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Original Article

Rational Use of Vancomycin Among Inpatients in Shahid Chamran Hospital; A Cross-Sectional Study

Running Title: *Rational Use of Vancomycin Among Inpatients in Shahid Chamran Hospital*

Parichehreh Jorkesh[1], Golnaz Sadat Afzal[1*], Mehrnoush DianatKhah[2]
[1]Department of Clinical Pharmacy, Faculty of Pharmacy, Shahid Sadoughi University of Medical Sciences
[2]Department of Clinical Pharmacy, School of Pharmacy, Isfahan University of Medical Sciences, Isfahan, Iran

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Corresponding author
Department pf Clinical Pharmacy, Faculty of Pharmacy, Shahid Sadoughi University of Medical Sciences
.
Tel: +9835 732151

E-mail
dr.golnaz.afzal@gmail.com

Introduction

Antibiotics, which are known as a sub-group of antibacterial agents, have been widely applied in clinical practice due to the universality and complexity of infectious diseases. Antibiotics play a key role in the inhibition of substantial bacterial functions. They are widely used for treating and preventing bacterial infections, and, consequently, save the lives of countless patients worldwide. However, overuse of antibiotics may cause negative impacts on individual users and social groups (1-5). Recent studies revealed that a minimum of 700,000 people die from antimicrobial-resistant infections each year around the world, and drug-resistant infections are expected to kill 10 million people a year within 30 years, greatly exceeding deaths from cancer. It has also been estimated that this resistance problem will be the biggest challenge facing healthcare systems by 2050 (2, 6).

Antimicrobial resistance is defined as a worldwide impacting burden, affecting inpatients in critical wards of hospitals, like intensive care units (ICU). Based on previous studies, hospitalized patients are facing an increased risk of developing infections. It may maybe due to exposure to several invasive devices, such as mechanical ventilation, urinary tract catheters, and so on (7-10).

Vancomycin is one of the most utilized antibiotics in the case of severe infections. It may be administered to patients with infections related to resistant microbes, patients with sensitivity to penicillin, patients with endocarditis, and patients with infections of the central nervous system (CNS). Irrational uses of antibiotics, like vancomycin, may be associated with increased morbidity and mortality among patients, as well as antibiotic resistance (11-14). This cross-sectional study aimed to evaluate the rational uses of vancomycin among patients admitted to Shahid Chamran Hospital, Isfahan, Iran. The accessibility and lower costs of vancomycin, rather than other antibiotics, are the reasons for choosing vancomycin in the study.

Keywords: Vancomycin, Rational Use of Drugs, Antibiotic

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Methods

This cross-sectional study was conducted on 402 patients admitted to Shahid Chamran Hospital, Isfahan, Iran between September 2021 to March 2022. Shahid Chamran Hospital is the main university hospital and referral center in Isfahan for heart diseases. This study was approved by the research deputy of Shahid Sadoughi University of Medical Sciences, Yazd, Iran (Code: IR.SSU.MEDICINE.REC.1400.166). In this study, informed consent was obtained from all included patients. Patients hospitalized in Shahid Chamran Hospital between September 2021 to March 2022 who received at least one dose of Vancomycin were found eligible for inclusion in the study.

In this study, according to CDC and up-to-date guidelines, demographic information and characteristics of patients related to vancomycin administration were recorded for all eligible patients. This information was composed of the patient's age, sex, weight, marital status, comorbidities reason for hospitalization (first diagnosis), length of treatment with vancomycin, suitability of vancomycin indication, and compliance with the recommended guidelines. In addition, possible adverse effects related to the drugs, the appropriate dose of the prescribed medicines, and the findings of cultures, and antibiograms were recorded via a pre-designed checklist.

Statistical Analysis was performed by SPSS ver. 16 for Windows (IBM Inc, NY). Quantitative and qualitative variables were presented as mean ± standard deviation (SD), and frequency counts (percentage), respectively.

