Drug Use Evaluation of Three Widely Prescribed Antibiotics in a Teaching Hospital in East of Iran

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Background: Drug utilization studies are helpful in understanding the current practice. We have conducted a retrospective study to evaluate the relevant use of a group of most commonly prescribed antibiotics in a teaching hospital in Iran. The results of this study may be of help for clinicians to improve the patient care.

Methods: Patients who received parenteral ceftazidim, vancomycin and amikacin from December 2010 to May 2011 were enrolled in this study. Patient's data including demographic, length of Hospital stay, drug allergy, first and final diagnosis were recorded in a predesigned data collection form. American Hospital Formulary Services (AHFS) book were used as a reference for evaluation of study drug indication and dosing according to diagnosis and microbiological culture. Defined Daily Dose (DDD) of each drug extracted from Anatomic and Therapeutic Chemical classification system (ATC/DDD) and drug usage data evaluated by calculating the ratio of prescribed drug to its DDD.

Results: The ratio of prescribed daily dose to DDD was 0.78, 0.95 and 0.86 for amikacin, ceftazidime and vancomycin respectively. Between amikacin group, 43 patients (86%) received drug empirically, the number of empiric treatments for ceftazidim and vancomycin were 45(90%) and 44 patients (88%). The renal function tests (Blood Urea Nitrogen, Serum Creatinin) were evaluated in 56% of amikacin group, 64% in ceftazidime group and 78% in vancomycin group.

Conclusion: The results of this study indicate the need to establish continuing medical education (CME) courses for physicians to familiarize them with standards required to use and monitor these agents.

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Introduction

Antibiotics are among the most commonly used drugs in Hospital settings. Irrational use of antibiotics can be associated with a number of serious consequences to the patients and community (1). Developing resistance has been worrisome early after these agents became available for widespread use (2). Drug Use Evaluation (DUE) of commonly used antibiotics not only will result in improved treatment efficacy but also in conserving cost and preventing unwanted adverse effects (3).

We have conducted a retrospective study to evaluate the relevant use of a group of most commonly prescribed antibiotics in a teaching hospital in Iran. Ceftazidim, vancomycin, and amikacin are the primary focus of this study. We agreed on these three antibiotics based on data extracted from Hospital Information System about extensive use of them. There are only limited number of DUE surveys conducted in our hospital care centers concerning antibiotic use.

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Patients and Methods

The study was a cross sectional retrospective DUE study conducted in Amir teaching Hospital with 263 beds. This Hospital is affiliated to Zabol University of Medical Sciences (ZUMS) and it is the only Hospital providing medical care in Zabol city.

Study population

Patients who received parenteral ceftazidim, vancomycin and amikacin from December 2010 to May 2011 were enrolled in this study. The data extracted from Hospital information system included record number of patients who received study drugs, Clinical data retrieved from patient charts.

Data collection

Patient's data including demographic, length of Hospital stay, drug allergy, first and final diagnosis were recorded in a predesigned data collection form. Drug's indicator including treatment regimen, dosing, microbiological culture/sensitivity testing. Clinical outcome and adverse drug reaction verified as study outcome.

Audit criteria

American Hospital Formulary Services (AHFS) (4) book were used as a reference for evaluation of study drug indication and dosing according to diagnosis and microbiological culture. Defined daily dose (DDD) of each drug extracted from Anatomic and therapeutic chemical classification system (ATC/DDD) and drug usage data evaluated by calculating the ratio of prescribed drug to its DDD. Defined Daily Dose is a unit based on the average daily dose used for main indication for consumption of certain medication (5).

Descriptive analyses of data were performed using SPSS software (version, 16).

Results

Total of 2755 patient's records evaluated in the study time window of one month and 50 patients for each drug have been analyzed. Ceftazidim has been used most commonly in internal medicine ward (42%); amikacin (66%) and vancomycin (40%) were most common in pediatric ward (Table1).

The median length of treatment for amikacin, ceftazidim and vancomycin were 4 days for each drug. The range of treatment duration for amikacin, ceftazidim and vancomycin were 1-13 days, 1-11 days and 1-15 days respectively (Table 2).

