Research Paper: Financial Burden of Inappropriate Vancomycin Use for Patients With Cancer

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ABSTRACT

Background: As an antibiotic, vancomycin presents numerous benefits in controlling methicillin-resistant staphylococcal infections; however, if used inappropriately, it can lead to bacterial resistance in patients. The current study aimed to evaluate the financial burden of inappropriate use of Vancomycin in patients with cancers in selected university hospitals in Shiraz.

Methods: This descriptive cross-sectional study was conducted in 2017-2018. The required data were collected using a checklist. In total, 150 adult patients with cancer were selected by the census method. moreover, the t-test, Chi-squared test, and Analysis of Variance (ANOVA) were used to examine the relationship between the study variables where appropriate.

Results: The present study results suggested that inappropriate prescribing of vancomycin had a frequency of 61 (59.2%) in Namazi Hospital and 22 (46.8%) in Amir Hospital; thus, there was no significant difference between these hospitals concerning the types of prescriptions (P=0.15). It was also found that the inappropriate use of vancomycin cost the patients $1974.2 and $1046.5 in Namazi and Amir hospitals, respectively.

Conclusion: The present study data indicated that the most frequent problems were the inappropriate prescription of vancomycin in hematology wards, the lack of drug discontinuation at the proper time, and the continuation of drug administration more than the patients' needs. Thus, conducting regular educational programs for physicians per relevant guidelines could help reduce unreasonable administration of the drug and the financial burden imposed on patients.

Keywords: Antibiotic vancomycin; Patients with cancers; Prescriptions; Inappropriate prescription

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1. Introduction

Attempts to rationalize drug use have always been considered as key issues in pharmaceutical policymaking. According to the World Health Organization (WHO), to achieve a rational drug administration, it is necessary to use the drugs with appropriate treatment effects that can meet the clinical needs of the patients within specific geographical areas and with the minimum adverse effects and the lowest cost [1]. Pharmacotherapy is among the commonly used treatment methods; thus, providing scientific and standard models for the rational prescription and administration of drugs is on health policymakers. In this regard, mutual interactions of physicians, pharmacists, and patients through the proper diagnosis of diseases, rational selection, and prescription of drugs, delivery, and correct use of medicines are of great importance [2].

Antibiotics are frequently used to treat various infections; accordingly, the proper use of them is essential for the prevention and treatment of infectious diseases. However, the prevention of excessive and inappropriate use of antibiotics is a critical approach to rationalizing their prescription [3]. In numerous countries, using antibiotics accounts for approximately 30%-50% of drug prescriptions [4]. Having examined the statistics of 114 countries, the WHO identified antibiotic resistance as a major global threat [5]. As a result, like before penicillin discovery, some bacterial diseases have become incurable [4]. Inappropriate and excessive use of antibiotics has consequences, such as increased drug resistance, the inattention of physicians to drug interactions, patient dissatisfaction, lengthening, and severity of diseases; hazardous adverse effects and hospitalization; reduced physician-patient communication, and increased healthcare costs for individuals and the healthcare system [2]. The cost of global antibiotic use was estimated as 40 billion dollars in 2005; one-third of which belonged to developing countries [6]. Besides, >235 million doses of antibiotics are consumed annually worldwide. Statistics reflect that the sale of antibiotics, compared to other drugs, is ranked first in Iran, with an estimated cost of $97879.2 to $146818.9 per year [5]; thus, using antibiotics in this country is roughly equivalent to the total consumption in Europe and 16 times higher than that of the global mean [5]. Antibiotics account for 10% of the health share per capita in Iran [7]. In Iran, the excessive and inappropriate use of antibiotics has led to a large financial burden [8]; one-third to half of the administrations are unnecessary [5]. According-

ing to the National Committee on Rational Prescription and Use of Drugs, >25% of the patients in Iran received antibiotics in 2013. Moreover, the rate of antibiotic prescriptions by Iranian physicians and specialists was high. In other words, 89% of the patients referring to general dentists, 50% to otolaryngologists, 48% to general practitioners, and 45% to gynecologists had received antibiotics [9]. Most antibiotic resistance cases were reported in the countries with the highest consumption rates; therefore, there is a need for new and effective policies to control their overuse in the world, including Iran [10, 11]. A commonly used antibiotic in hospitals is vancomycin. Vancomycin is widely administered to treat the infections caused by methicillin-resistant staphylococcus aureus. However, the inappropriate use of vancomycin is the main cause of resistance. Such a practice may lead to the expansion of the methicillin-resistant staphylococcus aureus with heterogeneous resistance to the drug, causing great concern in various regions of the world [12].

