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Original Article

Retrospective Drug Utilization Evaluation of Vancomycin Usage in Infectious Wards and Intensive Care Units in Hamedan Teaching Hospitals, April to September 2020

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Abstract

Background: Drug utilization evaluation (DUE) was performed to assess using drugs with special conditions such as antibiotics. Vancomycin is one of the essential antibiotics that is effective on methicillin-resistant *Staphylococcus aureus*, but unreasonable use of vancomycin, in addition to cost, leads to outbreak microbial resistance, which is a concern for health care systems all around the world. The aim of this study was to evaluate vancomycin use in teaching hospitals in Hamedan, Iran.

Methods: This retrospective study was performed on patients who received vancomycin for at least 72 hours in intensive care units and infectious wards between April and September 2020 in the teaching hospitals of Hamedan. Data were obtained from patients' medical records and entered into predesigned checklists.

Results: From 661 patients, 441 were males and 247 were females. They received vancomycin for an average of 5.75 days. The most prevalent indication for vancomycin use was surgery. Only 40 patients had sensitive microbial culture to vancomycin, while 356 of them (53.9%) had no microbial culture at all. According to HICPAC guidelines, the overall appropriate use of vancomycin was 44.8%.

Conclusion: According to the results, the irrational use of vancomycin must be corrected to achieve maximum optimal use; thus, performing and adhering to microbial culture, deploying clinical pharmacists, and holding explanatory sessions for health care are recommended for this purpose.

Keywords: Drug Utilization Evaluation, Vancomycin, Microbial culture, HICPAC guidelines

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Introduction

Drug utilization evaluation (DUE) is a strategy that is designed to analyze drug consumption patterns and is in accordance with guidelines in a medical center. These studies are performed on drugs with a narrow therapeutic index, expensive drugs, or drugs the improper use of which can cause serious problems, including antibiotics (1,2). For rational use of medications, patients must receive drugs in appropriate doses and terms and based on their clinical conditions. Successful implementation of DUE leads to the assurance of appropriate, safe, and effective use of medications (3).

Vancomycin is a member of the glycopeptide family antibiotics that is widely used worldwide because of its proper impact on aerobic and anaerobic gram-positive bacteria, especially on methicillin-resistant *Staphylococcus aureus*. Unfortunately, inappropriate use of this antibiotic causes vancomycin-resistant bacterial strains (e.g., vancomycin-resistant *Enterococcus*), which is a global issue. As for remarkable therapeutic effects and the outbreak of microbial resistance, rational use of vancomycin is indispensable. On the other hand, irrational use can lead to ineffective treatment, toxicity, increased prevalence of resistant strains, increased mortality, intensification, and disease prolongation, and vancomycin-resistant *Enterococcus* gene transfer to other bacteria, and force high costs to patients and the healthcare system (4,5).

Therefore, DUE is essential for vancomycin and must be accurately performed until physicians are aware of the potentially inappropriate use of vancomycin. This awareness improves the effectiveness of treatment, prevents unwanted side effects, and reduces costs and the prevalence of antibiotical resistance (6,7).

This study aimed to survey the rational prescription of vancomycin in infectious wards and intensive care units in Hamedan Teaching Hospitals.

Materials and Methods

This cross-sectional, retrospective study was performed on patients who had received vancomycin for at least 72 hours in infectious wards and intensive care units in four Hamedan Teaching Hospitals between April and September 2020. Intended data such as vital signs, microbiological results, laboratory results, site of infection, dosing regimen, duration of administration, demographic data, cause of hospitalization, final diagnosis, medical history, and concurrent diseases were obtained from medical records, patient's history, medical orders, and nursing reports in the patient's records.

Table 1 presents the required criteria for vancomycin use based on Healthcare Infection Control Practices Advisory Committee (HICPAC). The collected data were compared to these criteria and analyzed by SPSS software, version 16.

Results

Out of a total of 661 patients from 4 hospitals included in the study, 267 (40.39%), 187 (28.29%), 109 (16.49%), and 98 (14.83%) patients were admitted to Farshchian Cardiovascular Subspecialty, Beheshti, Besat, and Farshchian (Sina) hospitals, respectively. Six hundred ten (92.4%) and 51 (7.6%) patients were treated in the intensive care and infection units, respectively. Among these patients, 414 (62.6%) and 247 (37.4%) cases were males and females, respectively. The mean age of patients was 60.54 years, and 64-68 years old patients received vancomycin more than other age groups.

Patients on average were bedridden for 12.03 days in mentioned units and received vancomycin for 5.75 days on average. Finally, 459 patients (69.4%) were discharged with partial recovery.

