency of the case or unavailability of sensitivity test. In both cases physicians treat patients empirically either according to signs and symptoms or available laboratory data. Our results were less than other studies such as that in Istanbul which showed that culture-based prescribing was (21.2%), and so the appropriate use rate was higher [18].

Number of doses given per day was also investigated. Meropenem should be given in 3 doses daily, or 2 – 1 doses according to the renal function. References do not mention 4 doses nor 6 doses. Therefore only 15% of cases were given more than the recommended number of doses.

According to the methodology of this research, the indicated cases were considered those mentioned in the British national formulary 70. Therefore, about 94% of the cases complied with this criteria. Results near to these were found in other studies such as those of Sumitsawan *et al* [19] and Sumret *et al* [20]. However, as this study did not evaluate the outcome of the use of meropenem therefore our results did not represent the real situation of rational drug use.

Due to the fact that our study depended on recorded evidence, there may be a situation of incomplete data. So the actual rate of inappropriate use of meropenem may be slightly more or less than what we found. Therefore, it is possible that there may be a misclassification regarding appropriateness of meropenem use.

The large number of patient records in our study could be beneficial in giving an impression of the general use of meropenem. They are comparative with other studies that used small number of patients in general hospitals, which could be helpful for the antimicrobial management in small and large settings and even for drug regulatory authorities [21]

Our study was carried out in 152 hospitals out of 260 hospitals in the whole country. These were secondary and tertiary specialized hospitals. According to the strict regulations for meropenem use in hospitals set by the drug regulatory authority in the ministry of health it was suspected to have a low rate of inappropriate use. The inappropriateness could be in indications or doses or duration. We have no data of meropenem use before these regulations as they were set prior to using meropenem in hospitals. An Egyptian study showed a similar conclusion in that promising results will be if a restriction policy is adopted in hospitals [22]. This same problem was studied in other countries which showed the beneficial effect of setting antibiotic restriction policies like the Turkish study which showed that inappropriateness of use was reduced from 59.3% to 22.4% upon application of restriction policies [23].

The cost of antibiotics is an important issue nowadays in our country. The average cost of meropenem alone was calculated to be about $74.52. If we compare this figure with other studies such as those in turkey ($16.8, and $13.8 for all antibiotics) [24] we can realize the size of the problem. The above costs do not include other expenses related to antibiotic use such as appliances used in conjunction with injections (cannulas, syringes, IV sets, …. etc) as well as nursing services and hospitalization expenses and probable adverse effects, and monitoring.

The role of clinical pharmacist, as a member of the patient care team, is pivotal in providing proper consultation for the physician regarding utilization of antibiotics. There are regulations utilizing the presence of clinical pharmacists in all wards in hospitals in Iraq. There are stewardship committees for antibiotic use in all hospitals. Studies in other countries have stated the expectation that clinical pharmacists can lead to better utilization of antibiotics in general [25], however, we have not designed this study to find this effect.

Conclusion

Strict guidelines and valid policies should be implemented in hospitals to decrease the antibiotic misuse and decrease the risk of microbial resistance against the current known antibiotics. The study confirms that there is a misuse of antibiotics in hospitals and that the physician needs to follow strict guidelines to prescribe antibiotics. Also, the study revealed that the acceptance of physicians to the pharmacist recommendations is low while it should be taken in

consideration when prescribing antibiotics to the patients.

Recommendations

Being the first research in this field it is recommended that further studies be designed to validate criteria of inappropriate use of meropenem in a variety of settings. Parameters to be studied would be errors in dosing, in indications, in duration and differences between wards as well as the effects of guidelines and the role of clinical pharmacists in meropenem use in hospitals.