A study on the cost-effectiveness of oral administration of vancomycin in the United States suggested that the cost of each dose of the drug varied from $5 to $33 [13]. Hatam et al. estimated that the cost of vancomycin consumption in Shiraz hospitals to be 1.6% of the total cost of antibiotics in 2012 [8]. Chiu et al. conducted a study in Boston in 2011; they concluded that the guidelines for the rational use of vancomycin reduced its administration by 35% in the Women Hospital and 65% in Massachusetts Hospital [14]. Hammer et al. suggested that 10.2% of the prescriptions in Maryland were inappropriate [15]. Additionally, Salehifar researched Mazandaran based on the Healthcare Infection Control Practices Advisory Committee (HICPAC) guidelines. Subsequently, Salehifar attributed 23.6% of vancomycin prescriptions to infectious disease specialists; 36.5% of which to surgeons, and 38.5% to other physicians; only in 32.7% of the cases, post-treatment cultures were requested [16]. Vancomycin is known to be the savior of the patients whose treatment with other antibiotics is of no hope; thus, the proper administration of this drug and the prevention of resistance against it is of great importance. Therefore, the present study examined the financial burden of inappropriate vancomycin use in patients with cancer.

2. Methods

This cross-sectional study was performed among all patients with cancer who were admitted to the hematology ward of Namazi Hospital and the adult cancer and emergency wards of Amir Hospital in Shiraz City, Iran, in

2017-2018. The sample size was determined as 150, using data from a similar study [17] with a prevalence of 56% proper vancomycin prescription, 95% confidence level, the accuracy of 0.08, and the following formula: n=z²p(1-p)/ d² (z=1.96, P=0.56, d=0.08).

The sampling was conducted by convenience sampling method, including all cancer patients who were receiving vancomycin. The sample size per hospital was determined based on the proportion of consuming vancomycin by patients with cancer in that hospital. The frequencies of consuming vancomycin in Namazi and Amir hospitals were respectively 8439 and 5000 vials in 2016 in the preliminary study. Therefore, considering the frequency of drug administration, the sample size in Namazi Hospital was estimated to be 105 out of the total 150 patients, and 45 in Amir Hospital.

To collect the necessary data, we used a checklist similar to the one employed by Askarian et al., i.e., applied to assess the appropriateness of vancomycin prescription [18]. The checklist consisted of 3 parts. to the first part covered basic information (age, gender, patient's health record number, type of insurance, physician's specialty, hospital ward, date of initiating vancomycin, the number of received doses, & culture result). The second part of the checklist addressed the appropriate administration of vancomycin and included 5 questions. Finally, the third part concerned inappropriate vancomycin prescriptions and included 12 items.

To investigate the status of the currently hospitalized patients, the researcher visited the hospitals on weekdays from June 2017 to August 2018. The researcher discussed with the physicians and nurses in the intended wards. Furthermore, the researcher reviewed medical prescriptions, nursing reports, drug kardexes, the results of the cultures obtained from current hospitalized cancerous patients in the 3 inpatients wards of Namazi Hospital (45 beds) and the 4 adult cancer wards of Amir Hospital (76 beds). Moreover, these data were collected and recorded as per confidentiality principles. This study was approved by the Ethics Committee of Shiraz University of Medical Sciences (Code: IR.SUMS.REC.1397.456).

To calculate the financial burden of inappropriate vancomycin administration in this study, the number of inappropriate doses prescribed per patient was calculated. Moreover, the price of each vancomycin dosage was explored from a pharmacy unit. Eventually, the number of inappropriate doses of the drug was multiplied by the price of each dose.