Vancomycin was mostly used for surgery (51.6%) and in respiratory diseases (33.3%). It should be noted that 199 patients were suffering from coronavirus disease 19 and sepsis (7%). The most common prescription pattern was 1 gram of vancomycin every 12 hours, which was performed for 520 patients (78.7%). Of all the patients, only 40 (6.1%) cases had a microbial culture that proved the entity of microorganisms that were sensitive to vancomycin (Figure 1). Eighty-two patients (12.4%) had microbial cultures which were sensitive to other antibiotics. However, no microbial culture was found for 356 patients (53.9%) in their files (Figure 2). Vancomycin was prescribed as prophylaxis treatment for 358 patients (54.2%). According to HICPAC guidelines, vancomycin indications were 44.8% appropriate in infectious wards and intensive care units in Hamedan Teaching Hospitals from April to September 2020 (Figure 3).

Cockcroft-Gault formula evaluated the patient's kidney function. Based on the findings, 481 patients (63.2%) needed to adjust the dose. In 281 of them, no dose adjustment was made at all; in 96 of them adjustment was inappropriately performed, and it was correctly performed only for 41 patients. It should be noted that a significant number of patients required dose adjustment, but no action was taken in this regard for them. They could receive vancomycin much more every 8 hours, but they were treated with a less dose, which is inappropriate according to UpToDate® 2012. In 49.5% of patients, the body temperature or number of white blood cells and in 14.4% of them, both factors were beyond the standard value; this could partly justify vancomycin use, along with the patient's clinical signs.

The rational use of vancomycin form, which is recommended by the Ministry, was found in 266 patient files (40.2%), of which only 4 cases were fully completed. Therapeutic drug monitoring (TDM) was not performed for all patients. Slow infusion order was observed only in 4 patients' files, while those orders were not relevant to guidelines. Fourteen patients were allergic to beta-lactams according to the section related to their drug allergies in their files. The remaining results are presented in Table 2.

Discussion

This was the first DUE study in Hamedan. As previously mentioned, this study evaluated the rate of inappropriate use of vancomycin in 4 teaching hospitals in Hamedan

Table 1. Criterions for Vancomycin Use Based on Healthcare Infection Control Practices Advisory Committee

Appropriate or Acceptable	Non-appropriate
Serious infections caused by beta-lactam-resistant gram-positive microorganisms Infections caused by gram-positive microorganisms in patients who have serious allergies to beta-lactam antimicrobials Prophylaxis for endocarditis following certain procedures in patients at high risk for endocarditis	Routine surgical prophylaxis for patients without life-threatening allergy to beta-lactam antibiotics Empiric antimicrobial therapy for a febrile neutropenic patient unless initial evidence indicates that the patient has an infection caused by gram-positive microorganisms and the prevalence of infections caused by MRSA in the hospital is substantial treatment in response to a single blood culture positive for coagulase-negative *Staphylococcus* if other blood cultures taken during the same time frame are negative Continued empiric use for presumed infections in patients whose cultures are negative for beta-lactam-resistant gram-positive microorganisms Systemic or local prophylaxis for infection or colonization of indwelling central or peripheral intravascular catheters Eradication of MRSA colonization Routine prophylaxis for patients on continuous ambulatory peritoneal dialysis or hemodialysis Treatment (chosen for dosing convenience) of infections caused by beta-lactam-sensitive Gram-positive microorganisms in patients who have renal failure

Note. MRSA: Methicillin-resistant *Staphylococcus aureus*.

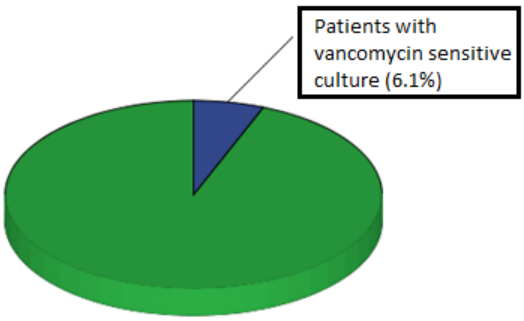

Figure 1. Patients Having a Microbial Culture That Proved the Entity of Microorganisms Sensitive to Vancomycin.

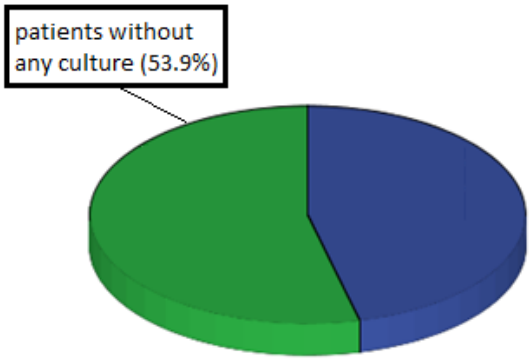

Figure 2. Patients Without Any Microbial Culture in Their Files.

