



Research Article

# Drug Utilization Evaluation of Vancomycin in a Teaching Hospital in Tabriz-Iran

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## ABSTRACT

**Background:** Drug Utilization Evaluation (DUE) studies are designed to evaluate drug usage appropriateness. In this study we evaluated the relevant use of vancomycin in a teaching hospital in Iran. The results of this study may be of help for clinicians to improve the patient care. **Methods:** The use of vancomycin was evaluated in a cross-sectional and prospective study from October 2011 until June 2012. Vancomycin administration was assessed according to CDC and ASHP guidelines. Predesigned data collection was implemented in this study. Information collected from medical records, patient's history, medical orders, nursing reports and the experimental results available in the patient's records. **Results:** During the study period, 75 cases were been evaluated from all of the hospital wards. The median age of patients was  $46.65 \pm 20.04$  years (mean  $\pm$  SD). The median time of vancomycin use in the study population was  $9.35 \pm 5.70$  days. most of the patients received vancomycin, had been hospitalized for trauma problems. In this study 30.7% of cases received vancomycin appropriately and in accordance to standard guidelines. **Conclusion:** Based on the results of our study, a substantial percentage of the patients (69.3%), received vancomycin inappropriately. It is essential to promote practical guidelines about utilizing culture and sensitivity testing when considering the use of important and broad spectrum antibiotics. Also educational programs for health care professionals regarding rational use of antibiotics can be helpful in improving antimicrobial medications utilization and monitoring.

## Introduction

Drug Utilization Evaluation (DUE) studies are designed to evaluate drug usage appropriateness.<sup>1</sup> 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. Considerable therapeutic effects of antibiotics and the emergence of resistance make antibiotics very valuable worldwide drugs so appropriate use of them is necessary.<sup>2</sup> Vancomycin is a potent antibiotic with a definite indications and has important role in the management of infections in patients who are recognized to have resistance to other intravenous and oral antibiotics or in patients who have

allergy to beta-lactam antibiotics. Vancomycin is usually administered with slow intravenous infusion and has a beneficial therapeutic effect at trough Concentrations between 15-20 mg/L for treatment of infections caused by gram-positive pathogens, such as staphylococcus, streptococcus pyogenes, betalactamase producing streptococcus, streptococcus pneumonia, enterococci and clostridium. Vancomycin acts by the inhibition of bacterial cell wall development and blocks it in an earlier stage in comparison to beta-lactam antibiotics.<sup>3-5</sup>

In drug resistance settings, vancomycin is considered an alternative to other antibiotics such as penicillin and methicillin until 2002 but nowadays, as a result of

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inappropriate use, resistance to vancomycin is reported high, worldwide. Irrational use of vancomycin may result in increased morbidity or mortality due to toxicity and the emergence of resistant organisms and also impose additional costs.<sup>6,7</sup>

Hence, it is necessary to do DUE programs for this drug. Accurate and constant studies should be done to inform clinicians from inappropriate and illogical use of vancomycin and help them to find out a way to use and prescribe this valuable drug in a logical and rational pattern. In this study, a concurrent, drug utilization evaluation program was conducted in one of the educational Hospitals in Tabriz University of Medical Sciences to assess the pattern of vancomycin usage and prescription and its concordance with international standard treatment guidelines.

### Materials and Methods

The use of vancomycin was evaluated in a cross-sectional and concurrent study from October 2011 until

June 2012. The study was conducted in Shohada Hospital, which is one of the teaching hospitals of Tabriz University of Medical Sciences and the major trauma center in Tabriz.

Vancomycin administration was assessed according to CDC and ASHP guidelines.<sup>8,9</sup>

Predesigned data collection was implemented in this study. Information collected from medical records, patient's history, medical orders, nursing reports and the experimental results available in the patient's records. Parameters which were recorded include: duration of vancomycin use, history of drug allergy, first and final diagnoses, type of administration, monitoring necessity, dosing regimen, microbiological culture/sensitivity testing and occurrence of adverse drug reaction. Indications for Vancomycin use according to CDC and ASHP guidelines are presented in Table 1 and 2, respectively.

Information was collected and Data were analyzed using SPSS16 software.

**Table 1.** 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.** 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, 75 cases were been evaluated from all of the hospital wards. The median age of patients was 46.65±20.04 years (mean ± SD). The youngest patient was 9 years old and the oldest one was 104 years. The median time of vancomycin use in the study population was 9.35±5.70 days. Maximum duration of vancomycin use was seen in a patient with pneumonia for 25 days and the minimum duration was for a patient with cellulite diagnosis for 1 day. In this study, 34 patients (45.3%) were female and 41 patients were male (54.7%). Since this study was conducted in

the referral center for trauma, most of the patients received vancomycin had been hospitalized for trauma problems (28 cases), other reasons for hospitalization and vancomycin use were: cerebrospinal disease (15 cases), Postoperative infections (14 cases), osteomyelitis (7cases), factitious and cellulitis (4 cases), septic arthritis (3 cases), spinal stenosis (2 cases) and osteoarthritis (2 cases). The most frequent indication for vancomycin use, during 6 months of study period, appeared to be for prophylaxis purposes (24 patients) (Table 3).

