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ARTÍCULO ORIGINAL

Hemato-Oncological Disease and Other Factors Associated with Subtherapeutic Vancomycin Levels in a High Complexity Hospital

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Abstract

Introduction: Measuring trough serum levels of vancomycin is recommended by current guidelines for monitoring treatment, with values between 15-20 mg/L for severe infections. Various variables are associated with failing to reach effective levels, which this study seeks to determine. This study aimed to identify factors associated with subtherapeutic serum levels, their relationship with hemato-oncological diseases, and other pharmacokinetic variables.

Materials and methods: This was an observational case-control study of hospitalized adults in whom serum vancomycin levels were measured. A total of 857 medical records were analyzed, of which 377 met the inclusion criteria of this study. A random selection of 92 cases and 202 controls was made at a 1:2 ratio without matching.

Results: The median age was 59 years, and 56.8% of the patients were male. Hemato-oncological diagnoses were present in 23.1% of patients, with non-Hodgkin lymphoma and acute leukemia being the most frequent. Four variables were statistically associated with subtherapeutic levels: hemato-oncological disease (OR 2.12; 95% CI 1.53–4.88; p=0.004), BMI ≥25 kg/m² (OR 1.15; 95% CI 1.07–1.21; p<0.001), age >75 years (OR 0.96; 95% CI 0.93–0.96; p<0.001), and creatinine >0.7 mg/dL (OR 0.08; 95% CI 0.01–0.11; p<0.001).

Discussion: Hemato-oncological disease and increased body mass index were significantly associated with subtherapeutic vancomycin levels. In contrast, older age and higher creatinine levels acted as protective factors, possibly due to reduced renal clearance. These findings support the need for therapeutic drug monitoring and dose adjustment in oncologic patients.

Keywords: vancomycin; drug monitoring; neoplasms; hematology; pharmacokinetics

Enfermedad Hemato-Oncológica y Otros Factores Asociados con Niveles Subterapéuticos de Vancomicina en un Hospital de Alta Complejidad

Resumen

Introducción: La medición de niveles séricos valle de vancomicina es recomendada por las guías actuales para la monitorización del tratamiento, esperando valores entre 15-20mg/L en infección severas. Existen distintas variables que se asocian a no alcanzar niveles efectivos las cuales se buscan determinar en este estudio. El objetivo de este estudio fue determinar los factores asociados con niveles séricos subterapéuticos, su relación con la enfermedad hemato-oncológica y otras variables farmacocinéticas.

Materiales y métodos: Estudio observacional de casos y controles en adultos hospitalizados a quienes se les midieron niveles séricos de vancomicina. Se analizaron un total de 857 historias clínicas, de las cuales 377 cumplieron con los criterios de inclusión. Se seleccionaron aleatoriamente 92 casos y 202 controles en una proporción 1:2, sin apareamiento.

Resultados: La mediana de edad fue de 59 años, y el 56,8 % de los pacientes eran hombres. El 23,1 % presentó diagnóstico hemato-oncológico, siendo los más frecuentes los linfomas no Hodgkin y las leucemias agudas. Se encontraron cuatro variables estadísticamente significativas: enfermedad hemato-oncológica (OR 2,12; IC 95 % 1,53–4,88; p=0,004), índice de masa corporal mayor de 25 (OR 1,15; IC 95 % 1,07–1,21; p<0,001), edad mayor de 75 años (OR 0,96; IC 95 % 0,93–0,96; p<0,001) y creatinina mayor a 0,7 mg/dL (OR 0,08; IC 95 % 0,01–0,11; p<0,001).

Discusión: La enfermedad hemato-oncológica y un mayor índice de masa corporal se asociaron significativamente con niveles subterapéuticos de vancomicina. Por el contrario, la edad avanzada y niveles más altos de creatinina actuaron como factores protectores, posiblemente debido a una menor depuración del fármaco. Estos hallazgos respaldan la necesidad de monitorización terapéutica y ajuste de dosis en pacientes oncológicos.

Palabras clave: vancomicina; monitoreo de medicamentos; neoplasias; hematología; farmacología

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Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) infections acquired in hospital settings are becoming increasingly common. These infections are associated with prolonged hospital stays and higher mortality rates[1-2]. Currently, the first-line treatment is vancomycin, which remains effective against nosocomial infections owing to the infrequent resistance observed in our region[3,4,5]. Guidelines recommend trough levels of 15-20 mg/L for severe MRSA infections[3], although this target is debated because of variable correlations with clinical outcomes. Despite this, it remains recommended for monitoring vancomycin treatment. The issue of high variability lies in the factors affecting the pharmacokinetics of the drugs. Multiple studies have established the need for higher doses when certain factors are present, such as a presumed high volume of distribution or increased renal clearance[4]. Because of the heterogeneity of patients starting vancomycin treatment, nomograms have been developed to calculate the initial doses for special populations. Currently, there is disagreement about the factors influencing the achievement of optimal serum vancomycin levels, especially in populations with hematologic-oncologic neoplasms[5].