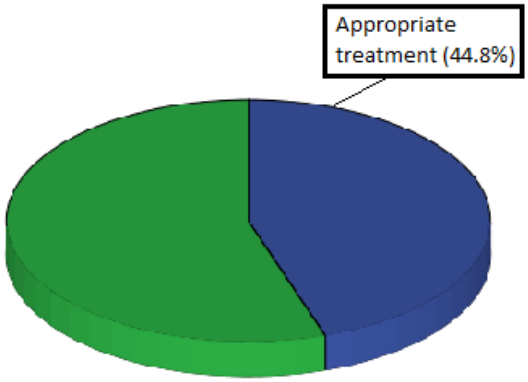

Figure 3. Appropriateness of Vancomycin Use in the Mentioned Hospitals.

about 55.2%. Several studies of this kind have been performed on vancomycin use. In a similar study performed on 75 patients, Hamishehkar et al reported a 69.3% rate of inappropriate use of vancomycin based on the American Society Health-System Pharmacists (6).

In another study performed in a teaching hospital in Bandar Abbas, Dehghan et al (8) announced the rate of inappropriate use of vancomycin as 43.9% according to the Centers for Disease Control and Prevention, American Society of Health-System Pharmacists and Infectious Diseases Society of America (IDSA).

Similarly, Ayazkhoo et al performed a 3-month study in a teaching hospital in Tehran, according to American Public Health Association, and reported that 64.4% and 88.8% of vancomycin use and dosing based on body weight were inappropriate, respectively (9).

In their study, Ayubi et al focused on 100 patients who received vancomycin for at least 72 hours, The survey results showed 29%, 69%, 90%, and 28% unapproved indications, inappropriate doses according to the American Hospital Formulary Service, inappropriate regimens based on tailoring culture results, and inappropriate regimens based on clinical response, respectively (10).

Vazin et al performed a similar study in Namazee hospital in Shiraz. The information of 95 patients hospitalized in intensive care units was collected, and 47.5% accordance to IDSA was reported based on their results (11).

Evidence indicated that compliance to the guidelines and appropriate use of vancomycin in the current study were more than noticeable compared to other studies; nonetheless, it can be because of citing different guidelines and performing studies in different units of the hospital. It should be noted that the interval between this study and the other ones can represent more probable attention to the rational use of vancomycin, which is the yield of previous studies.

In this regard, studies were performed in other countries. Zeleke and Engidawork conducted a study on 125 patients in Tikur Anbessa specialized hospital in Ethiopia and concluded that only 8% of vancomycin use was appropriate based on the HICPAC (12).

Al Za'abi et al evaluated 365 patients who received vancomycin in Sultan Qaboos University Hospital in Oman and found that 79.1% of use was considered inappropriate based on HICPAC. This was mainly due to the continuous use of vancomycin following negative microbiological cultures for β-lactam-resistant gram-positive microorganisms (13).

As is evident, the rational use of vancomycin is highly variable in developing countries and depends on the health progress level and health care in each of them. However, most countries, including Iran, should conduct more DUE studies to improve the rational use of drugs, especially antibiotics. Nowadays, there has been a limited number of such studies in developed countries since the 1990s.

Performing microbial culture can have a crucial role in preventing increased microbial resistance and the appearance of new organisms. In this study, from 661 patients receiving vancomycin, only 40 (6.1%) cases had a microbial culture in which the existing microorganism was sensitive to vancomycin. Overall, 267 patients were hospitalized in Farshchian cardiovascular subspecialty hospital for cardiac surgery and received vancomycin for endocarditis prophylaxis. Based on HICPAC, they did not need to perform a microbial culture. Based on the findings, 14 patients had a severe allergy to beta-lactams (9 cases in Farshchian cardiovascular subspecialty hospital), and it seems that vancomycin was prescribed because of this allergy. In other words, there was no microbial culture for 349 patients (52.8%), which could prove the existence of vancomycin-sensitive organisms, thus prescription

