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Vancomycin Utilization Evaluation in a Tertiary Teaching Hospital in Mashhad, Iran

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ABSTRACT

***Background*:** Inappropriate use of antibiotics in health care systems can lead to bacterial resistance, nosocomial infections and increased hospital costs. So, evaluation programs for these medications are needed. This study evaluates the pattern of vancomycin utilization in Imam Reza hospital, Mashhad, Iran.

***Methods*:** At first, according to drug information sources a check list was designed for the appropriate indication and dosing of vancomycin. One hundred patients were selected randomly from different wards of the hospital during a 6 month period and their data were collected in predesigned check list. Then, data were evaluated according to prepared checklist.

***Results*:** In this study, 100 patients (48 female and 52 male) were evaluated. Empiric therapy in 20% of patients was not initiated appropriately based on prepared checklist.

Empiric regimen was changed in 10 patients based on culture results and in 28 patients regarding clinical response. Prescribed doses were, according to the guideline in only 31% of patients. Duration of treatment were inappropriate in 35 patients. Vancomycin induced nephrotoxicity occurred in 7 patients and red man syndrome in 1 patient. Administration procedure was correct in all patients.

***Conclusion*:** According to the results, lots of error occurred in vancomycin administration and dosing in our center. It is necessary to develop localized guideline for vancomycin utilization in this hospital to prevent unwanted adverse reactions and antimicrobial resistance and also reduce treatment cost.

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Introduction

Drug use evaluation (DUE) is a necessary process that implemented by pharmacists to ensure rational drug administration and use. The rational use of drugs requires that "patients receive medications appropriate to their clinical conditions, in doses that meet their own individual requirements for an adequate period of time, at the lowest cost to them and their community"

(1). Worldwide, more than half of all medicines are prescribed, dispensed, or sold improperly, and 50% of patients fail to take them correctly. Moreover, about one third of the world's population lacks access to essential medicines (2). Irrational prescribing is a global problem. Bad prescribing habits lead to ineffective and unsafe treatment, exacerbation or prolongation of illness, distress and harm to the patient, and higher costs. The over-use of antibiotics, in particular, inappropriate use is a global public health concern. The inappropriate use of antibiotics is a significant global public health problem.

The unnecessary use of antibiotics exposes the community to unwarranted medication use and contributes to the development of antimicrobial resistance (3).

Many clinical and non-clinical factors contribute to inappropriate or unnecessary use of antibiotics. These include doctor and consumer knowledge, perceived patient demand, pressure of promotion, fear of poor clinical outcomes, peer norms and local medical culture and supply mechanisms (4, 5). The workload of general practitioners (GPs) and impact of health-care structures have also been noted as influencing factors (6).

Vancomycin is a broad-spectrum antibiotic with activities against aerobic gram-positive microorganisms including staphylococci, streptococci and enterococci. This antibiotic should be kept as an alternative therapy for critical infections not susceptible to the other antibiotics (5,6). This study evaluated the pattern of vancomycin use in Imam Reza hospital, Mashhad, Iran.

Methods

This prospective study was done in a 918-bed teaching hospital, affiliated to Mashhad University of Medical Sciences. The hospital includes all major departments and services, including twenty-five medical and surgical wards. This study was conducted to evaluate the use of vancomycin in Imam Reza Hospital from April to September 2015 for 6 months. In order to collect data, firstly, highly-administered ward were identified, including burn, intensive care unit (ICU) and internal medicine. Based on the cardholder at the nursing station, all patients who received vancomycin and the number of days received vancomycin were identified. For more appropriate monitoring, patients who received medication for more than 72 hours were included in the list. Finally, 100 patients were randomly selected from this list.

In each case, the patient's paraclinical records and lab data were fully reconsidered every day, from the beginning of the medication to the time of discharge or discontinuation of the medication.