**Table3.** Indications of vancomycin use in the study population.

Indication	Number(% of total)	Appropriate(%)	Inappropriate(%)
Prophylaxis <sup>1</sup>	24(32)	7(29.16)	17(70.84)
Osteomyelitis	22(29.30)	9(40.90)	13(59.10)
Pneumonia	11(14.7)	1(9)	10(91)
Fasciitis and Cellulitis	8(10.70)	5(62.50)	3(37.50)
Septic Arthritis	5(6.70)	1(20)	4(80)
Meningitis	3(4)	0(0)	3(100)
Pseudomembranous Colitis	2(2.70)	0(0)	2(100)

<sup>1</sup> - Prophylaxis before and after Neurosurgery and Orthopedic surgery

In our study, 30.7% of cases received vancomycin in accordance to standard guideline(reference) which the reasons for its appropriate use were:

- 1) Treatment of serious infections caused by  $\beta$ -lactam-resistant gram-positive microorganisms (65.2 %).
- 2) Prophylaxis for postoperative infections and before major surgical procedures in patients with the risk of MRSA infection (17.39 %).
- 3) Treatment of gram-positive infections in patients with a serious allergy to  $\beta$ -lactam antimicrobials (13.05 %).
- 4) Discontinuation of treatment in negative culture results (4.35 %).

73 Patients received the drug intravenously and 2 patients received it orally.

63 patients received 1 g every 12 hours, 4 patients 1 g every 5 to 7 days, 2 patients 500 mg every 8 hours, 2 patients 500 mg every 6 hours, 2 patients received 1 g every 24 hours and 2 patients regimen was different from what was mentioned in the guideline as a result of dose adjustment. Hence, considering indications and patient's GFR vancomycin dosage was appropriate in 67 (89%) patients.

The need for monitoring of vancomycin serum levels was essential in 13 patients. Trough levels measurement had been ignored in all patients. 8 patients had renal failure, 4 patients were at risk of renal toxicity due to Concomitant use of aminoglycosides and it was observed that one sepsis case was infected with staphylococcus aureus.

The infusion time for vancomycin was one hour in 65 Patients, 4 patients received intravenous infusion for 30 minute , 2 patients with pseudomembranous colitis received the drug orally and 4 patients received it for an unusual time.

12 patients required dose adjustments but only 4 cases were properly adjusted. Dose adjustment of vancomycin should be based on CL Cr and patient's actual body weight.

In the 75 hospitalized patients, 3 cases had allergic reaction to  $\beta$ -lactams but none were sensitive to vancomycin.

In our study population, 38 patients (50.6%) had bacterial culture results. Among these, in 15 patients, resistance to betalactam antibiotics was indicated in the results of culture and sensitivity test. Among 38 patients, 13 cultures were gram-positive and 13 cultures were gram-negative. In specimen of 8 patients no microorganism was observed and 4 patients had mix culture of gram positive and gram negative microorganisms. It should be noted that Among patients which had microbial culture results, in more than 50% of patients vancomycin use was continued without considering the culture results.

## Discussion

Our study, was conducted to assess the appropriateness of vancomycin use in a teaching hospital in Tabriz. Nowadays, the methicillin resistant staphylococcus has become a major health care problem and its resistance

to vancomycin is increasing. It is reported that the percentage of methicillin resistant staphylococcus aureus (MRSA), has increased from 35.9% to 64.4% during 1992 till 2003 in the united state hospitals and the significant and incorrect use of broad spectrum antibiotics led to this important problem.<sup>10</sup>

Hence, it seems to be essential to do strategic studies such as DUE. Drug Utilization evaluation of commonly used antibiotics not only will result in improved treatment efficacy, but also in conserving cost and preventing unwanted adverse effects.<sup>11</sup>

So, we select vancomycin because of its important role in treatment of MRSA infection.

The results of our study indicated that 69.3% of patients received vancomycin inappropriately.

In a case-series study, Fahimi et al, reported that 97.7% of their study population, had inappropriate indication and dosing regimen of vancomycin and they concluded that Vancomycin irrational use was high compared to other countries.<sup>12</sup>

In our study, Vancomycin frequently was administered for prophylaxis purposes before and after surgery (32%). Among those who received vancomycin for prophylaxis, only 16.29% of cases, had correct indication for receiving vancomycin. Also In a similar study Misan and colleagues, evaluated 59 patients who received vancomycin in a teaching hospital for 5 month. they reported that in the first phase of their study, 97% of patients who received vancomycin for prophylaxis purposes, were classified as inappropriate use.<sup>13</sup>

Since the type of surgery and patients with risk factors for MRSA infections not mentioned in that study we can not judge about the appropriateness of vancomycin prescription.

