



Cross-sectional Study

Drug Utilization Evaluation (DUE) of vancomycin: A cross-sectional study

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ABSTRACT

Objective: Evaluating the use of antibiotics leads to identifying drug problems, preventing antibiotic resistance, and controlling the cost of medication. The aim of this study was to Drug Utilization Evaluation (DUE) of vancomycin.

Methods: This study was a descriptive retrospective cross-sectional study. Sampling method was the census. The information was collected through a checklist and referring to patients' files.

Results: 170 children and 120 adults who received vancomycin were studied. The dose of vancomycin in the studied adults was 40.6% and 61% was in accordance with the Uptodate guideline. Also, the duration of treatment in the studied children was 10.6% and 15.3% according to the Uptodate guideline and in adults 30%, 39.2% was in accordance with the Uptodate guideline. Also, the indication for vancomycin in children was 14.1% and 18.8% in accordance with the Uptodate guideline, and in adults 40% and 52.5% was in accordance with the Uptodate guideline. The highest initial diagnosis in children was RDS 54.1%, seizure 9.4%, jaundice 9.4% and pneumonia 8.2%, and in adults 30% CRF and 11.7% catheter. In children, the most common complications were related to shortness of breath 41.2%, fever 18.8% and jaundice 11.8%, and in adults were related to fever 32.5%, lethargy 26.7% and shortness of breath 20%, respectively.

Conclusion: It is recommended to improve the administration and rational use of antibiotics and prevent the occurrence of microbial resistance, to follow the treatment patterns based on international standards in hospitals.

1. Introduction

Drug Utilization Evaluation (DUE) is a practical, flexible, extensive and continuous method, which evaluates the quality and economics of drug use. These studies include the steps of prescribing, delivering, and consuming drugs and focuses mainly on treatment problems that a large number of patients face and are at high risk. DUE studies should analyze and evaluate this information implicitly, using pre-determined criteria and standards, away from any kind of bias. After analyzing the information obtained in order to improve performance, it designs and implements the necessary programs. After modifying the necessary functions, the effect of these changes is collected and reported again by performing the necessary follow-ups [1–3]. DUE are mainly qualitative and focus on the rationale for drug use [4]. Retrospective DUE studies have no effect on the course of drug therapy in discharged patients.

However, it identifies appropriate patterns of drug administration and suggests appropriate educational programs to improve the drug treatment process [5,6].

Given that studies examining and evaluating the trend of drug use in developing countries are considered a nascent program, the use of experiments related to the dramatic development of DUE studies in industrialized and developed countries seems useful. The weakness of the Third World has led to the DUE being in the early stages of development and development. At present, the problems facing these countries, apart from the weaknesses and shortcomings at the academic level, are the existence of executive problems and the lack of government planning for conducting such studies. Considering the many benefits of these studies in the field of quality improvement of the drug treatment situation, we find that a step should be taken to implement this series of activities and provide the necessary national and state support for its

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implementation [7,8].

Vancomycin is one of the antibiotics used in severe infections, patients with infections related to resistant organisms, patients sensitive to penicillin, endocarditis, infections of the central nervous system, etc [9–12]. Irrational use of vancomycin as an antibiotic can lead to the growth of resistant microorganisms [13]. Nephrotoxicity has been observed in a number of patients which is associated with a gradual increase in serum creatinine concentration [14]. Furthermore, the drug might be associated with increased health-care cost in terms of readmission, cost of the drug, and readmission reimbursement compared to fidaxomicin [15].

Today, the resistance of microorganisms to antibiotics has become a worrying issue in the treatment of infectious diseases worldwide. Some studies have shown that the widespread and inappropriate use of vancomycin not only increases the cost but also increases the number of positive gram-positive organisms, especially Vancomycin-resistant enterococci (VRE) [16]. Due to the necessity of performing DUE in order to achieve rational administration and use of vancomycin and prevent the consequences of its misuse, we decided to conduct a retrospective study of vancomycin consumption pattern to determine compliance with standards in Shahid Rahimi Hospital.