The mean dosage of amikacin was 783mg/day for adults (>12years old) and 247mg/day for pediatrics (<12years old).The mean ceftazidim dosage was 3803mg/day for adults and 695mg/day for pediatrics. Vancomycin mean dosage was 1734mg/day for adults and 303mg/day for pediatric. The ratio of prescribed daily dose to DDD was 0.78, 0.95 and 0.86 for amikacin, ceftazidime and vancomycin respectively (Table 2).

The length of Hospital stay (mean ± SD) was 6.32±3.13 days in amikacin group, 6.94±3.34 days for ceftazidim group and 8.14±5.17 days in vancomycin group (Table 2).

In amikacin group, 43 patients (86%) received drug empirically, the number of empiric treatments for ceftazidim and vancomycin were 45(90%) and 44 patients (88%) respectively (Table 3).

The initial diagnosis and the final diagnosis were same in 86% of patients in amikacin group, this rate for ceftazidim and vancomycin were 88% and 64% respectively. Among the patients who received amikacin, 84% have shown clinical response to antibiotic treatment, the response was 62% in ceftazidim group and 74% in vancomycin group. There were 6 death in vancomycin group and 2 death in ceftazidim unrelated to drug effects (Table 3).

Most common diagnosis at the starting time for both ceftazidim (13 patients) and vancomycin (6 patients) were pneumonia. Urinary tract infection was the most common cause (11case) of initiation amikacin therapy.

Microbiological cultures were utilized in the course of therapy for 62% of patients receiving amikacin and only 16% of all group had a culture with antibiotic sensitivity test, the rate of culture and sensitivity tests was 54% and 12% for vancomycin , 30% of patients in ceftazidim group had culture results, antibiogram was performed for none of them.

The renal function tests (blood urea nitrogen, serum creatinin) were evaluated in 56% of amikacin group, 64% in ceftazidime group and 78% in vancomycin group. Nineteen patients (12%) had abnormal results and none of them received dosage adjustment based on their renal function.

Discussion

Drug utilization studies are helpful in understanding the current practice in clinical settings. The results of this study may be helpful for clinicians to improve the patient care. It is also very helpful for health systems decision makers to reduce the costs of treatment by utilizing the TDM and culture and sensitivity testing in hospitals.

Vancomycin, ceftazidime and amikacin are among the most common used antibiotics (6). These drugs are mainly utilized as empirical therapy in our Hospital setting.

In this study, none of the patients treated with amikacin received extended-interval dosing schedule. It has been frequently stated that this method bears the advantages of enhanced efficacy and lesser toxicity (7). Incorrect concerns of greater renal toxicity with a single high-dose of aminoglycosides may have led to such approach. Educational programs can be employed to improve physicians' attitude regarding this dosing schedule.

Relatively high percentage of antibiotic courses was not based on culture results and clinical judgment was

Table 1. Distribution of antibiotics between wards based on their use.

Wards	Ceftazidim N (%)	Vancomycin N (%)	Amikacin N (%)
Pediatrics	4(8)	20(40)	33(66)
Internal	21(42)	10(20)	7(14)
Infectious disease	3(6)	7(14)	3(6)
Gastrointestinal	7(14)	0(0)	0(0)
Intensive Care Unit(ICU)	1(2)	5(10)	0(0)
Neonate	2(4)	1(2)	4(8)
Surgical ward (men)	5(10)	1(2)	0(0)
Surgical ward (women)	5(10)	0(0)	2(4)
Emergency	1(2)	0(0)	0(0)
Neonatal-ICU	0(0)	2(4)	0(0)
Pediatric-ICU	1(2)	0(0)	0(0)
Gynecology	0(0)	0(0)	1(2)

made on improvement of symptoms to guide treatment. The rate of empirical vancomycin use was similar to other studies performed in Iran. Vazin et al., showed a high prevalence of empirical use in febrile neutropenic patients (8). In another cross-sectional study, khalili et al., enrolled all patients receiving vancomycin in a 6-months period and reported about 80 percent empiric use (9). Lack of documented microbial growth and antibiogram results may be associated with prolonged courses of unnecessary combined antibiotic regimens. Such methods of antibiotic usage are associated with development of microbial resistance. Optimization of sampling methods and laboratory techniques can improve the culture yield.

