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Evaluation of Vancomycin Administration After Pharmacist Intervention in the Intensive Care Unit of an Educational Hospital

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Abstract

Background: Vancomycin is a glycopeptide antibiotic used to treat infections caused by Gram-positive bacteria. Irrational administration of this antibiotic may result in increased morbidity or mortality due to toxicity and the emergence of resistant organisms and also impose additional costs.
Objectives: The current study aimed at evaluating the effect of pharmacist intervention on vancomycin administration, and discussing appropriate and inappropriate applications of this drug.
Methods: The current study was performed on all patients receiving vancomycin intravenously in the intensive care unit (ICU) of Loghman educational Hospital in Tehran, Iran, from May to September 2015. Relevant data were collected by a pharmacist from each patient and their datasheets such as medical records, patient's history, medical orders, nursing reports, and the experimental results available in the patient's records, duration of vancomycin use, history of drug allergy, first diagnoses, type of administration, monitoring necessity, dosing regimen, and occurrence of adverse drug reaction. Patients then were followed until discharge from ICU.
Results: About 82% of patients had received vancomycin without noticing their body mass index (BMI) or calcium-induced calcium release (CICR). In addition, 2.63% had inappropriate indication, and in general, the duration of therapy was somehow correct in 44.73% of patients, and 55.26% received vancomycin for more than the appropriate period. Most of the wrong administration was for postoperative prophylaxis. The appropriate duration is maximum 48 hours. But in 63.33% of the patients, it continued for more than 2 - 3 days. And this inappropriate usage could increase vancomycin resistance.
Conclusions: Due to the increasing resistance rate to antibiotics, indication and duration of administration and dosing should be more accurate, and for each patient must be according to his/her ideal body weight (IBW).

Keywords: Vancomycin, Drug Use Evaluation, Pharmacist Intervention

1. Background

Vancomycin is a glycopeptide antibiotic used to treat infections caused by Gram-positive bacteria (1). In recent years inappropriate prescription of vancomycin led to the emergence of resistant Gram-positive microorganisms such as vancomycin-resistant enterococci (VRE) (2, 3). The current study aimed at evaluating the effect of pharmacist intervention on vancomycin administration.

Drug utilization evaluation (DUE) is a structured process to analyze the pattern of drug administration in various practice settings including hospitals in relation to guidelines or predetermined standards (4). Considerable therapeutic effects of antibiotics and the emergence of resistance make antibiotics very valuable worldwide drugs; therefore, it is necessary to use them appropriately (5).

Vancomycin acts by the inhibition of bacterial cell wall development and blocks it earlier in comparison with beta-lactams (6).

Irrational administration of vancomycin may result in increased morbidity or mortality due to toxicity and the emergence of resistant organisms and also impose additional costs. Hence, it is necessary to apply the DUE programs for this drug. Accurate and constant studies should be conducted to inform clinicians about inappropriate and illogical administration of vancomycin and help them to find out a method to use and prescribe this valuable drug in a logical and rational pattern.

2. Methods

2.1. Subject Recruitment

The current study was performed on all patients receiving vancomycin intravenously in the intensive care unit (ICU) of Loghman educational Hospital in Tehran, Iran, from May to September 2015.

2.2. Data Collection

Relevant data were collected by a pharmacist from each patient and their datasheets such as medical records, and orders, nursing reports and the paraclinical data available in the patient's records, history of vancomycin therapy and drug allergy, first diagnoses, type of administration, monitoring necessity, dosing regimen, and history of adverse drug reaction. Then, patients were followed until discharge from ICU.

2.3. Study Indicators

Nephrotoxicity and rate of acute kidney injury was assessed based on RIFLE (risk, injury, failure, loss, and end-stage kidney disease) and acute kidney injury (AKIN) criteria (Table 1). Vancomycin administration was assessed according to AHFS (American Hospital Formulary Service) guidelines.

The recorded parameters included duration of vancomycin use, diagnoses, type of administration, dosing regimen, and occurrence of adverse drug reaction. Indications for vancomycin therapy according to AHFS guideline are presented in Box 1.