Results

In this study, a total of 402 patients (113 females (28.1%), and 289 males (71.9%)), with a mean age of 60.53±13.51 (range: 20 to 100) years old were included. The mean weight of patients was reported as 71.19±11.3 Kg with a range of 39 to 112 Kg. Descriptive statistics of the patient's age and weight were reported in **Table 1.**

Table 1: Descriptive Statistics (Mean± SD) of Age and Weight of Patients

	N (%)	Min	Max	Mean±SD
Age	402 (100)	20	100	60.53±13.51
Weight	402 (100)	39	112	71.19±11.30

In the present study, hypertension (192 cases, 47.8%) was reported as the most frequent comorbidity, followed by diabetes (125 cases, 31.1%), dyslipidemia (96 cases, 23.9%), angina pectoris (83 cases, 20.6%), a history of heart attack (38 cases, 9.5%), hypothyroidism (37 cases, 9.2%), heart failure (21 cases, 5.2%), chronic obstructive pulmonary disease (COPD) (13 cases, 3.2%), and Asthma (10 cases, 2.5%). Out of 402 patients enrolled in the study, 230 subjects (57.21%) were hospitalized in intensive care units **(Table 2)**.

Table 2: Frequency of Hospitalized Patients Based on Their Hospitalities

		N	Valid Percent
Medical Wards	ICU	230	57.2
	Internal Medicine	109	27.1
	CCU	27	6.7
	VIP	21	5.2
	Gynecology	8	1.9
	Emergency	5	1.4
	Post Angioplasty	2	0.05
	Total	402	100

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In this study, 150 cases (37.2%), out of 402 cases, were reported with a history of using smoking and alcohol **(Table 3).** In terms of bacteria culture tests, blood culture test was presented as the most frequent test with a frequency of 25 cases (6.2%), followed by sputum (10 cases, 2.5%), wound (7 cases, 1.7%), urine (7 cases, 1.7%), pleural (2 cases, 0.5%), and pericardia (1 case, 0.2%).

Table 3: Frequency of Using Substances Among Inpatients

		N (%) Valid Percent		
		Yes	No	Total
Used Substances	cigarettes	66 (16.4)	336 (83.6)	402 (100)
	opium	61 (15.2)	341 (84.8)	402 (100)
	methadone	14 (3.5)	388 (96.5)	402 (100)
	alcohol	9 (2.2)	393 (97.8)	402 (100)

In the present study, a total of 5908 vials of vancomycin were administered with an average of 14.7±19.7 vials per patient (range: 1 to 166) **(Table 4).**

Table 4: Descriptive Statistics (Mean±SD) of Vancomycin Vials Utilized in Included Patients

	N (%)	Min	Max	Mean±SD
Vancomycin Vilas	5908 (100)	1	166	14.7±19.7

The frequency of antibiotics prescribed for all included patients were presented in **Table 5**, in detail. Based on **Table 5,** more than half of patients used ceftriaxone (148 cases, 36.8%) and ciprofloxacin (106 cases, 26.4%) besides vancomycin.

Based on the vancomycin uses indications, as shown in **Table 6**, prophylaxis (329 cases, 81.8%) was reported as the most common indication for using vancomycin among patients, followed by pneumonia (28 cases, 7%), endocarditis (15 cases, 3.7%), wound infection (14 cases, 3.5%), sepsis (8 cases, 2 %), pericarditis (2 cases, 0.5%), urine tract infection (2 cases, 0.5%), and peritonitis (1 case, 0.2%). Out of 402 cases, 11 patients (2.7%) were administered vancomycin with unknown indications.

Table 5: Frequency of Antibiotics Used in Included Patients

	N (%) Valid Percent		
	Yes	No	Total
Vancomycin	402 (100)	0 (0)	402 (100)
Ceftriaxone	148 (36.8)	254 (63.2)	402 (100)
Ciprofloxacin	106 (26.4)	296 (73.6)	402 (100)
Meropenem	53 (13.2)	349 (86.8)	402 (100)
Amikacin	51 (12.7)	351 (87.3)	402 (100)
Ampisulbactam	12 (3)	390 (97)	402 (100)
Ceftazidime	9 (2.2)	393 (97.8)	402 (100)
Levofloxacin	7 (1.7)	395 (90.3)	402 (100)
Rifampin	7 (1.7)	395 (98.3)	402 (100)
Tazocin	7 (1.7)	395 (98.3)	402 (100)
Metronidazole	5 (1.2)	397 (98.8)	402 (100)
Cefepime	4 (1)	398 (99)	402 (100)
Clindamycin	4 (1)	398 (99)	402 (100)
Cefazolin	3 (0.7)	399 (99.3)	402 (100)
Gentamicin	3 (0.7)	399 (99.3)	402 (100)
Azithromycin	2 (0.5)	400 (99.5)	402 (100)
Cotrimoxazole	2 (0.5)	400 (99.5)	402 (100)
Linezolid	2 (0.5)	400 (99.5)	402 (100)
Cefalotin	1 (0.2)	401 (99.8)	402 (100)
Imipenem	1 (0.2)	401 (99.8)	402 (100)

in terms of rational use of vancomycin, in 59 cases (14.4%), vancomycin was prescribed appropriately based on current guidelines. The frequency of rational uses of vancomycin based on its indications was presented in **Table 7,** in detail.