To calculate the costs of appropriate and inappropriate vancomycin prescriptions, the appropriate and inappropriately prescribed doses in 2017 and 2018 were first separately determined in the 7 wards of both study hospitals. Then, considering the price of the drug in the two years, the appropriate and inappropriate costs were calculated.

The price of 500 mg of vancomycin equaled $8.18 in 2017 and $0.818 as out of pocket for those under the coverage of insurance in the same year. Furthermore, the price of each mentioned vial and insurance-covered prices changed to $7.24 and $0.724 in 2018, respectively. Additionally, the dollar exchange rate was respectively 34214 and 42000 Rials in 2017 and 2018 according to the mean exchange rate announced by the Central Bank of Iran[1]. Subsequently, the total dollar exchange rate in the two years was measured and recorded.

In this study, t-test and Analysis of Variance (ANOVA) were used in SPSS to examine the relationships between the continuous variables. The Chi-squared test was also used to assess the dependent variables, including appropriate and inappropriate prescriptions.

3. Results

A majority of the study participants were selected from Namazi Hospital. In other words, of the 150 explored patients, 103 (68.66%) were selected from Namazi Hospital and 47 (44.76%) from Amir Hospital. The Mean±SD hospitalization duration was 7.77±2.24 days. Furthermore, the highest frequency of the study participants belonged to the age group of 31-40 years (23.33%). Besides, 76 (50.66%) research participants were male. In total, 92% of the researched patients were covered by insurance, most of whom (39.33%) had Social Security insurance. The main cause of hospitalization in the present research (38%) was acute myeloid leukemia. Of those patients, 64 (42.66%), 80 (53.33%), and 6 (4%) presented positive, negative, and no culture results, respectively.

Table 1 demonstrates no significant difference between the investigated hospitals respecting appropriate and inappropriate prescriptions of the drug (P=0.156).

As per Table 2, there was no significant difference between appropriate and inappropriate prescriptions in culture type between the explored hospitals (P≤0.0001). The most inappropriate prescriptions for negative culture results were 21 (100%) in Amir Hos-

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Table 1. Comparing the study hospitals concerning appropriate and inappropriate prescriptions

Hospital	No. (%)		P
	Appropriate Prescription	Inappropriate Prescription	
Namazi	42 (40.8)	61 (59.2)	0.15
Amir	25 (53.2)	22 (46.8)	

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pital and 56 (94.4%) in Namazi Hospital. Regarding the prescribing physicians in Namazi and Amir hospitals, there was no significant difference (P=0.28 & P=0.83, respectively) between appropriate and inappropriate prescriptions.

The total days of taking vancomycin and the total expenditure and the total dose of the drug used in the present study were 1166 days and $5523.2, and 3169780 mg, respectively. For comparing the extent of inappropriate prescription of this medication, it should be considered that the minimum monthly salary of a worker was $286.63 in 2017[2] and $264.21 in 2018.

Table 3 indicates that the most inappropriate costs imposed on the patients amounted to $1974.2 (54%) in Namazi Hospital and $1046.5 (55%) in Amir Hospital.

4. Discussion

Vancomycin is an antibiotic with a great effect on β-lactamase streptococci, enterococci, Staphylococcus aureus, staphylococcus epidermidis, and clostridium [19]. The excessive use of this drug, as the first-line therapy for the infections caused by this organism, has become an essential health challenge. This is due to the increased formation of vancomycin-resistant enterococci and staphylococci [12]. Prescribing vancomycin per guidelines is an issue that most countries need to consider to prevent the onset of resistance and financial burden on patients. In this research, the financial burden of inappropriate use of vancomycin in patients with cancers in Namazi and Amir Hospitals was investigated.

The obtained data revealed that 61 (59.2%) cases of vancomycin prescriptions in Namazi Hospital and 22 (46.8%) cases in Amir Hospital were inappropriate. However, there was no significant difference between these hospitals respecting appropriate and inappropriate prescriptions (P=0.15). However, previous studies reported different numbers of inappropriate drug administrations. For instance, Hammer et al., Alfandari et

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al., Wright et al., Melo et al., and Askarian et al. in Shiraz reported 10.2%, 29%, 40%, 5%, and 94% inappropriate prescriptions, respectively [15, 18, 20-22].