2. Material and methods

In this descriptive retrospective cross-sectional study, the records of patients admitted to (XXX) from January 2020–June 2020 who received vancomycin were reviewed. In accordance with CDC and Up to date guidelines, information related to vancomycin administration was collected such as demographic information including age, sex and weight of patients, dose of vancomycin, monitoring of serum creatinine level, length of treatment with vancomycin, calculation of creatinine clearance based on Cockcroft-Gaulten equation, evaluate the suitability of vancomycin indication and compliance with the recommended instructions. The results were accurately recorded and by comparing each with the existing valid guidelines, we examined the rationality of vancomycin in terms of indication for vancomycin, treatment costs, side effects of the drug, and so on. The main sources for collecting information were pharmacy drug cases, patient records, and nursing records.

After data collection, the data were entered into SPSS18 (IBM, Chicago, IL, USA) software and statistically analyzed. Using descriptive statistics (frequency and percentages), the results were presented in tables and statistical charts. Analytical statistics were used to measure the relationship and the effect of variables. $P < 0.05$ was considered statistically significant.

The research followed the tents of the Declaration of Helsinki. The

Ethics Committee of (XXX).

Unique identifying number is: researchregistry7896.

The methods are stated in accordance with STROCSS 2021 [17].

3. Results

In this study, 170 children and 120 adults referred to (XXX) who received vancomycin during our study period were analyzed. Table 1 lists the information about these patients.

Table 2 provides information on the percentage and frequency of doses appropriate to the CDC (a) and Uptodate (b) guidelines and disproportionate (c) to them separately. For this purpose, creatinine clearance for all patients was first calculated using the Cockcroft-Gault formula. Then, considering the normal creatinine level (0.6–1.3 mg/dl for men and 0.5–1.1 mg/dl for women), the prescribed dose of vancomycin was compared to CDC and Uptodate guidelines for people with abnormal creatinine levels. The results showed that out of 120 adults studied, 56 cases (46.7%) had normal creatinine levels and 64 cases (53.3%) had abnormal creatinine levels. Out of the 64 individuals with abnormal creatinine levels, the dose of vancomycin in 46% of the studied adults was in accordance with the CDC guideline and 61% was in accordance with the uptodate guideline. As mentioned in Table 2, the comparison of a and b, a and c, b and c parameters in children and adult groups separately showed that there was no significant difference between a and b in the adult group ($P = 0.166$), but in other cases there was a significant difference.

Table 3 provides information on the percentage and frequency of cases of proportional length of treatment with CDC (a) and Uptodate (b) guidelines and non-compliance with CDC and Uptodate guidelines (c) are listed separately. As can be seen, the length of treatment in the studied children was 10.6% according to the CDC guideline, 15.3% complied with the Uptodate guideline and 74.1% complied with the other guidelines. Also, the length of treatment in the studied adults was 30% in accordance with the CDC guideline and 39.2% in accordance with the guideline Uptodate. As mentioned in Table 3, the comparison of a and b, a and c, b and c parameters in children and adult groups separately showed that there was no significant difference between a and b in the children group ($P = 0.057$), but in other cases there was a significant difference.

Table 4 provides information on the percentage and frequency of prescription indications in accordance with CDC (a) and Uptodate (b) guidelines and non-compliance (c) with them. As can be seen, the indication for vancomycin administration in the studied children was 14.1% according to Guideline CDC, 18.8% according to Guideline Uptodate and 74.1% according to other guidelines. Also, the indication

Table 1
The information about patients.

	Children		Adult			
			Frequency	Percentage	mean	Std. Deviation
Age	Neonate (0–4 week)		116	68.2	(13–96years)	
	Infant(1month2years)		42	24.7		
	Children(2–12years)		12	7.1		
	Total		170	100.0		
Sex			Frequency	Percentage	Frequency	Percentage
	Male		94	55.3	Male	52
	Female		76	44.7	Female	68
	Total		170	100.0	Total	120
Average length of treatment	Mean		Std deviation		mean	Std deviation
	12.07		8.354		6.30	6.864
Mean creatinine level at the beginning of treatment (mg/dl)	Mean		Std deviation			
	0.53482		0.351454			
Average total cost of treatment	Mean		Std deviation		mean	Std deviation
	708715		779180.82		851052	869129.62
Average cost paid by the patient	Mean		Std deviation		mean	Std deviation
	59178.94		71707.84		59598.98	64335.83
Average cost of insurance	Mean		Std deviation		mean	Std deviation
	667710.35		724926.61		845766.85	1031063.68

Table 2

Percentage and frequency of dose administration in accordance with up-to-date, CDC guidelines and non-compliance with up-to-date and CDC guidelines.