Patients with the following conditions are considered to be at high risk of MRSA infection: Patients who hospitalized and receive long-term care facilities for a long time, patients undergo hemodialysis, Receiving cancer treatment or medications that compromise their immune systems, Inject illegal drugs, Had surgery in the past year, People who have tattoos, Members of the millenarians, athletes and other people who may share items such as towels or razors.<sup>14,15</sup>

In our study, the patients who had received inappropriate vancomycin prophylaxis were for pre and post orthopedic surgery and Neurosurgery. In accordance to CDC guidelines for using vancomycin as a prophylaxis before and after surgery, microbiology laboratory should report recurrent staphylococcus aureus infection after surgery or the patient recognized to have a risk factor for MRSA infection or the patient has allergy to  $\beta$ -lactams. In the absence of mentioned conditions cefazolin is offered for prophylaxis.<sup>8</sup>

Among 22 patients who had received vancomycin for the treatment of osteomyelitis, 9 patients (40.9%) had appropriate administration because of gram-positive infections known to be resistant to  $\beta$ -lactams by culture/sensitivity results. In 13 cases of inappropriate use of vancomycin for osteomyelitis, 5 cases had no

culture. although one of the 5 cases had chronic osteomyelitis, but in accordance with guideline sampling from the bone discharge should be considered and treatment should be modified based on the culture/sensitivity results. One case was reported to have co-administration with vancomycin and teicoplanin. Not only the administration of vancomycin without collecting specimen is inappropriate, but also co-administration of 2 antibiotics from the same category is Contrary to the guidelines. Although 1 patient, had gram-positive culture (*staphylococcus aureus*), vancomycin was inappropriate choice due to age limitation and sensitivity to cloxacillin. The Starting time of vancomycin in 1 case was incorrect. In this case, though Gram-positive culture was resistant to beta-lactam antibiotics and patient was intermediate to vancomycin, and in spite of this report, Thirteen days after the culture report vancomycin was started. 5 patients demonstrated infection with Gram-negative strains, which in these cases vancomycin treatment had no indication and was inappropriate. Continuing vancomycin administration in spite of these culture results may have the following reasons:

- 1) Physician's distrust to hospital laboratories.
- 2) Physicians fear that patients do not receive the proper treatment when vancomycin is discontinued.
- 3) Physicians do not pay attention to paraclinical tests and follow the treatment as they have accustomed.

Among 11 patients who had received vancomycin for pneumonia only 1 case was appropriate. 4 cases didn't demonstrated any evidence of positive culture results and 6 cases had irrelevant culture results (gram-negative).

Among 8 patients who received vancomycin for fasciitis and Cellulitis 3 cases were inappropriate. Two patients without culture and 1 patient had negative culture.

Among 5 patients with diagnosis of septic arthritis only 1 case was administered according to guideline. 4 cases shouldn't have received vancomycin due to gram negative culture result or no sign of growth on culture.

In our study, 3 cases received vancomycin empirically in meningitis and because of the negative spinal fluid culture continuing treatment with vancomycin had no indication.

Two patients inappropriately had received vancomycin for pseudomembranous colitis. Administration in these cases was only based on diarrhea, fever and other symptoms that were not specific for *Clostridium difficile*.

Lipsky and colleagues in a prospective 3-phase study as baseline and 2 follow-up periods monitored vancomycin use. They demonstrated that irrational use of vancomycin can further be decreased by proper education to medical staff, however this effect appeared to be transient.<sup>16</sup>

Based on the results of our study, a substantial percentage of the patients (69.3%), received vancomycin inappropriately. Since , inappropriate use of vancomycin can increase the risk of development of

vancomycin resistant pathogens such as vancomycin resistant staphylococcus<sup>10</sup>, It is essential to promote practical guidelines about utilizing culture and sensitivity testing when considering the use of important antibiotics such as vancomycin. Also educational programs for health care professionals regarding rational use of antibiotics can be helpful in improving antimicrobial medications utilization and monitoring.

### Conclusion

In conclusion, the following hints are recommended to achieve rational use of vancomycin in our hospitals:

1. Accomplishment the vancomycin standard treatment guideline modified according to local resistance pattern in hospitals
2. Conducting antibiotic usage review studies
3. Sending periodically feedbacks to physicians and nurses involved mostly in vancomycin administration
4. Setting pharmaceutical and therapeutic infection control committees in hospitals to discuss issues regarding antibiotic usage patterns and approaches
5. Reevaluating laboratory tests and processes related to infection control
6. Conducting educational programs for health care professionals regarding rational use of antimicrobial medications.

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### Conflict of Interest

The authors report no conflicts of interest.

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