Compared to the study by Askarian et al. in Namazi Hospital (2003), the present study signified an improved trend of guideline-relevant vancomycin administration by physicians. Physicians' knowledge of the guideline seems to have increased compared to 2003.

The total dose of administered vancomycin was equal to 3169780 mg; of which, 895300 mg (28.25%) and 2274480 mg (75.71%) were administered appropriately and inappropriately, respectively. Fahimi et al. [23] and Ayazkhoo et al. [24] and concluded that a high percentage of vancomycin administrations was inappropriate, and the doses of the drug used inappropriately in the two studies were approximately 50% and 97.7%, respectively. Nateghian et al. argued that >50% of the vancomycin administrations were inappropriate, and most of the inappropriate administrations concerned surgical prophylaxis. This finding was consistent with those of our study, indicating that 75.71% of the drug administration was inappropriate [17].

In this study, vancomycin prescription for the mentioned group was not according to the standards. Inappropriate prescriptions were found for 95% of negative culture results in Namazi Hospital and 100% of negative results in Amir Hospital. Thus, most cases of inappropriate vancomycin administration were empirically performed despite the negative culture results. This result was consistent with those of Mahmoudian Darvishiani et al. in Al-Zahra Hospital in Isfahan; no drug prescription was found based on the culture results [19].

Keyserling et al. stated that 79% of the drug prescriptions were empirical. Moreover, if an antibiotic was administered without regard to the culture results, it would take longer [25].

Askarian et al. investigated Namazi Hospital. They concluded that a major cause of inappropriate vancomycin

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Table 2. Comparing of the variables of Namazi and Amir hospitals concerning appropriate and inappropriate prescriptions

Hospital No. (%)							
Namazi				Amir			
Variable	Appropriate Prescription	Inappropriate Prescription	P	Variable	Appropriate Prescription	Inappropriate Prescription	P
Ward							
Hematology 1	18 (42.9)	24 (57.1)		Emergency	9 (47.4)	10 (52.6)	
Hematology 2	13 (36.1)	23 (63.9)	0.77	female surgical	6 (66.7)	3 (33.3)	0.29
Hematology 3	11 (44)	14 (56)		Male surgical	4 (36.4)	7 (63.6)	
				Adults 3	6 (75)	2 (25)	
Culture result							
No culture	1 (16.7)	5 (83.3)		No culture	0 (0)	0 (0)	
Negative	3 (5.09)	56 (94.91)	≤0.0001	Negative	0 (0)	21 (100)	≤0.0001
Positive	38 (100)	0 (0)		Positive	25 (96.2)	1 (3.8)	
Age, y							
18-40	19 (45.2)	23 (54.8)		18-40	10 (47.6)	11 (52.4)	
41-60	12 (32.4)	25 (67.6)	0.43	41-60	9 (52.9)	8 (47.1)	0.63
≥61	11 (45)	13 (54.2)		≥61	6 (66.7)	3 (33.3)	
Gender							
Male	23 (45.1)	28 (54.9)	0.28	Male	13 (54.2)	11 (45.8)	0.89
Female	18 (35.3)	33 (64.7)		Female	12 (52.2)	11 (47.8)	
Cancer type							
ALL	11 (36.7)	19 (63.3)		ALL	12 (63.2)	7 (36.8)	
AML	20 (40)	30 (60)	0.70	AML	2 (28.6)	5 (71.4)	0.28
Solid tumors	11 (47.8)	12 (52.2)		Solid tumors	10 (50)	10 (50)	
Having insurance							
Yes	40 (41.2)	57 (58.8)	0.52	Yes	22 (53.7)	19 (46.3)	0.63
No	2 (33.3)	4 (66.7)		No	3 (50)	3 (50)	

administration was using surgical prophylaxis in patients with negative culture [18]. Hadavand et al. documented that among 103 examined patients, only 18 (4.17%) were examined for cultures, and 9 (7.8%) of the 13 cases presented positive culture results. Furthermore, 31% of the patients received vancomycin without any indications during their admission. Besides, in several cases, vancomycin was administrated regardless of their indications. This might increase the risk of resistance to this drug [12]. Ayazkhoo et al. reported that most cases of vancomycin therapy were experimental and initiated regardless of cultures and other treatment conditions [24]. In the present study, it is possible that physicians in Namazai and Amir hospitals prescribed vancomycin empirically and regardless of the patients' culture results.