The emergence of antibiotic-resistant pathogens is a global concern challenging healthcare systems due to the difficulty in diagnosis and treatment. Various alternatives, such as broad-spectrum antibiotics, have been developed to cover different pathogens[6,7,8,9,10]. Vancomycin is a complex tricyclic glycopeptide composed of non-ribosomal glycosylated cyclic or polycyclic peptides. It inhibits peptidoglycan synthesis in aerobic and anaerobic gram-positive bacteria[10] and is characterized as a time-dependent antibiotic[11,12,13,14]. In patients with cancer, especially those with hematologic neoplasms, increased creatinine clearance and vancomycin distribution volume have been demonstrated[15,16,17], increasing the risk of subtherapeutic vancomycin levels[18,19,20,21,22]. Additionally, adverse effects and toxicity associated with vancomycin have been observed during treatment, linked to patient comorbidities, concomitant use of nephrotoxic drugs, hypotension, and renal function deterioration[23,24,25]. Other described adverse effects include phlebitis (13%), red man syndrome characterized by erythema, pruritus, hypotension, and angioedema caused by a histaminergic response to rapid infusion, with a variable incidence of 3.4% to 11.2%, and neutropenia in approximately 2% of cases[8].

Due to variability and a narrow therapeutic range compared to other antimicrobials, serum measurements of vancomycin levels are necessary to maximize efficacy and minimize toxicity[23]. Recommendations for monitoring have evolved over time with better drug characterization. Higher levels are expected, especially in severe infections and depending on the pathogen[26]. Evaluations consider the duration vancomycin concentration remains above the minimum inhibitory concentration (MIC), the area under the curve (AUC) to MIC ratio (AUC/MIC), and the peak serum concentration to MIC ratio (Cmax/MIC)[24]. Current guidelines recommend an AUC/MIC value >400 to evaluate the clinical effectiveness of vancomycin[24]. A target trough level of 15-20 mg/L is recommended for severe MRSA infections, to be taken before the fourth dose at treatment initiation or dose adjustment[26-30]. Therefore, it is essential to determine how frequently adequate serum levels are achieved and which independent factors may influence these levels. In Colombia, no studies have evaluated vancomycin serum levels in the hematologic-oncologic population, despite its frequent use against methicillin-resistant *Staphylococcus aureus*[26]. The importance of these levels lies in monitoring treatment, making necessary adjustments, reducing potential toxicity, and preventing resistance associated with subtherapeutic levels. This study aimed to determine the factors associated with subtherapeutic vancomycin serum levels and their impact on the hematologic-oncologic population.

Materials and methods

We conducted an observational analytical case-control study in hospitalized patients over 18 years of age who were receiving vancomycin treatment at a high-complexity institution in Colombia, in whom serum levels were measured before the fourth dose. Patients undergoing renal replacement therapy at the time of antibiotic administration, those with incomplete medical records (such as missing basic data: age, sex, height, weight, loading dose, maintenance dose, creatinine), and those with vancomycin serum levels > 25 mg/L were excluded. Cases were defined as hospitalized patients with subtherapeutic vancomycin levels (<10 mg/L), and controls were defined as those with therapeutic levels (≥10 mg/L).

To estimate the association between subtherapeutic vancomycin levels and hematologic disease, a 1:2 case-control sample size calculation was performed using Epidat software with the following parameters: 95% confidence level, two controls per case, expected OR of 1.6, 18% of exposed cases, and 83% statistical power. A total of 92 cases and 202 controls were included, considering a 10% loss rate.

The variables included were: age (years), sex, weight (kg), height (m), body mass index (kg/m^2), admission diagnosis, infectious diagnosis, hematologic-oncologic diagnosis, type of hematologic-oncologic disease, time since last chemotherapy (days), concomitant use of aminoglycosides, vancomycin loading dose (grams), maintenance dose (grams), vancomycin levels (mg/L) before the fourth dose, time difference between level measurement and the fourth dose, presence of fever, febrile neutropenia, volume of intravenous fluids, creatinine (mg/dL), albumin (g/dL), glomerular filtration rate (according to Cockcroft-Gault and CKD-EPI), volume of distribution, and patients admitted to the intensive care unit (ICU).