3. Results

The current study was performed on 50 patients in the ICU receiving vancomycin. Most of indications were infection prophylaxis in patients with brain and cerebrovascular surgery, and also meningitis. The mean± standard deviation (SD) of patients' age was 46.2 ± 18.63 years. The youngest patient was 3 months old and the oldest 76 years old. The mean ± SD period of vancomycin therapy in the study population was 7.31 ± 6.62 days. Maximum duration of vancomycin therapy was observed in a patient with meningitis after brain surgery for 30 days and the minimum duration was a single dose before foot surgery and intracerebral hemorrhage (ICH). In the current study, there were 22 female (46.8%) and 25 male (53.19%) patients. The rate of infusion in the patients varied from 105 mg/hour (qid for an infant) to 1,250 mg/hour based on the patient's condition.

Eighty-two percent of the patients received the same dose of 1 g twice daily, without noticing their body mass index (BMI) or calcium-induced calcium release (CICR). In 4 patients the administration was different from the first day. In a 3-month infant with meningitis 105 mg/6 hours was administered; 250 mg/6 hours was prescribed in a 3-year-old male after brain surgery with fever and seizure after surgery; 150 mg/6 hours in a 5-year-old female with the same indication, but without fever and seizure; 600 mg/6 hours in a 13-year-old female with brain tumor surgery.

In 1% after 12 days, dosage of vancomycin was increased from 1 g/BD to 1250 mg/BD and in 3 patients doses were decreased from 1 g/BD that in one of them it was due to dermatologic and sensitivity reactions and in the others the reason had not been mentioned in patients file. The preparation of intravenous (IV) vancomycin is generally as follows: first the drug is dissolved in 10 mL of WFI (water for injection), then, it is diluted up to 200 mL WFI, and the resulting solution is injected in 3 hours. One of the patients developed dermatologic and sensitivity reactions, which the dose was decreased from 1 gr qid to 1 gr each 72 hours to overcome. In reviewing their SrCr (scavenger receptor cysteine-rich family) and glomerular filtration rate (GFR) profiles, based on RIFLE and AKIN criteria, no acute kidney injury was observed in the patients. The results of appropriate or inappropriate duration of therapy are shown in Table 2.

4. Discussion

Almost all of the patients (97.36%) had indication of receiving vancomycin according to AHFS (postoperative prophylaxis), but as already reported, 36.66% received vancomycin in appropriate duration for postoperative prophylaxis according to AHFS.

The correct indication was more than it was reported in the study by Salehifar et al. they showed that only 58% of patients had the correct indication to receive vancomycin (7).

Preparation and the rate of infusion was acceptable by AHFS.

One patient showed dermatologic and sensitivity reactions following the vancomycin administration, but the drug did not stop that was an incorrect regimen. In addition, this patient did not have the indication to receive vancomycin (the 2.63% inappropriate usage).

Nowadays, the methicillin-resistant Staphylococcus aureus (MRSA) is a major health care problem and its resistance to vancomycin is increasing. It is reported that the percentage of MRSA increased from 35.9% to 64.4% from 1992 to 2003 in the United State hospitals and the significant and incorrect prescription of broad spectrum antibiotics led to this health threatening problem (8).

Table 1. Criteria for Acute Kidney Injury

	SrCr Criteria			Urine Output Criteria
	RIFLE	AKIN	KDIGO	
Definition	Increase in SrCr of > 50% developing over < 7 d	Increase in SrCr of 0.3 mg/dL or > 50% developing over < 48 h	Increase in SrCr of 0.3 mg/dL developing over 48 h or > 50% developing over 7 d	Urine output of < 0.5 mL/kg/h for > 6 h
			Staging	
RIFLE-risk AKIN/KDIGO stage 1	Increase in SrCr of > 50%	Increase in SrCr of 0.3 mg/dL or > 50%	Increase in SrCr of 0.3 mg/dL or > 50%	Urine output of < 0.5 mL/kg/h for > 6 h
RIFLE-injury AKIN/KDIGO stage 2	Increase in SrCr of > 100%	Increase in SrCr of > 100%	Increase in SrCr of > 100%	Urine output of <0.5 mL/kg/h for > 12 h
RIFLE-failure AKIN/KDIGO stage 3	Increase in SrCr of > 200%	Increase in SrCr of > 200%	Increase in SrCr of > 200%	Urine output of < 0.3 mL/kg/h for > 12 h or anuria for > 12 h
RIFLE-loss	Need for renal replacement therapy for > 4 wk			
RIFLE-End-stage	Need for renal replacement therapy for >3 mo			