After selecting patients, extraction, evaluation and analysis of data were fully conducted. This sample size chose based on time and human resource limitations. Random case selection performed by searching in HIS system by the pharmacist. A standard protocol on vancomycin indications, dosing and monitoring was designed by clinical pharmacists based on updated international consensus guidelines in literature that best matched local condition like American Hospital Formulary Service (AHFS) drug information, drug facts and comparisons, Applied clinical pharmacokinetics, Applied therapeutics: The clinical use of drugs, Mandell Infectious Disease Inventory, Douglas and Bennett's Principles and Practice of Infectious Diseases, and Up to date version 21.6 (6, 9-12). A form for collection of vancomycin consumption data was also developed by clinical pharmacists.

Patients were evaluated on a daily basis and their charts and hospital information system (HIS) were reviewed and clinical and paraclinical information was recorded in a designed questionnaire, from vancomycin initiation day to the time of discharge or its discontinuation. Patient hospital information system (HIS) was reconsidered and crucial data for evaluation, were gathered and recorded in designed. These data included diagnosis, vital signs and other clinical sign and symptoms, paraclinical test like computed tomography (CT) scan and magnetic resonance imaging (MRI), biochemical tests, demographic data and also an indication checklist for vancomycin prescription, its dose and duration and co-prescribed antibiotics.

The results were analyzed using Excel 2013 software. The results of this study are presented descriptively. The results were shown as mean ± standard deviation or median continuous variables, respectively, and the number (percentages) for nominal variables.

Results

This prospective study was conducted during 6 months on 100 patients treated with vancomycin in Imam Reza Hospital, Mashhad, Iran. Patients' demographic and laboratory data are listed in Table 1. Most of the patients were admitted to ICU ward (45%).

In 29% of patients, vancomycin administered without approved indication. Most of the errors occurred in ICU wards (72%).

Culture were requester for 80% of cases and only in 10 cases (10%) the initial empiric treatment was changed based on the culture results and in other patients vancomycin was continued regardless of the culture results. As the evaluation presented, in ICU ward clinicians paid less attention to the culture results.

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

Age (year), (mean±SD)		33.8 ± 25.7
Duration of Hospitalization (Day,) (mean±SD)		37.4 ±5.6
Female/Male ratio		48/52
Body weight (Kg), (mean±SD)		49.7 ±27.4
Renal failure (GFR[1]<60 ml/min), N (%)		46)46%(
Patients with hepatic failure[3], N (%)		17)17%(
Wards, N (%)	ICU[2]	45)45%(
	Burn	29)29%(
	Internal	26)26%(

[1] glomerular filtration rate

[2] intensive care unit

[3] Patients with coagulopathy (INR>1.5) and encephalopathy distinguished in 28 days–6 months

Culture results were reported in only 40% of cases 72 hours after culture request.

Clinical improvement was carefully evaluated according to the criteria mentioned in the method section, and it was found that 28 cases (28%) had not shifted to direct antibiotic therapy despite of the appropriate therapeutic response. The majority of errors occurred in ICU and Internal ward (43%).

Inappropriate dosing were occurred in 69 patients; 32 cases out of them were due to dosing vancomycin regardless of patients' GFR (24 patients received higher dose and 8 patients were given lower than recommended dose) and another 37 cases received the wrong dose regarding their body weight (Seven patients received a higher dose, based on body weight, while in 30 cases the prescribed dose was lower than the required dose). Overall, 82% of these errors happened in ICU and burn ward. Table 2 shows detailed data, gathered about errors in indication and dose from different wards.

Regarding vancomycin induced adverse reactions, the red man syndrome was happened in one patient in a burn ward, resulting in discontinuation of the drug. Nephrotoxicity did not happen during the study period. It is worth-mentioning that therapeutic drug monitoring (TDM) was not requested in any cases as checking vancomycin trough level is not performed in Mashhad.