Participants were selected using the Athenea® laboratory software, identifying patients with vancomycin serum level studies during the study period. With each participant's identification number, digital records were reviewed in the Servinte® software to select those with subtherapeutic antibiotic levels, verifying compliance with all inclusion and exclusion criteria. The investigators recorded the clinical information in Excel.

For statistical analysis, a univariate description was first performed, obtaining frequencies and proportions for qualitative variables and measures of central tendency (mean, median) and dispersion (standard deviation, interquartile range) for quantitative variables, depending on their distribution assessed by the Shapiro-Wilk test. Cases and controls were compared across independent variables to identify the frequency of occurrence in each group. In the bivariate analysis, categorical variables were evaluated using the chi-square and Fisher's exact tests, while continuous variables with normal distribution were analyzed using Student's t-test, and non-normally distributed variables using the Mann-Whitney U test. Finally, a multivariate logistic regression analysis was conducted on variables of interest, which were those with statistical significance in the bivariate analysis or considered clinically relevant, followed by diagnostic testing of the final model using the Hosmer and Lemeshow goodness-of-fit test. Statistical significance was set at $p < 0.05$, and the data were analyzed using Stata version 14.

Ethical Considerations

This study was approved by the Ethics Committee of the Fundación Cardioinfantil-La Cardio and adhered to the ethical principles for human research described in the Nuremberg Code, Belmont Report, and Declaration of Helsinki, as well as Resolution 008430 of 1993 by the Ministry of Health of the Republic of Colombia.

Results

We analyzed 857 clinical records of patients who had vancomycin serum levels measured in the Athenea® database. A total of 251 patients were excluded due to improper sample collection, 145 due to end-stage renal disease or acute kidney injury, 65 due to supratherapeutic vancomycin levels, and 19 due to insufficient records. A total of 377 patients met the selection criteria, of which 40.8% (157/377) were cases with vancomycin levels <10 mg/dL. In this study, 92 cases and 202 controls were randomly selected in a 2:1 ratio.

Regarding the characteristics of the patients treated with vancomycin included in the study, the median age was 59 (46–69) years, and 56.8% (167/294) were male. The median weight was 64 (55–73) kg, median height was 1.65 (1.57–1.70) m, and median body mass index was 23.6 (21.3–27.0) kg/m². Table 1 presents the clinical and sociodemographic characteristics of patients treated with vancomycin, and Figure 1 shows the infectious diagnoses of these patients.

Among the patients included in the study, 23.1% (68/294) had a hematologic-oncologic diagnosis, with other diagnoses being more frequent. Non-Hodgkin lymphoma was the most common neoplasm, followed by acute myeloid leukemia. The median time since the last chemotherapy was 10 (7–14) days. Table 2 shows the characteristics of the patients according to the distribution between cases (vancomycin <10 mg/L) and controls (vancomycin >10 mg/L).

Table 1. Sociodemographic characteristics of Patients Treated with Vancomycin.

Variable	Result n=294
Concomitant aminoglycoside medications, n (%)	11 (3.8)
Vancomycin loading dose (mg/kg), Median (IQR)	30 (25.4-33.3)
Vancomycin maintenance dose (mg/kg), Median (IQR)	15 (13.5-17.8)
Vancomycin level before fourth dose (mg/kg), Median (IQR)	12.6 (8.6-16.8)
Presence of fever, n (%)	170 (45.2)
Febrile neutropenia, n (%)	49 (13.0)
Intravenous fluid volume, Median (IQR)	3893 (1544-6979)
Patients admitted to the ICU, n (%)	127 (33.8)
Creatinine (mg/dL), Median (IQR)	0.8 (0.6-1)
Albumin (g/dL), Median (IQR)	2.7 (2.3-3.0)
Cockcroft-Gault GFR, Median (IQR)	83.5 (63.0-112.0)
CKD-EPI GFR, Median (IQR)	92.3 (72.6-107.4)
Volume of distribution, Median (IQR)	57.7 (39.8-105.1)

(ICU) intensive care unit
(GFR) glomerular filtration rate

The cases were younger, had a higher median body mass index, and had a higher frequency of hematologic-oncologic diagnoses, particularly acute lymphoblastic leukemia. In addition, they had a lower maintenance dose of vancomycin, lower median creatinine levels, and a higher glomerular filtration rate by any formula than the controls, with these differences being statistically significant.