	^a CDC		^b up-to-date		Non-compliance with ^{UpToDate} and CDC guidelines		P value		
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage	p ^{a,b}	p ^{b,c}	p ^{a,c}
Children	0	0%	0	0%	170	100%	<0.01*	<0.01*	<0.01*
Adult	26	40.6%	39	61%	18	28.1%	0.166	<0.01*	<0.01*

*Statistically significant difference (P < 0.05).

Table 3

Percentage and frequency of treatment lengths in accordance with guidelines CDC, up-to-date date and non-compliance with guidelines CDC and UpToDate.

	^a CDC		^b up-to-date		Non-compliance with ^c up-to-date and CDC guidelines		P value		
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage	p ^{a,b}	p ^{b,c}	p ^{a,c}
Children	18	10.6%	26	15.3%	126	74.1%	<0.057	<0.01*	<0.01*
Adult	36	30.0%	47	39.2%	37	30.8%	<0.01*	<0.01*	<0.01*

*Statistically significant difference (P < 0.05).

Table 4

Percentage and frequency of prescription indications in accordance with guidelines CDC, Uptodate and non-compliance with guidelines CDC and UpToDate.

	^a CDC		^b up-to-date		^c Other		P value		
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage	p ^{a,b}	p ^{b,c}	p ^{a,c}
Children	24	14.1%	32	18.8%	126	74.1%	<0.01*	<0.01*	<0.01*
Adult	48	40.0%	63	52.5%	28	23.3%	0.021*	<0.01*	<0.01*

*Statistically significant difference (P < 0.05).

for vancomycin administration in the studied adults was 40% in accordance with Guideline CDC, 52.5% in accordance with Guideline Up-to-date and 23.3% in accordance with other guidelines. As mentioned in Table 4, the comparison of a and b, a and c, b and c parameters in children and adult groups separately showed that there was significant difference between them.

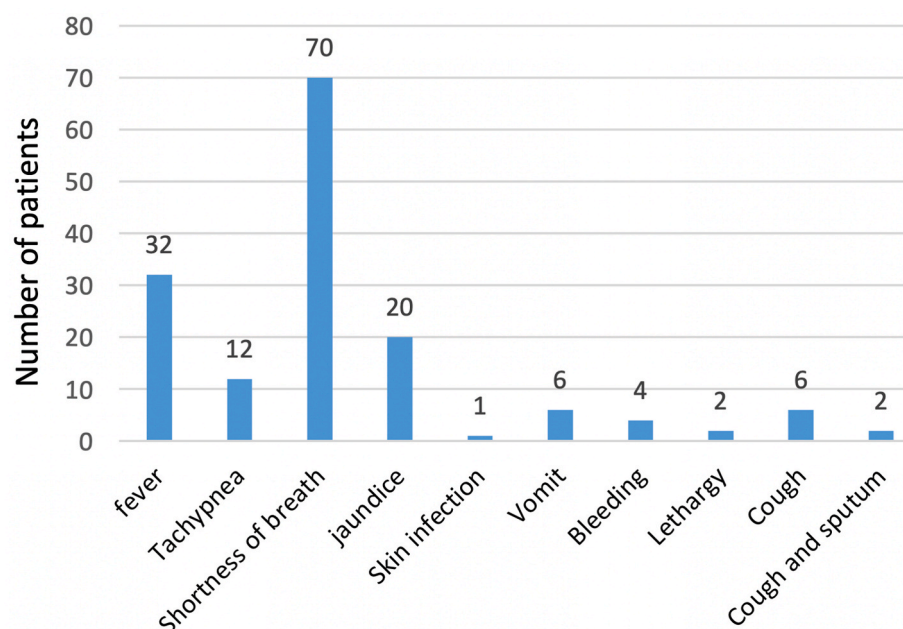
The most primary diagnoses in the children were RDS (54.1%), seizures (9.4%), jaundice (9.4%) and pneumonia (8.2%), respectively. Also, in the studied adults, the highest initial diagnosis was related to CRF (30%) and catheter (11.7%), respectively.

