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Vancomycin Utilization Evaluation in a Major Teaching Hospital in West of Iran

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ABSTRACT

Background: Vancomycin is a potent antibiotic and has central role in the managing of infections with known resistance to other antibiotics or in patients with allergy to beta-lactams. Irrational use of vancomycin is associated with increased morbidity and mortality as well as the antibiotic resistant.

Methods: The DUE was done in Imam Reza Hospital, Tabriz, Iran. A total of 100 patients were included during a 6-month period. We aimed to evaluate vancomycin administration pattern and assess its compliance with Centers for Disease Control and Prevention (CDC) and the American Society of Health-System Pharmacists (ASHP) protocols as the primary outcome and its adverse effects as the secondary outcome.

Results: The mean duration of hospitalization and antibiotic therapy were 22.11 ± 1.76 and 19.08 ± 1.51 respectively (mean ± SD). The most causes of vancomycin administration (51%) were for surgery prophylaxis. In 38% of patients, vancomycin administration was not in accordance to standard guidelines. Dose and duration of vancomycin therapy was according to ASHP and CDC guidelines in 74% and 59% of patients. Dose readjustments of antibiotics were necessary in 28 patients which were done in 12 of them. A total of 140 samples were collected from 60 patients. In 30% of patients, vancomycin use was continued without considering the culture results.

Conclusion: It is important to set practical pharmaceutical and therapeutic infection control committees in hospitals under the clinical pharmacists' observation. Furthermore, educational programs for health care professionals regarding rational use of antibiotics can be helpful in improving antimicrobial medications utilization and monitoring.

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Introduction

Drug Utilization Evaluation (DUE) studies are defined to assess drug use appropriateness. DUE is an authorized, structured process to analyze prescribing, dispensing and drug usage in numerous practice settings, such as hospitals (1- 3).

Vancomycin is a potent antibiotic and has central role in the managing of infections in patients with known resistance to other intravenous and oral antibiotics or in patients with allergy to beta-lactam antibiotics. The mechanism of bactericidal action of vancomycin is inhibition cell wall synthesis and damage to the cytoplasmic membrane. All strains of Staphylococcus aureus and Staphylococcus epidermidis, including the methicillin –resistant species, are susceptible to vancomycin for the treatment of infections in patients who cannot receive or who failed to respond to penicillin and cephalosporins. Vancomycin is considered the treatment of choice for infections caused by methicillin-resistant staphylococci, both S. aureus and S. epidermidis,

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a major pathogen whose prevalence in hospitals and institutions is being reported with increasing frequency, leading to renewed interest in its use. The drug is indicated in gram-positive endocarditis, osteomyelitis, pneumonia, septicemia, and soft tissue infections. With rare strains of tolerant enterococci, an aminoglycoside must be added to the regimen as vancomycin is only bacteriostatic under this condition. Vancomycin is not active against gram-negative organisms, fungi, or yeasts (4- 7).

Irrational use of vancomycin is associated with increased morbidity and mortality because of toxicity as well as the emergence of resistant organisms (8, 9).

Considering increasing resistance to vancomycin and treatment cost, careful consideration should be given to their choice. Therefore, doing DUE programs for this drug is required. The present study was done to evaluate the pattern of vancomycin use and prescription as well as its concordance with standard guidelines in Imam Reza hospital, Tabriz, Iran.

Methods

The present prospective DUE study was done to evaluate usage pattern of vancomycin in Imam Reza Hospital which is one of the major teaching hospitals of Tabriz University of Medical Sciences. All patients prescribed vancomycin during a 6-month period, from January to August 2017 were included. The patients' medical records were examined for demographic information of patients as well as dose, duration, rout of administration, adverse effects, and indication of vancomycin, dose adjustment in renal failure, history of drug allergy and microbiological culture/sensitivity testing. Patients with incomplete medical records were excluded. In the present study, we aimed to evaluate vancomycin administration pattern in our center and assess its compliance with Centers for Disease Control and Prevention (CDC) and the American Society of Health-System Pharmacists (ASHP) protocols as the primary outcome (10, 11). Indications for vancomycin use according to CDC and ASHP guidelines are presented in Table 1, and 2 respectively. The secondary outcome of our study was evaluation of adverse effects of vancomycin. All the data were coded and a SPSS 22 was used for the statistical analysis.

Table 1. Centers for Disease Control and Prevention (CDC) recommended indications for vancomycin use.