References

1. Fishman N. Antimicrobial stewardship. Am J Med. 2006; 119:553-561.
2. Mauldin PD, Salgado CD, Hansen IS, Durup DT, Bosso JA. Attributable hospital cost and length of stay associated with health care-associated infections caused by antibiotic-resistant gram-negative bacteria. Antimicrob. Agents Chemother. 2010; 54(1):109-115.
3. Wise R, Hart T, Cars O, Streulens M, Helmuth R, Huovinen P, Sprenger M. Antimicrobial resistance. Is a major threat to public health? BMJ. 1998; 317(7159):609-10.
4. Osama Mohamed Ibrahim, Maha Saber-Ayad. Antibiotics misuse in different hospital wards (A pilot study in an Egyptian hospital). Asian Journal of Pharmaceutical and Clinical Research. 2012; Vol 5, Issue 2.
5. Hulscher ME, Grol RP, Van Der Meer JW. Antibiotic prescribing in hospitals: a social and behavioural scientific approach. Lancet Infect Dis. 2010; 10(3):167-75.
6. Hersh AL, Shapiro DJ, Pavia AT, Shah SS. Antibiotic prescribing in ambulatory pediatrics in the United States. Pediatrics, 2011; 128(6):1053-1061.
7. Cusini A, Rampini SK, Bansal V, *et al*. Different patterns of inappropriate antimicrobial use in surgical and medical units at a tertiary care hospital in Switzerland: a prevalence survey. PLoS One 2010; 16:5(11):e14011
8. Lemos EV, de la Hoz FP, Alvis N, Einarson TR, Quevedo E, Castaneda C, *et al*. Impact of carbapenem resistance on clinical and economic outcomes among patients with Acinetobacter baumannii infection in Colombia. Clinical Microbiology and Infection, 2014; 20(2):174-180.
9. French G. Clinical impact and relevance of antibiotic resistance. Advanced Drug Delivery Reviews, 2005; 57(10):1514-1527.
10. Cunha BA. Antibiotic Essentials. Jones and Barlette, 2010.
11. Kleinke J. The price of Progress: Prescription drugs in the health care market. Health Aff. 2001; 20(5):43-60.
12. Polk RE, Fishman NO. Antimicrobial stewardship. In: Mandell GL, Bennett JE, Dolin R, editors. Mandell, Douglas, and Bennett's Principle and Practice of Infectious diseases. 7th ed. Philadelphia: Elsevier Churchill Livingstone, 2010; 677-685.
13. Molton JS, Tambyah PA, Ang, BS, Ling ML, Fisher DA. The global spread of healthcare-associated multidrug-resistant bacteria: a perspective from Asia. Clinical Infectious Diseases. 2013; 56(9):1310-1318.
14. Dejsirilert S, Tiengrim S, Sawanpanyalert P, Aswapokee N, Malathum K. Antimicrobial resistance of Acinetobacter baumannii: six years of National Antimicrobial Resistance Surveillance Thailand (NARST) surveillance. Journal of the Medical Association of Thailand. 2009; 92(Suppl 4):S34-45.
15. Muhammad Umair Khan, Rabia Ismail Yousuf, Muhammad Harris Shoaib. Drug utilization evaluation of meropenem and correlation of side effects with renal status of patients in a teaching based hospital. Pak. J. Pharm. Sci. 2014; 27(5 Special):1503-1508.
16. Falagas ME. Fosfomycin: Use beyond Urinary Tract and Gastrointestinal Infections. Clinical Infectious Diseases, 2008; 46:1069-1077.
17. Luciana, Retnosari Andrajati, Alfina Rianti, Amer Hayat Khan. Rational Antimicrobial Use in an Intensive Care Unit in Jakarta, Indonesia: A Hospital-Based, Cross-Sectional Study. Tropical Journal of Pharmaceutical Research. 2015; 14(4):707-714.
18. Asuman İnan, Özgür Dağlı, Seniha Şenbayrak Akçay, Derya Öztürk Engin, Emin Karagül, Seyfi Çelik Özyürek. Antibiotic use and cost in a teaching hospital in İstanbul. Journal of microbiology and infectious diseases (JMID). 2011; 1(3):128-133.
19. Sumitsawan J, Samerkum K, Sumitsawan T, Kongthong A. Evaluation of meropenem for sepsis management. Buddhachinaraj Medical Journal. 2012; 29(1):9.
20. Sumret Wichai Santimaleeworagun, Kamonphop Saowakul, Thirawan Haephruek, Penprapa Pengsombat, Witchuda Kwanmuang Silpakorn. Evaluation of Meropenem Use Among Septic Patients at Hua Hin Hospital. Thailand, Science & Tech J. 2016; 10(1):21-26.
21. Wandee Sumret, Wichai Santimaleeworagun, Kamonphop Saowakul, Thirawan Haephruek, Penprapa Pengsombat, Witchuda Kwanmuang Silpakorn. Evaluation of Meropenem Use Among Septic Patients at Hua Hin Hospital, Thailand, Science & Tech J. 2016; 10(1):21-26.
22. Osama Mohamed Ibrahim, Maha Saber-Ayad. Antibiotics misuse in different hospital wards (a pilot study in an Egyptian hospital). Asian Journal of Pharmaceutical and Clinical Research. 2012; Vol 5, Issue 2,
23. Erbay A, Bodur H, Akinci E, Colpan A. Evaluation of antibiotic use in intensive care units of a tertiary care hospital in Turkey. J Hosp Infect. 2005; 59(1):53-61.
24. Asuman İnan, Özgür Dağlı, Seniha Şenbayrak Akçay, Derya Öztürk Engin, Emin Karagül, Seyfi Çelik Özyürek. Antibiotic use and cost in a teaching hospital in İstanbul. Journal of microbiology and infectious diseases (JMID). 2011; 1(3):128-133.
25. Osama Mohamed Ibrahim, Maha Saber-Ayad. Antibiotics misuse in different hospital wards (a pilot study in an Egyptian hospital). Asian Journal of Pharmaceutical and Clinical Research. 2012; Vol 5, Issue 2.