The total number of over used vancomycin vials during the 6-months period was 2934.5 vials. Taking into account the cost of each vial (about 70000Rials for each 500 mg vial), the total cost of consuming extra amounts of vancomycin is 205415000Rials (≈489210 USD).

Discussion

This study evaluated the rate of inappropriate vancomycin use in teaching tertiary hospital. In 29% of cases vancomycin therapy was not necessary. Several similar clinical studies have been conducted on vancomycin use. In a study performed by Fahimi and colleagues in a teaching hospital in Tehran between 2007 and 2008, 45 patients were evaluated and only in one (2.2%) of patients vancomycin was prescribed in accordance with the center for disease control and prevention (CDC) and infectious disease society of America (IDSA) guidelines (7). In a study conducted by Vazin et al., from 2008 to 2009 at Namazi Hospital in Shiraz, the administration of vancomycin was evaluated in 58 patients based on Healthcare Infection Control Practices Advisory Committee (HICPAC) and Infectious Diseases Society of America (IDSA) guidelines. Vancomycin administration was appropriate in 68.63% and 71.43% (5 out of 7) of patients with febrile neutropenia (42 out of 51) and patients with other diagnosis, respectively (8).

In a pre-post study carried out by Tavakoli et al., in Taleghani Hospital of Tehran, Iran between 2011 and 2012 on 77 patients, , the administration of vancomycin was evaluated based on HICPAC and Centers for Disease Control (CDC) guidelines. In the first phase only in 38.96% of cases vancomycin administration was based on guideline which improved to 59.76% after pharmacists' intervention (9). In a study conducted by Salehifar et al., in Razi teaching Hospital in Mazandaran province, Iran, in 2012, based on HICPAC and Up to date 2012 guidelines, evaluating 146 patients treated with vancomycin, only 58% of the cases had accepted indication for vancomycin (10). In a study conducted by Hamishekar et al., in Tabriz Shohada teaching Hospital from 2011 to 2012, vancomycin indication was evaluated in 75 patients who treated with it based on CDC and American Society of Health-System Pharmacists (ASHP)

Table 2. Inappropriate indication and dose of vancomycin in different wards.

	Wards			
	Error (%)	ICU[1] (%)	Burn (%)	Internal (%)
Unapproved indication	29	72	6.8	20.6
Inappropriate Dose	69	41	41	18
Inappropriate regimen based on tailoring culture results	90	44	28	26
Inappropriate regimen based on clinical response	28	43	14	43

[1] intensive care unit

guidelines. In this study, vancomycin was prescribed only in 30% of patients in accordance with guidelines (11). It seems that in our center there is more compliance with guidelines regarding vancomycin indication. However, it should be noticed that different guidelines were used in various studies for evaluating vancomycin indication.

It may be one of the causes of variety in findings.it may also be due to evaluation of multiple wards in our study instead of concentrating on a specific ward.

Similar studies are also performed in other countries. In a study by Salemi et al., conducted at a hospital in Fontana, USA, between 1993 and 1995, vancomycin use was evaluated based on HICPAC guideline. Of 758 evaluated patients, initial administration of vancomycin was appropriate in 71% of them(12). In a study by Evans and Kortas, in a hospital in Lexington, USA, in 1996, vancomycin administration was evaluated based on HICPAC guideline. Of 101 patients who received this medication, vancomycin was only correctly administered in 66 cases (about 66%) (13). The rate of appropriate vancomycin use is about our study in developed countries.

Preparing and implementing guideline for rational antibiotic use may be helpful in reducing errors in Iran hospitals. Infectious clinicians and clinical pharmacist play a vital role in this process. In Ozkurt et al., and Pestonic et al., studies after antibiotic restriction policy implementation, inappropriate antibiotic use reduction were 20%.