1. Gram-positive infections which are already recognized to be resistant to beta-lactam antibiotics
2. Hypersensitivity to beta-lactams
3. If the empirical treatment has been initiated, follow up treatment should be based upon antibiogram culture results.
4. If the report of culture results is negative, vancomycin should be discontinued
5. Methicillin-resistant staphylococcal infections
6. Betalactam-resistant pneumococcal infections
7. Enterococcal infections resistant to penicillin

Table 2. American Society of Health-System Pharmacists (ASHP) recommended indications for vancomycin use.

1. Confirmed Coagulase negative staphylococcus infection or confirmed methicillin-resistant Staphylococcus aureus according to culture tests
2. Intense gram-positive infections in patients with chronic renal failure or hemodialysis
3.Suspected gram-positive infections including staphylococcus and Streptococcus in patients who are not able to have oral intake and or have Penicillin allergy that cannot be desensitized

Results

During the study period, vancomycin was prescribed for 100 patients (including 62 men and 38 women) with mean age of 50.61 ± 2.15 years. The mean duration of hospitalization (22.11 ±1.76) and antibiotic therapy (19.08 ± 1.51) are shown in Table 3. The mean duration of vancomycin therapy was 18.86 ±1.53 days. The most reason of vancomycin administration (51%) was surgery prophylaxis (Table 4). In 38% of patients, vancomycin administration was not in accordance to standard guidelines. The reasons for inappropriate administration of vancomycin were as follow: prophylaxis for postoperative infections and before major surgical procedures in patients without the risk of MRSA infection (73.6%), continuing of vancomycin without considering of culture results (21%) and treatment of infections caused by β-lactam sensitive gram-positive microorganisms (5.3%).

Table 3. Demographic /Clinical Data.

Characteristic	Patients (n=100)
Sex, female, n (%)	38(38)
Age (years), mean±SD	50.61 ± 2.15
Serum creatinine (mg/dL), mean±SD	2.08 ± .22
Hospitalization (day), mean ± SD	22.11 ± 1.76
Antibiotic therapy (day), mean ± SD	19.08 ± 1.51
Vancomycin therapy (day), mean ± SD	18.86 ±1.53

The most frequently prescribed anti-infective concomitantly with vancomycin were as follow: cephalosporin (38.2%), carbapenems (24.8%), fluoroquinolones (18.5%), aminoglycosides (4.5%), penicillin (3.8%) and other anti-infective (10.2%) (Table 5).

All of the patients received vancomycin intravenously. Dose and duration of vancomycin therapy was according to ASHP and CDC guidelines in 74% and 59% of patients respectively. Dose readjustments of antibiotics were necessary in 28 patients which were done in 12 of 28 patients. The need for monitoring of vancomycin serum levels was necessary in 34 patients. 22 patients had renal failure, 10 patients were at risk of renal toxicity due to concomitant use of aminoglycosides or sulfamethoxazole-trimethoprim. Furthermore, two sepsis cases were infected with staphylococcus aureus.

Among patients, 2 cases of allergic reaction to β-lactams, one case of Redman syndrome and two cases of nephrotoxicity due to vancomycin were observed.

A total of 140 samples were collected from 60 patients. In 18 patients, no bacterial growth was reported. Positive bacterial culture was observed in 21 and 18 for gram positive and gram negative bacteria respectively. Four patients had both gram positive and gram negative microorganisms. It should be noted that among patients which had microbial culture results, in approximately 30% of patients vancomycin use was continued without considering the culture results.

Table 4. Indications of vancomycin use in the study population.

Indication	Number (% of total)	Appropriate (%)	Inappropriate (%)
Surgery prophylaxis	51 (51)	23 (45.1)	28 (54.9)
Dialysis catheter placement	19 (19)	15 (78.9)	4 (21.1)
Pneumonia	16 (16)	13 (81.2)	3 (18.8)
Meningitis	7 (7)	5 (57)	2 (43)
Osteomyelitis	3 (3)	2 (66.6)	1 (33.4)
Septicemia	3 (3)	3 (100)	0 (0)
Urinary tract infection	1 (1)	1 (100)	0 (0)

Table 5. Concomitant Anti-invectives with vancomycin.