For the association analysis, febrile neutropenia was included in the hematologic disease group to reduce collinearity. The other variables remained unchanged. The factors associated with subtherapeutic levels in the study patients are shown in Table 3. The presence of hematologic-oncologic disease, overweight, and obesity were risk factors for subtherapeutic vancomycin levels. Some patients with normal weight also had subtherapeutic levels. Age > 75 years and creatinine greater than 0.7 mg/dL were protective factors against subtherapeutic levels. The model's R^2 was 76%, with a Bayesian index of -1832.3 and a Hosmer and Lemeshow goodness-of-fit test of 0.41, indicating a well-fitting model with the retained variables best explaining the phenomenon of subtherapeutic vancomycin levels.

Discussion

This study aimed to identify factors associated with subtherapeutic vancomycin levels in hospitalized patients and to determine whether there was a specific relationship with hematologic-oncologic diagnoses. The multivariate analysis

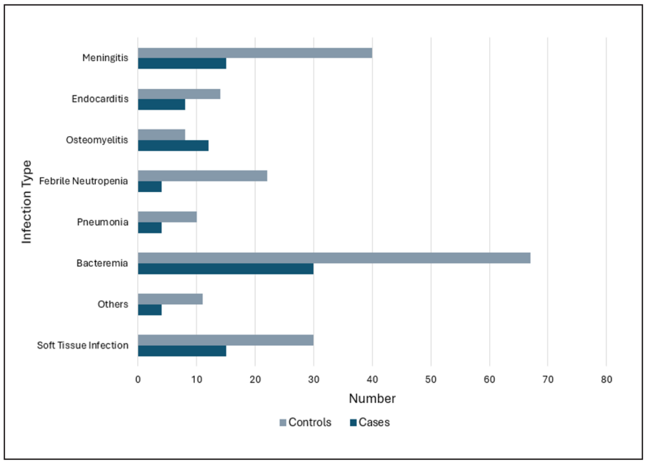

Figure 1. Infectious diagnosis of the study patients

revealed four statistically significant factors. Among them, hematologic-oncologic disease and a body mass index greater than 23 were associated with subtherapeutic vancomycin levels, while age > 75 years and creatinine levels greater than 0.7 mg/dL were protective factors.

The diagnosis of hematologic-oncologic disease showed a stronger association than the other variables, with the most frequent diagnoses including solid and mixed hematologic neoplasms, followed by non-Hodgkin lymphoma and acute myeloid leukemia. This result is primarily attributed to pharmacokinetic variables such as increased vancomycin clearance and a larger volume of distribution, as described in the study by Buelga et al., which included 215 patients in a one-compartment pharmacokinetic model with a diagnosis of hematologic-oncologic disease[14].

Additionally, the presence of febrile neutropenia can lead to subtherapeutic vancomycin levels due to increased distribution volume and clearance. In the study by Choi et al., which evaluated neutropenic versus non-neutropenic patients regarding subtherapeutic levels, an Odds Ratio of 1.72 (95% CI 1.06-2.79; P=0.029) was found between subtherapeutic vancomycin levels and the presence of neutropenia. Although the biological plausibility of this finding is not established, it is believed to be due to reduced neutrophil-bacteria interaction, increasing vancomycin binding to bacterial walls, resulting in higher consumption and consequently lower serum levels (reduced post-antibiotic effect)[5]. Another study by Haeseker et al. included 171 patients, 56 of whom were neutropenic, and found increased vancomycin clearance potentially related to increased renal blood flow, genetic factors, younger age, other medications, and neutropenia [31]. In our study, febrile neutropenia was present in 68 patients (23.12%), but no statistically significant differences were observed, unlike in other studies[5,31].

The increased distribution volume in patients with hematologic neoplasms suggests that higher vancomycin doses are required to achieve effective levels[30]. This was evaluated using a Monte Carlo simulation in a study by Fernández de Gatta et al. in a hemato-oncologic population, who found that doses of 3000-4000 mg/day were required to achieve a high probability of clinical response when *Staphylococcus aureus* was susceptible, and calculated the cumulative response fraction for different Staphylococcus strains[26]. Similarly, Haeseker et al. suggested a 33% dose adjustment to achieve therapeutic levels in neutropenic patients [31], which is presumed to be related to higher clinical effectiveness [30]. However, in this study, no statistically significant differences were found in the distribution volume values calculated using the Ambrose-Winter method[12].

Another evaluated variable was body mass index, where a value greater than 25 had an odds ratio of 1.15 (95% CI 1.07-1.21; P<0.001). Despite being statistically significant, the confidence interval was close to one, and the body mass index value was not clinically relevant nor directly related to obesity. Studies have concluded that obese patients exhibit different drug dispositions than non-obese patients, with changes in pharmacokinetic variables[30], including increased distribution volume, higher vancomycin clearance, and altered protein binding, reducing the free drug fraction. While this might suggest a relationship with low vancomycin levels, Richardson et al. documented serum levels of 16.6 mg/L versus 12.1 mg/L (P = 0.004) in obese versus non-obese patients, respectively[30].