In the children studied, the most common complications were shortness of breath (41.2%), fever (18.8%) and jaundice (11.8%), respectively. Also, in the studied adults, the most complications were

related to fever (32.5%), lethargy (26.7%) and shortness of breath (20%), respectively. Figs. 1 and 2 illustrate this finding.

4. Discussion

Our study demonstrated that out of 120 adults, 64 had abnormal creatinine levels. The dose of vancomycin to 40.6% of them was in accordance with the CDC guideline and 61% was in accordance with the up-to-date guideline. Also, the mean creatinine level at the beginning of treatment in the studied children was 0.53 ± 0.35 mg/dl. However, in Askarian et al.'s study out of 200 vancomycin prescriptions, only 12 (6%) were considered appropriate [18]; which was very low compared to our results. In a study by Fahimi et al., it was shown that four of the 45

**Fig. 1.** Frequency of side effects of vancomycin in children.

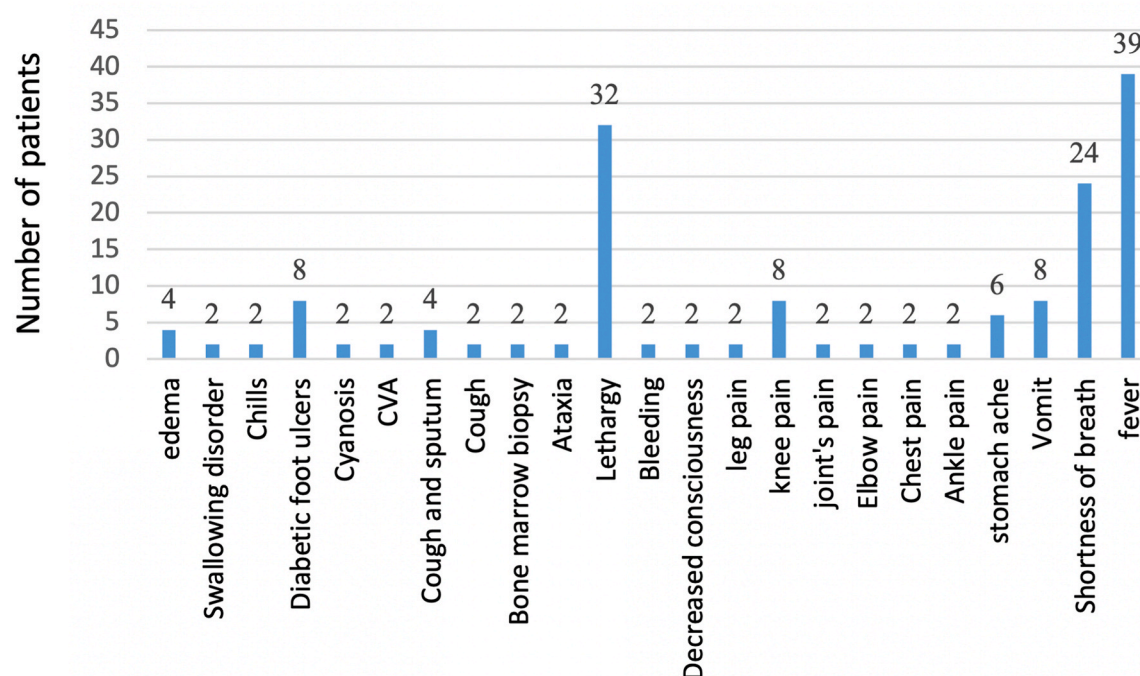


Fig. 2. Frequency of side effects of vancomycin in adult.

patients studied were given an unfavorable dose of vancomycin based on serum creatinine levels and only in one (2.2%) of the patients vancomycin was prescribed in accordance with the CDC and infectious disease society of America (IDSA) guidelines [13]. In evaluation of vancomycin use in university-affiliated hospitals in Southern Khorasan Province (East Iran) based on HICPAC guidelines it was shown that only 10.6% of the patients showed inappropriate vancomycin use according to the HICPAC criteria [19]. Creatinine clearance is a relatively good estimate for renal dose adjustment; therefore, daily monitoring of serum creatinine and estimation of creatinine clearance, in addition to ensuring the appropriate dose of the drug, can be effective in preventing renal toxicity [20–22]. The difference between the renal toxicities of vancomycin may be due to the different criteria used to define renal toxicity, different study populations, and concomitant administration of nephrotoxic agents. The effect of age on pharmacokinetics is due to the effect of age on kidney function. Vancomycin should be adjusted for renal excretion in renal failure [23].