Culture result plays an important role for optimization of antibiotic regimen. In our study only in 10 cases (10%) the initial experimental treatment was changed based on the cultures. For instance, in some cases, despite of the culture results that showed microorganism susceptibility to methicillin, vancomycin was still continued. Many clinicians do not pay attention to the culture results for various reasons. For example in burn ward, tissue culture is required for precise diagnosis instead of wound secretion culture. Moreover, since most blood samples for culture are not taken before the start of the empiric antibiotic regimen, the results of subsequent cultures cannot be helpful, as it is not obvious that the negative culture result is due to the infection absence or the initiation of antibiotic therapy. In some cases clinicians do not trust to the accuracy of the sampling process, kits and their results.

In a study performed by Hamishekar et al., in Tabriz on 75 patients who received vancomycin, continuation of antibiotic regimen was wrong in 50% of cases. And only in 4.35% of cases, vancomycin was discontinued due to negative culture (11). In Melo et al., study in Brazil which was performed on 126 patients who received vancomycin. Vancomycin should be discontinued in 8 cases based on culture results, which occurred only in one case (14). In Floret et al., study in eastern France, evaluating vancomycin use based on HICPAC guideline 53.1% of culture results were not implemented (17 out of 32 cases) (15). It appeared that culture results are implemented much less in our center than other countries and even different centers in Iran. Technical and methodological advancement should be made in this center in order to increase culture reliability and applicability.

Clinical improvement should be occurred a few days after initiation of empiric regimen, otherwise antimicrobial regimen should be changed. In our study 28 cases (28%) had not tailored despite the appropriate therapeutic response. In Tavakoli et al., study in Tehran the treatment duration was appropriate in 83.3% of cases (9). In Vazin et al., research in Shiraz treatment duration was improper in half of patients(8). In Salemi et al., study out of the 536 cases with approved indication for vancomycin therapy in 176 patients it was discontinued after 3 days, according to clinical and laboratory evidence (12). The most important reason for not discontinuing the medication, despite evidence of patient recovery is the fear of infection recurrence.

Vancomycin dose adjustment should be based on the trough serum concentration or available dosing nomogram and renal function. In this study serum trough concentration was not requested in any of the cases due to the lack of TDM facilities at Imam Reza Hospital. Vancomycin dosing in 31 cases (31%) was completely

correct based on our guideline. In 32% of patients the dosing was wrong based on creatinine clearance of patients and in remaining cases, the error was due to inappropriate dosing based on body weight. In Ayazkhoo et al., study in Tehran, 64.4% of vancomycin dosing was wrong according to the American Pharmacists Association (APhA) guideline and also in 88.8% of cases dose was not adjusted properly based on patients' GFR and body weight (16). In Tavakoli et al., study In Tehran, 54.5% of patients received wrong dosage(9). In Khalili et al., study In Tehran, dosing in 97.4% of cases was consistent with ASHP guidelines (17). In Fahimi et al., study out of 45 patients 4 patients received an undesired dose based on the serum creatinine. Also, in 6 cases, inappropriate dosing implemented according to the patients' body weight (7). In Vazin et al., research in Shiraz, 35% of patients experienced vancomycin induced nephrotoxicity but a proper dose adjustment was done in only half of them (8). The differences in findings of mentioned studies can be due to the variation between applied guidelines in them.

Beside antibiotic resistance occurrence which is the main result of antibiotic overuse, economic burden also imposes to the patients. In our study the total amount of extra vials used during the 6-months period was 2934.5 vials. Taking into account the cost of each vial, the total cost of consuming extra amounts of vancomycin is 205415000 Rials (≈489210 USD).

In conclusion, it appears that vancomycin administration in "Imam Reza" hospital of Mashhad, Iran, must be modified as there are lots of errors in its indication dosing and duration of therapy. It is crucial to optimize and execute standard guidelines to minimize improper use, costs and antibiotic resistance. Providing necessary equipment for vancomycin TDM also is critical for our medical center. Moreover, clinicians should pay more attention to culture results for timely modification of antibiotic regimen. Hospital and clinical pharmacists can play an important role in these processes to reduce current medication errors.

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