Table 6: Frequency of Vancomycin Uses Indications in Included Patients

	N (%) Valid Percent		
	Yes	No	Total
prophylaxis	329 (81.8)	73 (18.2)	402 (100)
pneumonia	28 (7)	374 (93)	402 (100)
endocarditis	15 (3.7)	387 (96.3)	402 (100)
wound infection	14 (3.5)	388 (96.5)	402 (100)
Unknown Indication	11 (2.7)	391 (97.3)	402 (100)
sepsis	8 (2)	394 (98)	402 (100)
pericarditis	2 (0.5)	400 (99.5)	402 (100)
urine tract infection	2 (0.5)	400 (99.5)	402 (100)
peritonitis	1 (0.2)	401 (99.8)	402 (100)

Table 7: Frequency of Rational Uses of Vancomycin Based on Indications in Included Patients

	N (%) Valid Percent		
	Rational	Irrational	Total
prophylaxis	8 (2.4)	321 (97.6)	329 (100)
pneumonia	23 (82.1)	5 (17.9)	28 (100)
endocarditis	15 (100)	0 (0)	15 (100)
wound infection	12 (85.7)	2 (14.3)	14 (100)
sepsis	7 (87.5)	1 (12.5)	8 (100)
pericarditis	2 (100)	0 (0)	2 (100)
urine tract infection	2 (100)	0 (0)	2 (100)
peritonitis	1 (100)	0 (0)	1 (100)
Unknown Indication	0 (0)	11 (100)	11 (100)

As shown in **Table 6**, endocarditis, pericarditis, urine tract infection, and peritonitis were reported as the most frequent indications. In this study, the process of vancomycin de-escalation was performed in 30 patients, out of 40 patients who had cultural tests. The length of treatment with vancomycin, as shown in **Table 8**, was reported with a mean of 4.89±5.4 days among patients.

The duration of vancomycin treatment based on the vancomycin use indications was also shown in **Table 8,** in detail. In addition, the appropriate dosage of vancomycin was evaluated in the study. In this regard, in 352 patients (87.6%), vancomycin was administered with the appropriate dosage. The incurred costs related to inappropriate vancomycin administration were evaluated in the study. In this regard, a total of 1069200000 IR (equal to about $2000 US) was calculated for 3960 inappropriately administered vials.

Table 8: The duration of vancomycin treatment based on the vancomycin uses, indications

	N (%)	Mean±SD (days)
prophylaxis	329 (81.8)	4.09±4.54
pneumonia	28 (7)	10.21±7.5
endocarditis	15 (3.7)	17.2±13.32
wound infection	14 (3.5)	9.0±5.49
sepsis	11 (2.7)	7.88±7.47
pericarditis	8 (2)	4.5±0.7
urine tract infection	2 (0.5)	4.5±0.7
peritonitis	2 (0.5)	5±0.0
Unknown Indication	1 (0.2)	5.55±3.44

Moreover, more than half of used vancomycin was administered by surgeons (228 cases, 56.7%), followed by cardiologists (129 cases, 32.1%), infectious diseases specialists (44 cases, 10.9%), and nephrologists (2 cases, 0.5%). In this study, the possible adverse events related to using of vancomycin were also evaluated for all included patients. In this regard, the red man syndrome was the only side effect reported among the patients with a frequency of 5 cases (1.2%). There were no serious side effects reported in the study.

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Discussion

Vancomycin, which is widely used to treat serious infectious diseases, plays a key role in the management of infections with known resistance to other antibiotics or in patients allergic to beta-lactams. Irrational uses of antibiotics may be associated with increased morbidity and mortality among patients, as well as antibiotic resistance (3-5, 11-14). In this study, we aimed to evaluate the rational use of vancomycin among inpatients in Shahid Chamran Hospital, Isfahan, Iran. The accessibility and lower costs of vancomycin, rather than other antibiotics, in developing countries, like Iran, were the reasons for choosing vancomycin in the study.