Therapeutic Drug Monitoring (TDM) is a well-established and necessary requirement for patients treated with amikacin and vancomycin and relevant guidelines have been published. Despite strong recommendations for employing TDM in patients treated with vancomycin and amikacin, it wasn't performed for any of treated patients. Another concerning issue in the study including similar population was higher than suggested therapeutic trough levels of vancomycin in more than half of treated patients who received standard recommended doses (8). Several factors may be involved; lack of required equipments, associated short-term costs and absence of clinical

pharmacists familiar with pharmacokinetic properties of these agents all may have contribute. Notifying physicians about long-term cost-saving quality of TDM and use of a consultant clinical pharmacist for dosing adjustments can improve the treatment standardization. Dose adjustments were necessary for about 14 percent of patients due to diminished renal function that were not performed accordingly in study population. Vazin et al., also reported that in the setting of diminished renal function, appropriate vancomycin dose adjustments were not performed. This again demonstrates the need for more widespread implement of pharmacist's role in Hospital wards.

Only in a minority of patients vancomycin use was matched to standard indications proposed by AHFS, which can lead in increased treatment failure and developing antimicrobial resistance. In the study conducted by Vazin et al., about 70% of cases were treated according to standard indications proposed by Infectious Disease Society of America (IDSA) guideline for empirical vancomycin use. Mark et al., conducted a retrospective study on 199 courses of vancomycin use at two institutions. It was noted that either initial selection or treatment continuation was inappropriate in a high proportion of patients treated with vancomycin. More concerning issue was that 27 courses included inappropriate use as prophylactic therapy before surgery. In a prospective survey by Junior et al., all patients receiving vancomycin were analyzed which demonstrated only about 30 percent appropriate use during first 72 hours of drug initiation (10).

The most prevalent primary indication for ceftazidim and vancomycin antibiotics in our study was pneumonia, while meningitis was the main indication in the study by Khalili and colleagues. According to the guidelines vancomycin is not a common choice for empiric treatment of outpatient pneumonia (11). With the highest use of these antibiotics in wards such as internal medicine and pediatrics knowing that the majority of patients have been admitted from emergency room; it seems probable that critical condition of patients admitted to these wards may have caused such a broad-spectrum antibiotic use. Meningitis is a life threatening problem and vancomycin empiric therapy is a standard of care while vancomycin in pneumonia is only justifiable by considering methicillin resistant staph aureous infection (12). It is reasonable to

Table 2. Mean and Defined Daily Dose (DDD), Mean duration of antibiotic treatment and Hospital stay.

	Mean Dose (mg/day)		DDD (mg/day)	Mean duration of treatment (day)	Mean length of hospital stay (day± SD)
	Children (<12 Years old)	Adult (>12Years old)			
Ceftazidim	695	3803	4000	4 (1-11)	6.94±3.34
Vancomycin	303	1734	2000	4 (1-15)	8.14±5.17
Amikacin	247	783	1000	4 (1-13)	6.32±3.13

Table 3. Clinical and monitoring data.

Monitoring/ Clinical parameters	Amikacin N (%)	Ceftazidim N (%)	Vancomycin N (%)
Culture	31(62)	15(30)	27(54)
Antibiogram	8(16)	0(0)	6(12)
Blood Urea Nitrogen/Creatinin	28(56)	32(64)	39(78)
Empiric therapy	7(14)	45(90)	44(88)
Prescription based on guideline	12(24)	11(22)	8(16)
Definite Therapy	43(86)	5(10)	6(12)
Therapeutic response	42(84)	31(62)	37(74)
Therapeutic failure	8(16)	17(34)	7(14)
Death	0(0)	2(4)	6(12)

promote practice guidelines about utilizing culture and sensitivity testing when considering the use of broad spectrum antibiotics.

In conclusion, the results of this study indicate the need to establish continuing medical education (CME) courses for physicians to familiarize them with standards required to use and monitor these agents. Also, it is recommended that a resident pharmacist and infectious disease specialist be consulted to optimize treatment outcome.

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