Anti-infective	N (%)
Cephalospurine	38.2 (38.2)
Carbapenem	24.8 (24.8)
Flouroquienelone	18.47 (18.47)
Amnigoglycoside	4.46 (4.46)
Penicillin	3.28 (3.28)
Others	10.19 (0.19)

Discussion

Our study demonstrated that the most common indication for prescribing vancomycin was for infection prophylaxis before and after surgery. In 62% of patients, the prescribing of vancomycin was based on appropriate indication. Numerous similar studies have been conducted on vancomycin usage pattern. Based on a study by Salemi et al., at a hospital in Fontana, USA, from 1993 to 1995, vancomycin usage was according HICPAC guideline in 71% of patients (12). In a study conducted by Evans et al., hospital in Lexington, USA, in 1996, vancomycin administration was appropriate in approximately 66% of patients (13). The rate of appropriate vancomycin usage in our study is slightly lower than these studies in developed countries. However, in comparison with most of similar studies in Iran, compliance with the guidelines is higher in our study. In a study conducted by Fahimi et al., at a territory teaching hospital in Tehran from 2007 to 2008, vancomycin prescription was according to the CDC and IDSA (infectious disease society of America) guidelines in 2.2% of patients (14). In a study performed by Vazin et al., between 2008 and 2009 at a teaching Hospital in Shiraz, the administration of vancomycin was based on the IDSA and HICPAC (Healthcare Infection Control Practices Advisory Committee) guidelines in approximately 30% of patients (15). Similarly based on a study by Hamishekar et al., in Tabriz Shohada tertiary teaching Hospital between 2011 and 2012, vancomycin prescription was in accordance with the CDC and ASHP guidelines in 30% of participations (16). In a study by Salehifar et al., at Razi teaching Hospital in Iran, it is demonstrated that only 58% of the patients had acceptable indication for vancomycin based on HICPAC and Uptodate 2012 guidelines (17). In another descriptive cross-sectional study by Khalili et al., in the Infectious Disease Department of Imam Khomeini Hospital in Tehran, vancomycin utilization was compatible with CDC and ASHP protocols in 28% and 35% of the patients respectively (18). In a prospective study in 2017 at Imam Reza Hospital of Mashhad, 71% of patients received vancomycin with approved indication that is slightly higher than our study (19). In our study, dose and duration of vancomycin therapy was

according to ASHP and CDC guidelines in 74% and 59% of patients. Based on the study of Elyasi et al., mentioned above, inappropriate dose prescription took place in 69% of patients. Furthermore, dose readjustment of antibiotics was not carried out based on GFR in 32% of patients in comparison with 57% in our study (19). In a study conducted by Ayazkhoo et al., in Tehran, 64.4% of vancomycin dose was incorrect based on the American Pharmacists Association (APhA) guideline. Furthermore, in 88.8% of patients, dose adjustment was not carried out properly based on patients' GFR and body weight (20). In another study by In Tavakoli et al., in Tehran, 54.5% of patients were prescribed wrong dose. The duration of treatment was appropriate in 83.3% of patients (21). In study by Khalili et al., in Tehran, in 97.4% of patients, dosage of vancomycin was consistent with ASHP guidelines (18). In study conducted by Fahimi et al., on 45 patients, 4 patients were prescribed an undesired dose according to the serum creatinine. In addition, 6 patients didn't receive appropriate dosing according to the body weight (14). It is important to mention that using different guidelines in the various studies as well as evaluating multiple wards instead of concentration in a specific area could affect the results. Furthermore, clinical pharmacy is a new specialty in Iran and hospitals are suffering from a shortage of clinical pharmacists. Numerous studies have indicated positive effects of clinical pharmacist presence in reducing prescription errors in hospitals (14-19). Two cases of allergic reaction to β-lactams, one case of Redman syndrome and two case of nephrotoxicity due to vancomycin were observed in our study. Furthermore, the need for monitoring of vancomycin serum levels was necessary in 34 patients. Vazin et al., demonstrated that vancomycin induced nephrotoxicity took place in 35% of patients but a proper dose adjustment was carried out in only half of them. (15). In a study conducted by Salemi et al., among 536 patients on vancomycin therapy, drug discontinuation was done in 176 patients after 3 days based on clinical and laboratory evidence (22).

Most cases of vancomycin administration were empirically and before getting the result of cultures. Among patients who had microbial culture results, in approximately 30% of patients' vancomycin use was continued without considering the culture results. Probable reasons for continuing vancomycin administration in spite of these culture results were physicians fear about inadequate antibiotic treatment and their distrust to hospital laboratories.

Presence of clinical pharmacists in different departments of the health care centers, setting pharmaceutical and therapeutic infection control committees in hospitals, providing educational information for health care professionals, implementation of vancomycin standard treatment guideline based on hospital resistance pattern, and conducting antibiotic utilization review studies are recommended to achieve rational use of vancomycin.

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