Vancomycin is 80-90% excreted through the kidneys, with body clearance related to renal creatinine clearance, requiring adjustments for renal clearance values. The literature classically uses the Cockcroft-Gault formula, with equations like Modification of Diet in Renal Disease (MDRD) and CKD-EPI included. In the study by Conil et al. in ICU patients, these equations were compared, finding CKD-EPI to be the best predictor for vancomycin clearance calculation[30]. Unlike other studies in which CKD-EPI has been shown to be the best method for calculating vancomycin clearance in intensive care units, in our study, patients with subtherapeutic levels showed higher glomerular filtration rates calculated by both CKD-EPI and Cockcroft-Gault, although no statistically significant differences were observed.

In recent years, increased renal clearance has been described as a new phenomenon with an unclear etiology, which is more frequent in ICU patients. Minkute et al. evaluated the incidence of increased renal clearance in patients with vancomycin levels, finding lower serum creatinine levels, associated with conditions like sepsis, trauma, surgery, hematologic neoplasms, and burns, with up to twice the risk of subtherapeutic levels[27]. In our study, cases had lower creatinine levels than controls, acting as a protective factor with creatinine levels above 0.7 mg/dL.

Vancomycin clearance is related to renal clearance and patient age. It has been found that elderly patients may have decreased clearance[13]. In the study by Sanchez et al., patients under

Table 2. Demographic, clinical, pharmacokinetic, and hemato-oncological characteristics between cases and controls

Variable	Controls (n=202)	Cases (n=92)	p-value
Age, Median (IQR)	64 (53-73)	45.5 (33-58)	<0.001
Male sex, n(%)	112 (55.4)	55 (59.8)	0.48
Body mass index, Median (IQR)	23.4 (21.0-26.3)	24.4 (21.8-27.9)	0.03
Hemato-oncological diagnosis, n(%)	41 (20.3)	27 (29.3)	0.03
Type of hemato-oncological disease			0.015
Acute lymphoblastic leukemia, n(%)	2 (4.9)	4 (14.8)	
Acute myeloid leukemia, n(%)	2 (4.9)	8 (29.6)	
Hodgkin’s lymphoma, n(%)	2 (4.89)	0	
Non-Hodgkin’s lymphoma, n(%)	12 (29.3)	6 (22.2)	
Multiple myeloma, n(%)	1 (2.4)	2 (7.4)	
Others, n(%)	22 (53.7)	7 (25.9)	
Time since last chemotherapy, Median (IQR)	8 (5-14)	10 (7-13)	0.26
Concomitant aminoglycoside medications, n(%)	6 (3.0)	5 (5.6)	0.3
Vancomycin loading dose (mg/kg), Median (IQR)	30 (25.4-33.4)	30 (28.8-30)	0.33
Vancomycin maintenance doce (mg/kg), Median (IQR)	15.5 (13.9-18.1)	14.9 (12.7-16.6)	<0.001
Vancomycin level before fourth dose (mg/kg), Median (IQR)	15.1 (12.2-18.4)	6.7 (5.4-8.4)	<0.001
Presence of fever, n(%)	82 (40.6)	45 (49.4)	0.16
Febrile neutropenia, n(%)	41 (20.3)	27 (29.3)	0.08
Intravenous fluid volume (milliliter), Median (IQR)	3615 (1480-6930)	3745 (1321-7010)	0.74
Patients admitted to the ICU, n(%)	79 (39.1)	27 (29.6)	0.12
Creatinine (mg/dL), Median (IQR)	0.8 (0.7-1.1)	0.7 (0.6-0.9)	<0.001
Albumin (g/dL), Median (IQR)	2.6 (2.2-3.0)	2.7 (2.4-3.2)	0.12
Cockcroft-Gault GFR, Median (IQR)	70.3 (53.2-89.1)	1108 (92-1403)	<0.001
CKD-EPI GFR, Median (IQR)	84.8 (62.2-97.7)	105 (96.2-120)	<0.001
Volume of distribution, Median (IQR)	56.6 (386-1122)	59.7 (41.6-87.1)	0.51

(ICU) intensive care unit
(GFR) glomerular filtration rate, (IQR) Interquartile Range

65 years were compared with those over 65 using a two-compartment model, finding clearance values of 4.03±1.7 L/h in patients under 65 years compared to 2.24±1.2 L/h in those over 65 years[30]. Similarly, in the previously mentioned study by Minkute et al., age was statistically significant, with younger patients having higher vancomycin clearance and lower creatinine values (P=0.001) and levels below 0.4 mg/dL associated with subtherapeutic vancomycin levels[27]. Based on these findings, age > 75 years was identified as a protective factor for achieving therapeutic vancomycin levels.