In other words, they prescribed the drug experimentally if a patient had a high fever, without considering other indications.

No significant difference was observed in drug prescriptions regarding the physicians' specialties between Namazi and Amir hospitals. In other words, most of the inappropriate drug prescription cases in Namazi Hospital belonged to general practitioners (n=36, 66.7%), as well as internists (n=1, 100 %), residents (n=2, 66.7%), and general practitioners (n=9, 50%) in Amir Hospital. Habibzadeh et al. revealed that the highest and lowest numbers of prescriptions were practiced by non-infectious and infectious disease specialists, respectively [26]. The obtained data suggested that except for infec-

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Table 3. Total costs of appropriate and inappropriate prescriptions of vancomycin in Namazi and Amir hospitals

Hospital Name	Appropriate Costs			Inappropriate Costs			Total Costs	
	Rial	Dollar	%	Rial	Dollar	%	Rial	Dollar
Namazi	66266200	1630.5	46	77620080	1974.2	54	143886280	3604.7
Amir	31416000	872	45	38379520	1046.5	55	69795520	1918.5
Total	97682200	2502.5	45.7	115999600	3020.7	54.3	213681800	5523.2

tious disease specialists and hematologists, other physicians lacked adequate knowledge of the guidelines on vancomycin prescription. Furthermore, there was no serious interaction between clinical pharmacists and physicians in prescribing drugs. Additionally, on holidays, physicians seemed to neglect the supervision on continuation or discontinuation of drug use.

Hamilton et al. demonstrated that physicians' consultation with infectious disease specialists and pharmacists improved the appropriate administration of vancomycin from 47% to 73% [27]. Gillon et al. in 2017 indicated that collaboration between pharmacists and infectious disease specialists reduced inappropriate use of vancomycin [28].

The present study results signified no significant difference between the types of prescriptions in the explored hospitals. However, in Namazi and Amir hospitals, the highest frequency of inappropriate administrations was observed in the age groups of 41-60 years (67.6%) and 18-40 years (52.4%), respectively.

Gram-positive bacteria contamination is frequently observed in patients with cancer. Moreover, vancomycin is often experimentally used to treat it. Therefore, patients with cancer might require higher doses of the drug for treatment. This is because vancomycin resistance is much more common in these patients [29]. The present study results revealed no significant difference in prescriptions concerning the type of cancer (P=0.49); however, in both hospitals, Acute Lymphoblastic Leukemia (ALL) and Acute Myeloid Leukemi (AML) cancers accounted for the most frequent inappropriate administrations. In the study by Nateghian et al., 73% of the children with ALL had enterococci; of whom, 25.3% presented resistance to vancomycin. Accordingly, it was concluded that increased vancomycin use could have increased enterococci [30].

In the study by Sung et al., the patients with AML were more prone to become infected with gram-positive bacteria [31]. It seems that physicians considered it possible that the patients with ALL and AML were more prone to infection than other cancer groups; thus, they experimentally prescribed vancomycin to prevent infections in those patients. Such measures could lead to inappropriate prescriptions.

The obtained results indicated no significant difference in the types of prescriptions, with or without insurance coverage (P=0.52). However, in Namazi Hospital, the number of inappropriate prescriptions was higher for those under insurance coverage, compared to the individuals who did not. Contrarily, the individuals without insurance coverage were more likely to be prescribed vancomycin in Amir Hospital. The collected findings indicated a significant difference in the total costs, as well as appropriate and inappropriate prescriptions regarding having or lacking insurance coverage. Therefore, in all cases, the lack of insurance coverage costed much more than having it. However, there was no significant difference between the costs of drug prescribing in the study hospitals; either in general or respecting appropriate and inappropriate prescriptions. Investigations on the relationship between vancomycin administration and insurance coverage are scarce; thus, this part of the study results was not comparable.