Table 2. The Remaining Results

Demographic Data	
Age (mean)	64.04
Height (mean)	165.5
Weight (mean)	72.63
Accompanying and background diseases	
Hypertension	43.4%
Diabetes mellitus	25.7%
Hyperlipidemia	15.3%
Heart diseases	14.8%
Heart surgery	8.3%
Cancer	8%
Lung diseases	7.7%
Renal diseases	6.5%
Vital signs during the first dose	
Sistol (mean)	119.26
Diastol (mean)	71.32
Respiratory rate(mean)	20.56
Hearth rate	87.29
Clinical data	
Hemoglobin (mean)	11.59
Platelets (mean)	201.16
White blood cells (mean)	11547.85
Creatinine (mean)	1.48
Blood urea nitrogen (mean)	35.97
Creatinine clearance (mean)	82.65
Site of infection	
Unrecognizable	43.4%
Respiratory system	26.3%
Catheter	11%
Bacteremia	8.2%
Central nervous system	4.7%
Intra-abdominal	3%
Skin and soft tissue	2%
Kidney and urinary ducts	1.2%
Other	0.4%
Prescribing physician	
Cardiovascular surgery specialist	42.2%
Infectious disease specialist	25.9%
Internal medicine specialist	14.1%
Neurosurgeon	4.8%
General Surgeon	4.8%
Neurologist	3%
Other	5.1%
Dosage regimen	
1 g every 12 hours	78.7%
1 g every 24 hours	8.6%
1 g every 48 hours	4.2%
1 g every 72 hours	1.7%
500 mg every 48 hours	1.7%
500 mg every 12 hours	1.2%
Other	4%
Dose amount	
1 g	94.1%
500 mg	4.5%
Other	1.4%
Dose frequency	
Every 12 h	80.2%
Every 24 h	8.6%
Every 48 h	6.5%
Every 72 h	2.7%
Other	1.8%
Chef complaint (primary diagnosis)	
Chest pain	34.5%
R/O COVID-19	31.5%
Respiratory problems	8.8%
Multiple traumas	5.1%
Septicemia	3.9%
Central nervous system problems	3.3%
Kidney problems	1.8%
Other	10.4%
Final diagnoses	
Surgery	51.6%
COVID-19	30.1%
Septicemia	7%
Respiratory diseases	3.2%
Kidney diseases	1.8%
Central nervous system diseases	1.5%
Cardiac diseases	0.9%
Other	3.9%

Note. COVID-19: Coronavirus disease 19.

was empiric and based on patients' clinical conditions. Furthermore, there was no culture for 98 patients (14.8%) at all (in addition to the patients of the Farshchian cardiovascular subspecialty hospital).

Some of the reasons for the lack of performing culture were not taking blood sampling before starting prescription and refusing to stop taking drugs after obtaining negative results, as well as late culture results and unreliable results because of the high incidence of false results (2).

In the study by Hamishehkar et al, microbial culture was performed for 50.6% of patients (6). This rate was reported as 80% and 20.5% in other studies by Ayubi et al (10) and Khalili et al (14), respectively. Nevertheless, some patients may need no microbial culture due to the guideline and disease.

Vancomycin dose adjustment must be performed based on body weight and creatinine clearance (renal function) or drug serum concentration. The TDM method must be used to obtain the serum concentration. Having drug

serum concentration helps in using accurate and effective dosages and reducing ineffective treatment and side effects. However, TDM is a costly laboratory method that, according to different guidelines, is performed for limited drugs in patients with special conditions.

There was no request for TDM in the study by Ayubi et al, and 69 patients received inappropriate doses. Moreover, dosing was completely correct and in accordance with the guidelines only in 31% (10). Likewise, 88.8% of dosing based on body weight was inappropriate as reported by Ayazkhoo et al (9). In another study by Hamishehkar et al, TDM was necessary for 13 patients, but it was not performed, and 12 patients needed dose adjustment based on a renal function, which was correctly performed only for 4 cases (6). In the current study, 418 patients required dose adjustment based on body weight and creatinine clearance, which was correctly performed for 41 patients, but TDM was not considered for all.

Conclusion

Eventually, it seems vancomycin use in teaching hospitals in Hamedan had many defects in performing microbial culture, dose adjustment, and empiric therapy. To reduce irrational use and accordingly microbial resistance, several approaches are suggested as follows:

1. Performing microbial culture as much as possible to deliberate pathogens' sensitivity to vancomycin.
2. Refusing to continue empiric therapy without laboratory evidence, performing TDM in required situations, and adhering to dose adjustment based on renal function and body weight obligations to vancomycin standard treatments mentioned in several guidelines.
3. Performing more antibiotic consumption patterns in health centers.
4. Offering feedback on suchlike studies to physicians who are more involved with vancomycin prescriptions.
5. Establishing review committees in hospitals to discuss antibiotic usage patterns.
6. Establishing educational programs for healthcare professionals regarding the rational use of antibiotics.
7. Deploying clinical pharmacists in hospitals.

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Conflict of Interests

The authors declare that they have no conflict of interests.

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