This study has several limitations. First, it was an observational, retrospective, unicentric study. Regarding the vancomycin serum levels, the record corresponded to the sample taken before the fourth dose. However, the exact time of the sample was not established, assuming it was taken according to nursing protocol. Another limitation is that febrile neutropenia was not analyzed as a subgroup of hematologic-oncologic patients, which may have influenced the statistical significance of this variable. Additionally, the distribution volume calculation was based on previous studies, as we did not have software for population analysis, and these measurements were estimations.

It emphasizes the importance of early and individualized monitoring in populations at higher risk of subtherapeutic vancomycin levels, particularly those with hematologic-oncologic disease, febrile neutropenia, or augmented renal

Table 3. Factors Associated with Subtherapeutic Levels in the patients.

Variable	Odds Ratio	[95% CI]	p-value
Age over 75 years, Yes	0.96	0.93-0.96	<0.001
Hemato-oncological disease, Yes	2.12	1.53-4.88	0,004
Body mass index ≥25, Yes	1.15	1.07-1.21	<0.001
Creatinine over 0.7 mg/dl, Yes	0.08	0.01-0.11	<0.001

clearance. Based on the evidence and our findings, we recommend measuring vancomycin levels within the first 48 h after treatment initiation, with repeat monitoring every 48–72 h during the acute phase.

This corroborates that in patients with hematologic neoplasms or febrile neutropenia, vancomycin clearance may be altered, leading to sub-therapeutic levels. Some Latin American studies have demonstrated that population pharmacokinetic models allow optimization of vancomycin dosing in intensive care units by adjusting loading and maintenance doses, achieving concentrations closer to the therapeutic target range[32]. In Colombia, one study showed that vancomycin doses of 1 gram every 12 hours were insufficient for some patients with normal or elevated clearance, suggesting the need for higher doses as well as stricter monitoring[33]. Therefore, based on our results, we provide additional evidence that should be used to adapt local vancomycin dosing guidelines in Latin American oncologic populations, employing population modeling and early monitoring strategies to adjust doses according to renal clearance, body mass index, and the presence of neutropenia.

In conclusion, this is one of the few studies in Colombia that describes the sociodemographic characteristics of patients treated with vancomycin. It was determined that hemato-oncological disease is a factor associated with subtherapeutic vancomycin levels. This finding sets a precedent for this population, particularly in the context of febrile neutropenia, where monitoring of serum levels is justified and higher doses are required to achieve effective levels that allow for an adequate presumptive clinical response and help prevent resistance.

Other independent factors, such as age, body mass index, and creatinine levels, were also identified. These variables are closely related to pharmacokinetic parameters, such as drug clearance and volume of distribution. Additional pharmacokinetic studies are needed in special populations in our region to establish relationships with clinical outcomes. Likewise, specific studies on hemato-oncological populations are necessary to allow independent analysis of this group.

Ethical considerations

Protection of persons. Participation in the study was conducted in accordance with the principle of respect for people. All eligible participants were included only after meeting the predefined inclusion criteria, and their autonomy and dignity were respected throughout the research process. As this study involved the secondary analysis of clinical data, no direct intervention or modification of standard medical care was performed. The study posed minimal risk to participants, and all procedures were consistent with accepted ethical standards for human research.

Protection of vulnerable populations. The study population included patients who may be considered vulnerable due to their clinical condition. To ensure their protection, no experimental procedures were performed, and data collection was limited exclusively to information obtained during routine clinical care. The study did not involve coercion, undue influence, or differential treatment, and special care was taken to ensure that participation did not expose individuals to additional risks beyond those inherent to their medical condition.

Confidentiality. Confidentiality of participant information was strictly maintained. All data were anonymized prior to analysis, and personal identifiers were removed or replaced with unique study codes. Access to the database was restricted to authorized members of the research team, and the information was used exclusively for scientific and academic purposes.

Privacy. The study respected the privacy of participants by ensuring that no identifiable personal information was disclosed in reports, publications, or presentations derived from the research. Data were stored in secure, password-protected databases in accordance with institutional policies and national data protection regulations.

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Conflict of interests. The authors have no conflict of interest to declare.

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Data Availability Statement. The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request.

Authors´ contribution. DSP contributed to the conceptualization, EFM, GCP developed the methodology, EFM, AFP performed the research analysis, GCP, EFM, AFP, DSP prepared the original document, GCP, EFM, AFP, DSP reviewed and edited, EFM supervised. All authors contributed, read, and approved the submitted version of the manuscript.