The current research results revealed that the cost of inappropriate vancomycin administration was higher in Namazi Hospital than that in Amir Hospital; however, the difference was not statistically significant (P=0.303). Additionally, the total costs of inappropriate prescriptions in both explored hospitals were higher than that of appropriate prescriptions. Furthermore, the patients with cancer in Namazi and Amir hospitals paid a total of 115999600 Rials or 3020.7 dollars for the inappropriate administration of vancomycin. This finding is consistent with that of the study by Hatam et al.; they reported that the cost of inappropriate administration of antibi-

otics in 6 hospitals in Shiraz equaled 54054210 Rials, or $6843.26. Thus, inappropriate drug administrations increased direct costs and required careful and regular management of antibiotic administrations [8]. Several studies also measured the average daily cost of vancomycin use in the United States to be about $15-$55 [13]. The cost of taking vancomycin in research in Shiraz hospitals (2012) was estimated to be 1.6% of the total cost of antibiotics administration [8]. Considering the lack of similar studies on the financial burden of vancomycin in Iran, these findings were not comparable.

5. Conclusion

Vancomycin is known as the savior of the patients whose treatment with other antibiotics is of no hope; thus, its proper administration and prevention of resistance are of particular significance. Accordingly, the inappropriate use of the drug will pose serious complications and put the patients' lives at a higher risk, instead of improving their health. Therefore, continuous personnel training as well as direct monitoring to reduce and discontinue inappropriate administrations of this antibiotic seems necessary. Additionally, due to the high price of vancomycin and the failure to report it to financial non-specialists (e.g. general practitioners), they may be unaware of the financial burden of administering the drug.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of Shiraz University of Medical Sciences (Code: IR.SUMS.REC.1397.456).

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Authors contributions

Conceptualization and Supervision: Nahid Hatam; Data collection, data analysis: Mehrdad Askarian and Nasrin Moradi; Methodology, investigation, Writing – original draft, and Writing – review & editing and final approval: All authors.

Conflict of interest

The authors declared no conflict of interest.

References

[1] Hajebi G, Mortazavi SA, Godarzi J. [A survey of consumption pattern of antibiotics in Taleghani Hospital (Persian)]. Research in Medicine. 2005; 29(2):157-64. https://pejouhesh.sbmu.ac.ir/article-1-140-en.html

[2] Zareshahi R, Haghdoost AA, Asadipour A, Sadeghirad B. [Rational usage of drug indices in the prescriptions of Kerman medical practitioners in 2008 (Persian)]. J Rafsanjan Univ Med Sci. 2012; 11(6):523-36. http://journal.rums.ac.ir/article-1-1606-en.html

[3] Llor C, Bjerrum L. Antimicrobial resistance: Risk associated with antibiotic overuse and initiatives to reduce the problem. Ther Adv Drug Saf. 2014; 5(6):229-41. [DOI:10.1177/2042098614554919] [PMID] [PMCID]

[4] Khoshdel A, Panahandeh G. [The pattern of antimicrobial utilization in patients of pediatric wards in Hajar hospital, Shahrekord, Iran in 2009-2010 (Persian)]. J Shahrekord Univ Med Sci. 2012; 14(5):54-62. http://journal.skums.ac.ir/browse.php?a_id=1025&sid=1&slc_lang=en

[5] Hosseinzadeh F, Sadeghieh Ahari S, Mohammadian-erdi A. [Survey the antibiotics prescription by general practitioners for outpatients in Ardabil City in 2013 (Persian)]. J Ardabil Univ Med Sci. 2016; 16(2):140-50. http://jarums.arums.ac.ir/browse.php?a_code=A-10-607-15&slc_lang=en&sid=1