Box 1. AHFS Recommended Indications for Vancomycin Use

	Indications
1	Methicillin-Resistant Staphylococcal Infections
2	Enterococcal infections resistant to penicillin or in patients with the history of immediate-type hypersensitivity to penicillin.
3	Clostridium difficile-associated diarrhea and colitis in seriously ill patients (i e, with severe or potentially life-threatening colitis) or those who cannot tolerate or do not respond to oral metronidazole.
4	Bacillus spp. infections
5	Respiratory tract infections in which penicillin-resistant S. pneumoniae especially when cephalosporins cannot be used.
6	Perioperative prophylaxis in neurosurgery, orthopedic, cardiac, thoracic, or vascular surgery at institutions where MRSA are the frequent causes of postoperative wound infections or the first drug of choice cannot be used.
7	Rhodococcus spp. infections in immunocompromised individuals (in combination with another antibiotic)
8	As an alternative to parenteral penicillin G or ampicillin for prevention of perinatal group B streptococcal disease.

Table 2. Vancomycin Therapy; Evaluation of Patients During the Study in ICU

Indications	Percentage	Appropriate Duration	Inappropriate Duration
Postoperative prophylaxis	78.9436.66	63.33%	
Meningitis	18.42100	-	
Colon surgery	2.63	100%	

Hence, it seems to be essential to do strategic studies such as drug utilization evaluation (DUE) in order to evaluate commonly used antibiotics, which results in improved treatment efficacy, but also conserves cost and prevents unwanted adverse effects (9).

In a case series study, Fahimi et al. reported that 97.7% of the study population had inappropriate indication and dosing regimen of vancomycin and they concluded that irrational administration of vancomycin was high in Iran compared to other countries (10) and according to the current study, in just 28.57% of patients, vancomycin dosing was somehow proportional to their BMI, and the others (71.42%) received doses higher or lower than the proper dosage.

In 44.73% of the patients, the duration of therapy was somehow correct, but 55.26% of the subjects received vancomycin for more than appropriate period. In comparison with the study by Salehifar et al. the rate of inappropriate duration was more; in that study about 55% of the subjects had the correct duration of therapy (7). Most of the wrong administration was for postoperative prophylaxis. The appropriate duration for this indication is maximum 48 hours. But, in 63.33% of the subjects it continued for more than 2 - 3 days and this inappropriate usage could increase vancomycin resistance.

In the current study, Red-man syndrome was not observed because the infusion rate in 100% of the cases was appropriate, the same as a prospective drug utilization review (DUR) study conducted by Vasin et al. (11).

In this study, vancomycin serum concentration was measured in 4 patients: 18.7, 22, and 24 μg/mL in 3 patients with brain surgery and 29.9 μg/mL in a patient with meningitis after surgery that after 7 days the serum concentration increased to 36.8 μg/mL.

Minimum trough serum concentration should be > 10 mg/L and in complicated infections (bacterimia, endocarditis, osteomyelitis, meningitis, and hospital-acquired pneumonia), trough serum concentrations of 15 to 20 mg/L

are recommended (11).

In the current study, the serum concentration was higher than normal level; it was somehow similar to that of Vasin et al. (11).

Due to the increasing resistance rate to antibiotics, indication, and duration of administration and dosing should be more concerned, and for each patient should be tailored to his/her IBW.

In conclusion, some points were recommended to achieve rational use of vancomycin in hospitals:

1- Antibiotics should be prescribed based on standard guidelines and microorganism type.

2- The duration of treatment should be proportional to references and patient should be monitored during the therapy.

3- Laboratory tests and processes related to infection control should be reevaluated.

4- Educational courses should be offered for physicians and nurses in order to obtain rational use of antibiotics.

5- Attention should be paid to adverse effects of drugs and appropriate decisions should be made on stopping or continuing the drug therapy.

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