References

1. Rodríguez-Rojas A, Rodríguez-Beltrán J, Couce A, Blázquez J. Antibiotics and antibiotic resistance: A bitter fight against evolution. Int J Med Microbiol. Elsevier GmbH.; 2013;303(6– 7):293–7. DOI: 10.1016/j.ijmm.2013.02.004
2. Rybak MJ. The pharmacokinetic and pharmacodynamic properties of vancomycin. Clin Infect Dis. 2006;42 Suppl 1(Suppl 1):S35–9. DOI: 10.1086/491712
3. Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the

treatment of methicillin-resistant Staphylococcus aureus infections in adults and children. Clin Infect Dis. 2011;52(3). DOI: 10.1093/cid/ciq146

4. Reardon J, Lau TTY, Ensom MHH. Vancomycin Loading Doses: A Systematic Review. Ann Pharmacother. 2015;29(5):557–65. DOI: 10.1177/1060028015571163
5. Hyuk M, Hwa Y, Lee S, Hoon S, Kim J. Neutropenia is independently associated with sub- therapeutic serum concentration of vancomycin. Clin Chim Acta. Elsevier B.V.; 2017;465:106– 11. DOI: 10.1016/j.cca.2016.12.021
6. Levine DP. Vancomycin : A History. Clin Infect Dis. 2006;48201:5–12. DOI: 10.1086/491709
7. Moellering RC. Vancomycin : A 50-Year Reassessment. Clin Infect Dis. 2006;42(Suppl 1):3–4. DOI: 10.1086/491708
8. Bruniera R. The use of vancomycin with its therapeutic and adverse effects: a review. Eur Rev Med Pharmacol Sci. 2015;19:694–700.
9. Mouton JW. Fundamentals of Antimicrobial Pharmacokinetics and Pharmacodynamics. 2014. 1- 467 p.
10. Bosso J a., Nappi J, Rudisill C, Wellein M, Bookstaver PB, Swindler J, et al. Relationship between vancomycin trough concentrations and nephrotoxicity: A prospective multicenter trial. Antimicrob Agents Chemother. 2011;55(12):5475–9. DOI: 10.1128/AAC.00168-11
11. Van Hal SJ, Paterson DL, Lodise TP. Systematic review and meta-analysis of vancomycin- induced nephrotoxicity associated with dosing schedules that maintain troughs between 15 and 20 milligrams per liter. Antimicrob Agents Chemother. 2013;57(2):734–44. DOI: 10.1128/AAC.01568-12
12. Leong J, Boro M, Winter M. Determining vancomycin clearance in an overweight and obese population. Am J Heal Pharm. 2011;68(119):599–603. DOI: 10.2146/ajhp100410
13. Marsot A, Boulamery A, Bruguerolle B, Simon N. Vancomycin A Review of Population Pharmacokinetic Analyses. Clin Pharmacokinet 2012; 2012;51(1):1–13. DOI: 10.2165/11596390-000000000-00000
14. Buelga DS, Fernandez M, Herrera E V, Dominguez-gil A. Population Pharmacokinetic Analysis of Vancomycin in Patients with Hematological Malignancies. Antimicrob Agents Chemother. 2005;49(12):4934–41. DOI: 10.1128/AAC.49.12.4934-4941.2005
15. Soni SS, Ronco C, Katz N, Cruz DN. Early diagnosis of acute kidney injury: The promise of novel biomarkers. Blood Purif. 2009;28(3):165–74. DOI: 10.1159/000227785
16. Turnidge JD, Kotsanas D, Munckhof W, Roberts S, Bennett CM, Nimmo GR, et al. Staphylococcus aureus bacteraemia: a major cause of mortality in Australia and New Zealand. Med J Aust. 2009;191(7):368–73. DOI: 10.5694/j.1326-5377.2009.tb02841.x
17. Paul M, Kariv G, Goldberg E, Raskin M, Shaked H, Hazzan R, et al. Importance of appropriate empirical antibiotic therapy for methicillin-resistant Staphylococcus aureus bacteraemia. J Antimicrob Chemother. 2010;65(12):2658–65. DOI: 10.1093/jac/dkq373
18. Robinson JO, Phillips M, Christiansen KJ, Pearson JC, Coombs GW, Murray RJ. Knowing prior methicillin-resistant Staphylococcus aureus (MRSA) infection or colonization status increases the empirical use of glycopeptides in MRSA bacteraemia and may decrease mortality. Clin Microbiol Infect. European Society of Clinical Infectious Diseases; 2014;20(6):530–5. DOI: 10.1111/1469-0691.12388