[6] Barari M, Afrasiabian S, Mohsenpour B, Hajibagheri K, Sheikhesmaili F. [Evaluation of appropriate antibiotic administration by general practitioners at the emergency department of a teaching hospital in Sanandaj, Iran (Persian)]. Sci J Kurdistan Univ Med Sci. 2018; 23(3):67-72. https://sjku.muk.ac.ir/article-1-4268-en.html

[7] Shabanian A, Karimi Nasab MH, Shayesteh Azar M, Esmaeilnezhad Ganji SM. Type and rate of prophylactic antibiotic use in the orthopedic patients underwent elective surgeries in Shahid Beheshti Hospital in Babol. J Babol Univ Med Sci. 2018; 20(5):68-73. http://jbums.org/browse.php?a_id=7407&sid=1&slc_lang=en

[8] Hatam N, Askarian M, Moravveji AR, Assadian O. Economic burden of inappropriate antibiotic use for prophylactic purpose in Shiraz, Iran. Iran Red Crescent Med J. 2011; 13(4):234-8. [PMID] [PMCID]

[9] Moradi G, Gouya MM, Eshrati B, Mohraz M, Molaei L, Piroozi B. National action plan of the Islamic Republic of Iran for combating antimicrobial resistance during 2016-2021. Med J Islam Repub Iran. 2018; 32:82. [DOI:10.14196/mjiri.32.82] [PMID] [PMCID]

[10] Zarezade M, Shaterzade F, Abedini S, Raadabadi M. [Evaluating pattern of prescribing antibiotics in surgical wards of Shahid Rahnemon Hospital compared to standard methods in 2015 (Persian)]. J Shahid Sadoughi Univ Med Sci. 2015; 23(7):679-90. http://jssu.ssu.ac.ir/browse.php?a_id=3250&sid=1&slc_lang=en

[11] Loeffler JM, Garbino J, Lew D, Harbarth S, Rohner P. Antibiotic consumption, bacterial resistance and their correlation in a Swiss University Hospital and its adult intensive care units. Scand J Infect

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Dis. 2003; 35(11-12):843-50. [DOI:10.1080/00365540310016646] [PMID]

[12] Hadavand F, Farkhonde S, Motamed N. [Study on observing the indications of vancomycin use in the surgical wards of Shohada Khalij Hospital of Bushehr in 2013 (Persian)][PhD dissertation]. Bushehr: Bushehr University Of Medical Sciences; 2013.

[13] Bunnell KL, Danziger LH, Johnson S. Economic barriers in the treatment of clostridium difficile infection with oral vancomycin. Open Forum Infect Dis. 2017; 4(2):ofx078. [DOI:10.1093/ofid/ofx078] [PMID] [PMCID]

[14] Chiu CH, Michelow IC, Cronin J, Ringer SA, Ferris TG, Puopolo KM. Effectiveness of a guideline to reduce vancomycin use in the neonatal intensive care unit. Pediatr Infect Dis J. 2011; 30(4):273-8. [DOI:10.1097/INF.0b013e3182011d12] [PMID]

[15] Hammer BM, Lardieri AB, Morgan JA. Appropriate use of vancomycin in NICU despite free-for-all policy. J Pediatr Pharmacol Ther. 2016; 21(3):207-12. [DOI:10.5863/1551-6776-21.3.207] [PMID] [PMCID]

[16] Salehifar E, Babamahmoodi F, Alikhani A, Ganji R, Fazli M. Drug utilization evaluation of vancomycin in a referral infectious center in Mazandaran Province. J Pharm Care. 2014; 2(2):55-9. https://jpc.tums.ac.ir/index.php/jpc/article/view/46

[17] Nateghian AR, Robinson J, Samadi B, Abdi N. Appropriate use of vancomycin in an educational tertiary care hospital in Tehran, Iran. Med J Islam Repub Iran. 2007; 21(1):43-9. http://mjiri.iums.ac.ir/article-1-274-en.html