In our study, it was shown that the indication for vancomycin in children and adults is 14.1% and 40% according to the CDC guideline, and 18.8% and 52.5%, according to the up-to-date guideline, respectively. Various studies have been performed to investigate the pattern of vancomycin use in different populations. For example a cross-sectional, pre-post interventional study conducted at Imam Hossein Hospital, Tehran, Iran, from 2014 to 2016 showed that total vancomycin consumption in the baseline and after the intervention phases was significantly reduced compared to the training program period [24]. In a study of 58 patients in Shiraz Namazi Hospital, it was shown that vancomycin was administered appropriately to 68.63% of patients with febrile neutropenia and 71.43% of patients with other diagnoses according to Healthcare Infection Control Practices Advisory Committee (HICPAC) and IDSA guidelines [25]. In the evaluation of 75 patients in Shohada Teaching Hospital in Tabriz, the indication for vancomycin in only 30% of patients was based on CDC and American Society of Health-System Pharmacists (ASHP) guidelines and 69.3% of the patients received vancomycin inappropriately [26]. Another study in Sudan showed that the most common indications for vancomycin use were sepsis (29%) and pneumonia (19.6%) and more than 30% of patients received vancomycin regardless of HICPAC criteria [27]. This is while in our study, the

most primary diagnoses in children and adults were RDS (54.1%) and CRF (30%), respectively. It should be noted that the use of different guidelines in different studies as well as the evaluation of different sections can affect the results.

Our data analysis showed that the mean duration of treatment in children and adults under study was 12.07 ± 8.35 and 6.30 ± 6.86 days, of which 10.6% and 30% were in accordance with the CDC guideline, and 15.3% and 39.2% were in accordance with the up-to-date guideline, respectively. The results of a study conducted by Afshin Shiva and Milad Azemoddeh showed that the Mean $\pm$ SD duration of treatment for patients was 4.45 ± 4.91 days [28].

Our study is retrospective in nature so a number of variables including long term therapeutic outcomes and associated cost could not be analyzed. Furthermore, comparative analysis with other antibiotics is also not presented in this study.

Conclusion: Based on the results of the present study, it can be concluded that most cases of vancomycin use are empirical and this can be due to routine drug use and uncertainty about antibiogram results; therefore, it seems those comprehensive programs to target drug use in all medical centers to be implemented and applied to prevent the spread and resistance. As a result, it is recommended to improve the administration and rational use of antibiotics and prevent the occurrence of microbial resistance, to follow the treatment patterns based on international standards in hospitals and to develop in-hospital instructions based on the microbial resistance pattern of each center. Microbial resistance and control of serum levels and training courses for physicians can be effective in the ratio of consumption of this antibiotic. It is suggested that in future studies, this type of study be carried out with a larger sample size and in different populations.

Ethical approval

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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No funding was secured for this study.

Author contribution

Dr. Ali Kharazmkia and Mina Rezvani: conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. Dr. Ali Amiri and Dr. Hamid Reza Sherkatolabbasieh: Designed the data collection instruments, collected data, carried out the initial analyses, and reviewed and revised the manuscript. Dr. Mehdi Birjandi: Coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Trial register number

1. Name of the registry: N/a
2. Unique Identifying number or registration ID: IR.LUMS.REC.1399.069
Hyperlink to the registration (must be publicly accessible): <https://ethics.research.ac.ir/ProposalCertificateEn.php?id=138271&Print=true&NoPrintHeader=true&NoPrintFooter=true&NoPrintPageBorder=true&LetterPrint=true>

Guarantor

Dr. Ali Kharazmkia.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Human and animal rights

No animals were used in this research. All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

Consent for publication

Informed consent was obtained from each participant.

Availability of data and materials

All relevant data and materials are provided with in manuscript.

Patient consent

Consent was not obtained to publish the case report. This report does not contain any personal information that could lead to the identification of the patient.

Declaration of competing interest

The authors deny any conflict of interest in any terms or by any means during the study. All the fees provided by research center fund and deployed accordingly.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2022.104169>.

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