19. Rodvold K a., Blum R a., Fischer JH, Zokufa HZ, Rotschafer JC, Crossley KB, et al. Vancomycin pharmacokinetics in patients with various degrees of renal function. Antimicrob Agents Chemother. 1988;32(6):848–52. DOI: 10.1128/AAC.32.6.848
20. Matzke G, McGory R, Halstenson, Charles Keane W. Pharmacokinetics of Vancomycin in Patients with Various Degrees of Renal Function. Antimicrob Agents Chemother. 1984;25(5):433–7. DOI: 10.1128/AAC.25.4.433
21. Janson B, Thursky K. Dosing of antibiotics in obesity. Curr Opin Infect Dis. 2012;25(6):1. DOI: 10.1097/QCO.0b013e328359a4c1
22. Shimamoto Y, Fukuda T, Tanaka K, Komori K, Sadamitsu D. Systemic inflammatory response syndrome criteria and vancomycin dose requirement in patients with sepsis. Intensive Care Med. 2013;39(7):1247–52. DOI: 10.1007/s00134-013-2909-9
23. Matsumoto K, Takesue Y, Ohmagari N, Mochizuki T, Mikamo H, Seki M, et al. Practice guidelines for therapeutic drug monitoring of vancomycin: A consensus review of the Japanese Society of Chemotherapy and the Japanese Society of Therapeutic Drug Monitoring. J Infect Chemother. Elsevier; 2013;19(3):365–80. DOI: 10.1007/s10156-013-0599-4
24. Rybak M, Lomaestro B, Rotschafer JC, Moellering R, Craig W, Billeter M, et al. Therapeutic monitoring of vancomycin in adult patients: A consensus review of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, and the Society of Infectious Diseases Pharmacists. Am J Heal Pharm. 2009;66(1):82–98. DOI: 10.2146/ajhp080434
25. Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children: Executive summary. Clin Infect Dis. 2011;52(3):285–92. DOI: 10.1093/cid/ciq146
26. Fernandez de gatta M, Buelga DS, Sánchez A, Dominguez-gil A, Garcia MJ. Vancomycin Dosage Optimization in Patients with Malignant Haematological Disease by Pharmacokinetic / Pharmacodynamic Analysis. 2009;48(4):273–80. DOI: 10.2165/00003088-200948040-00005
27. Minkute R, Briedis V, Steponavičiute R, Vitkauskiene a., Mačiulaitis R. Augmented renal clearance - An evolving risk factor to consider during the treatment with vancomycin. J Clin Pharm Ther. 2013;38(6):462–7. DOI: 10.1111/jcpt.12088
28. Mohr JF, Murray BE. Point: Vancomycin is not obsolete for the treatment of infection caused by methicillin-resistant Staphylococcus aureus. Clin Infect Dis. 2007;44(12):1536–42. DOI: 10.1086/518451
29. Steinmetz T, Eliakim-Raz N, Goldberg E, Leibovici L, Yahav D. Association of vancomycin serum concentrations with efficacy in patients with MRSA infections: a systematic review and meta-analysis. Clin Microbiol Infect. Elsevier Ltd; 2015;21(7):665–73. DOI: 10.1016/j.cmi.2015.04.003
30. Cataldo MA, Tacconelli E, Grilli E, Pea F, Petrosillo N. Continuous versus intermittent infusion of vancomycin for the treatment of gram-positive infections: Systematic review and meta-analysis. J Antimicrob Chemother. 2012;67(1):17–24. DOI: 10.1093/jac/dkr442
31. Haeseker MB, Croes S, Neef C, Bruggeman CA, Stolk LML, Verbon A. Vancomycin Dosing in Neutropenic Patients. PLoS One. 2014;9(11):e112008. DOI: 10.1371/journal.pone.0112008
32. Amador JS, Vega Á, Araos P, Quiñones LA, Amador CA. A Successful Experience of Individualized Vancomycin Dosing in Critically Ill Patients by Using a Loading Dose and Maintenance Dose. Pharmaceuticals (Basel). 2025;18(5):677. DOI: 10.3390/ph18050677.
33. Parra González D, Pérez Mesa JA, Cuervo Maldonado SI, Díaz Rojas JA, Cortés JA, Silva Gómez E, et al. Pharmacokinetics of Vancomycin among Patients with Chemotherapy-Associated Febrile Neutropenia: Which Would Be the Best Dosing to Obtain Appropriate Exposure? Antibiotics (Basel). 2022;11(11):1523. DOI: 10.3390/antibiotics11111523.