[18] Askarian M, Assadian O, Safaee GR, Golkar A, Namazi S, Movahed MR. Vancomycin use in a large teaching hospital in Shiraz, Islamic Republic of Iran, 2003. East Mediterr Health J. 2007; 13(5):1195-201. [DOI:10.26719/2007.13.5.1195] [PMID]

[19] Mahmoodian A, Abbasi S, Farsaei S. A new approach to Vancomycin utilization evaluation: A cross-sectional study in intensive care unit. J Res Pharm Pract. 2016; 5(4):279-84. [DOI:10.4103/2279-042X.192453] [PMID] [PMCID]

[20] Alfandari S, Levent T, Descamps D, Hendricx S, Bonenfant C, Taines V, et al. Evaluation of glycopeptide use in nine French hospitals. Med Mal Infect. 2010; 40(4):232-7. [DOI:10.1016/j.medmal.2009.10.019] [PMID]

[21] de Melo DO, Sasaki M, Grinbaum RS. Vancomycin use in a hospital with high prevalence of Methicillin-Resistant Staphylococcus aureus: Comparison with Hospital Infection Control Practices Advisory Committe Guidelines (HICPAC). Braz J Infect Dis. 2007; 11(1):53-6. [DOI:10.1590/S1413-86702007000100014] [PMID]

[22] Wright SW, Wrenn KD. Appropriateness of vancomycin use in the emergency department. Ann Emerg Med. 1998; 32(5):531-6. [DOI:10.1016/S0196-0644(98)70030-7] [PMID]

[23] Fahimi F, Soleymani F, Tavakoli-Ardakani M. Vancomycin utilization evaluation in a teaching hospital: A case- series study in Iran. J Pharm Care. 2013; 1(2):51-4. https://jpc.tums.ac.ir/index.php/jpc/article/view/12

[24] Ayazkhoo L, Mousavi S, Ramazani F, Ayatollahi-Tafti M, Sa'dabadi Z, Sistanizad M. Vancomycin utilization evaluation: Are we dosing appropriately? J Pharm Care. 2013; 1(4):149-52. https://jpc.tums.ac.ir/index.php/jpc/article/view/33

[25] Keyserling H, Sinkowitz-Cochran RL, Harris JM, Levine GL, Siegel JD, Stover BH, et al. Vancomycin use in hospitalized pediatric patients.

Pediatrics. 2003; 112(2):e104-11. [DOI:10.1542/peds.112.2.e104] [PMID]

[26] Ghasemi A, Habibzadeh Sh. [Vancomycin indications request form effects on its substandard using in Imam Khomeini Hospital (Persian)]. [MD. Dissertation]. Ardabil: Ardabil University Of Medical Sciences; 2011. https://eprints.arums.ac.ir/1824/

[27] Hamilton CD, Drew R, Janning SW, Latour JK, Hayward S. Excessive use of vancomycin: A successful intervention strategy at an academic medical center. Infect Control Hosp Epidemiol. 2000; 21(1):42-5. [DOI:10.1086/501703] [PMID]

[28] Gillon J, Xu M, Slaughter J, Pentima MCD. Vancomycin use: Room for improvement among hospitalized children. J Pharm Pract. 2017; 30(3):296-9. [DOI:10.1177/0897190016635478] [PMID]

[29] Al-Kofide H, Zaghloul I, Al-Naim L. Pharmacokinetics of vancomycin in adult cancer patients. J Oncol Pharm Pract. 2010; 16(4):245-50. [DOI:10.1177/1078155209355847] [PMID]

[30] Nateghian A, Robinson JL, Arjmandi K, Vosough P, Karimi A, Behzad A, et al. Epidemiology of vancomycin-resistant enterococci in children with acute lymphoblastic leukemia at two referral centers in Tehran, Iran: A descriptive study. Int J Infect Dis. 2011; 15(5):e332-5. [DOI:10.1016/j.ijid.2011.01.006] [PMID]

[31] Sung L, Lange BJ, Gerbing RB, Alonzo TA, Feusner J. Microbiologically documented infections and infection-related mortality in children with acute myeloid leukemia. Blood. 2007; 110(10):3532-9. [DOI:10.1182/blood-2007-05-091942] [PMID]