Based on the study results, the most frequently used vancomycin was administered in the intensive care unit (ICU) and general internal medicine wards. Despite the emphasis on bacteriologic profile and antibiogram of cultures, it seems that this practice is not commonly performed in medical centers. Bacteria cultural tests were only performed for 40 (about 10%) included patients. In terms of vancomycin use indications, the most commonly reported indications were prophylaxis, pneumonia, and endocarditis, respectively. The study results demonstrated that vancomycin was administered irrationally for most of the included patients. Prophylaxis and pneumonia were reported as the most frequent vancomycin use indications in the present study. However, the highest rate of irrationally prescribed vancomycin was also related to prophylaxis. In this study, vancomycin was administered to only three subjects based on their bacteria cultural tests, the remaining vancomycin was prescribed based on the experience of doctors (empirical uses of vancomycin). Based on the Centers for Disease Control and Prevention (CDC) and the Infectious Diseases Society of America (IDSA) guidelines, the empirical uses of vancomycin should be discounted if cultural results fail to reveal beta-lactam-resistant bacterial infections.

A study conducted by Jean G Dib et al. on the improvement of vancomycin utilization in adults in a Saudi Arabian Medical Center 15. Based on the mentioned study results, in 48 cases of 74 cases (65%), vancomycin administration was considered appropriate according to the CDC recommendations. Another study was performed by Al Za'abi et al. on "Utilization Pattern of Vancomycin in a University Teaching Hospital in Oman: Comparison with International Guidelines" (16). This retrospective study revealed that out of 478 prescriptions, 20.9% were considered appropriate based on the Hospital Infection Control Practices Advisory Committee (HICPAC) guidelines. Another study was carried out by Salehifar and his colleagues on the evaluation of drug utilization in a referral infectious center in Mazandaran, Iran (17). In the mentioned study, 146 medical records were reviewed over six months. This study demonstrated that vancomycin was administered irrationally in a great proportion of patients (nearly 42%). Following our study results, vancomycin was prescribed irrationally for most of the included patients (about 72.1%). The frequency of irrational uses of vancomycin in the present study was higher than in the mentioned studies.

In the present study, based on the vancomycin use indications, prophylaxis was reported as the most frequent indication for vancomycin use among patients. In a study conducted by Al Za'abi et al. (16), vancomycin was prescribed mostly for the treatment of sepsis, followed by prophylaxis. Another study was carried out by Mandana Naderi and her colleagues on the evaluation of vancomycin utilization at 72 hours post-admission (18). Based on their study, skin and soft tissue infections (SSTI), pneumonia, and positive blood cultures were defined as the most common indications for vancomycin use. The present study results were not consistent with the studies of Al Za'abi et al. and Naderi et al.

By the present study, like the study of Salehifar and his colleagues (17), most patients received vancomycin empirically without regard to bacteria cultural tests. Not having health insurance to cover medical expenses seems as the main reason for the low request rate for performing bacteria cultural tests in Iran. A study carried out by Alfandari et al. revealed that among 81 patients who received vancomycin empirically, only 33 percent of them were reported to appropriately using vancomycin (19). In our study, out of 40 patients with the results of vancomycin de-escalation, only 30 patients were reported with an appropriately using vancomycin. Alongside the unreliability of laboratory findings, acute and critical conditions of hospitalized patients in different medical wards, and the lack of a system for managing the uses of antibiotics after 72 hours might be defined as the main reasons for inappropriate uses of vancomycin in medical centers.

In this study, the appropriate dosage of vancomycin was evaluated based on current guidelines and recommendations. Based on the study results, in most cases (87.6%), vancomycin was administered with appropriate dosage. A study was performed by Khiali and his colleagues on the evaluation of vancomycin utilization in teaching hospitals in the west of Iran (20). Regarding the mentioned study, the dosage and duration of vancomycin utilization were reported as 74% and 59% based on ASHP and CDC recommendations. A study conducted by Fahimi et al. demonstrated that in 97.7 percent of patients, vancomycin was administered inappropriately in terms of indication and dosing regimen (21). It appears that the frequency of rational uses of vancomycin in the present study was higher than the mentioned ones.

Conclusion

This study demonstrated that vancomycin was administered inappropriately in most patients in terms of indications and duration of vancomycin utilization. In addition, the empirical uses of vancomycin were high in the present study. Implementation protocols of rational uses of vancomycin in medical centers besides standard treatment guidelines are highly recommended.

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Authors' contribution: PJ visited the patient and collected the data. PJ and GA wrote the primary draft of the manuscript. GA and MD revised and finalized the manuscript. All authors read and approved the final version of the manuscript

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