Vancomycin dosing in an obese patient with acute renal failure: A case report and review of literature

Kun-Yan Xu, Dan Li, Zhen-Jie Hu, Cong-Cong Zhao, Jing Bai, Wen-Li Du

Specialty type: Pharmacology and pharmacy
Provenance and peer review: Unsolicited article; Externally peer reviewed.
Peer-review model: Single blind

Abstract

BACKGROUND
Vancomycin is the most commonly used drug for methicillin-resistant Staphylococcus aureus. The empirical clinical doses of vancomycin based on non-obese patients may not be optimal for obese ones.

CASE SUMMARY
This study reports a case of vancomycin dosing adjustment in an obese patient (body mass index 78.4 kg/m²) with necrotizing fasciitis of the scrotum and left lower extremity accompanied with acute renal failure. Dosing adjustment was performed based on literature review and factors that influence pharmacokinetic parameters are analyzed. The results of the blood drug concentration monitoring confirmed the successful application of our dosing adjustment strategy in this obese patient. Total body weight is an important consideration for vancomycin administration in obese patients, which affects the volume of distribution and clearance of vancomycin. The alterations of pharmacokinetic parameters dictate that vancomycin should be dose-adjusted when applied to obese patients. At the same time, the pathophysiological status of patients, such as renal function, which also affects the dose adjustment of the patient, should be considered.

CONCLUSION
Monitoring vancomycin blood levels in obese patients is critical to help adjust the dosing regimen to ensure that vancomycin concentrations are within the effective therapeutic range and to reduce the incidence of renal injury.

Key Words: Vancomycin; Obesity; Acute renal failure; Pharmacokinetics; Case report

©The Author(s) 2022. Published by Baishideng Publishing Group Inc. All rights reserved.
Core Tip: We report the medical records of dose adjustment of vancomycin in an obese patient (body weight 240 kg), including the dose adjustment protocol in acute renal injury. This article also reviews the current literature on the application of vancomycin in the obese population and provides recommendations on how to make dose adjustments based on available evidence.

Citation: Xu KY, Li D, Hu ZJ, Zhao CC, Bai J, Du WL. Vancomycin dosing in an obese patient with acute renal failure: A case report and review of literature. World J Clin Cases 2022; 10(18): 6218-6226
URL: https://www.wjgnet.com/2307-8960/full/v10/i18/6218.htm
DOI: https://dx.doi.org/10.12998/wjcc.v10.i18.6218

INTRODUCTION
Since 1980, the prevalence of obesity has more than doubled worldwide. It is estimated that by 2030, 60% of the world's adult population will be classified as obesity[1]. In the United States from 2013 to 2014, the prevalence of obesity was 35.0% for male and 40.4% for female adults, and there was a significant linear increasing trend among women in the prevalence of obesity from 2005 through 2014 [2]. Obesity has also become a major public health burden in China. Over the past 40 years, the prevalence of obesity has increased significantly. The nationally representative survey showed that more than half of the Chinese adults are obese according to the Chinese standards[3]. The increased prevalence of obesity poses a challenge for clinicians to deliver optimized doses of antimicrobial drugs in the intensive care unit. Obesity is a key risk factor for community and hospital-acquired infections[4], and increases risks of incidence and mortality compared to non-obese individuals[5]. It may affect the pharmacokinetics of antimicrobial agents, particularly in patients requiring high-dose antimicrobial therapy[6], and can also influence the immune response and increase susceptibility to infections[7], resulting in a high risk of infection in obese patients[8]. As a consequence, clinicians are increasingly facing severely obese patients requiring antibiotic treatment. However, few studies have summarised the published data and provided clinical guidance for effective dosing in these patients.

Since the early 1980s, as the number of methicillin-resistant Staphylococcus aureus (MRSA) infections began to increase, vancomycin has become the drug of first choice for this microbial infection[9]. Vancomycin belongs to glycopeptide antibiotic which acts by inhibiting bacterial cell wall synthesis[10]. It is the most widely used antibiotic worldwide for the treatment of severe Gram-positive bacterial infections[11]. The binding of vancomycin to protein is approximately 50% to 55%[10]. The volume of distribution is 0.4-1 L/kg[9]. Vancomycin is primarily cleared via renal excretion[12]. The actual body weight of obese subjects increases the chance of vancomycin exposure and the incidence of vancomycin-associated nephrotoxicity[13]. Therefore, dose adjustment is required when vancomycin is used in obese patients, because of the effect of obesity on vancomycin pharmacokinetic parameters. One study shows that therapeutic drug monitoring (TDM) significantly improves the clinical curative effect and reduces the incidence of nephrotoxicity in patients treated with vancomycin[14].

Although the pharmacokinetics of vancomycin in the general population is well-described, to the best of our knowledge, only a few studies have investigated the effect of vancomycin dose in the obese population. This study reports the medical records of dose adjustment of vancomycin in an obese patient weighing up to 240 kg, including the dose adjustment protocol in the acute renal injury. This article also reviews the current literature on the application of vancomycin in the obese population and provides recommendations on how to make dose adjustments based on the available evidence.

CASE PRESENTATION
Chief complaints
A 40-year-old man was referred to our intensive care unit (ICU), with the complaints of chest tightness and shortness of breath with no obvious cause for 3 mo.

History of present illness
In November 2020, the patient reported chest tightness and shortness of breath with no obvious cause. Three days later, the patient’s symptoms aggravated with abdominal distension and edema of both lower limbs. He was admitted to the ICU of a local hospital for acute respiratory failure. After 2 wk of treatment, the patient still had persistent fever and was transferred to the ICU of our hospital on November 18, 2020.
History of past illness
The patient had suffered from hypertension for 3 years and erysipelas of the right lower extremity for 2 years.

Personal and family history
The patient had no specific personal or family history.

Physical examination
The patient’s height and body weight were 175 cm and 240 kg, respectively. The patient had necrotizing fasciitis of the scrotum and left lower extremity, and large brown skin pigmentation of the left calf, and two approximately 2-cm surgical incisions with built-in gauze drainage and cloudiness drainage fluid were visible in the left thigh and the middle of the left calf (Figure 1).

Laboratory examinations
The culture of secretion revealed *Staphylococcus hemolyticus* at a local hospital.

Imaging examinations
There were no abnormal imaging data findings.

FINAL DIAGNOSIS
The final diagnoses were: (1) Sepsis; (2) Acute respiratory distress syndrome; (3) Pneumonia; (4) Heart failure; (5) Necrotizing fasciitis of the scrotum and left lower extremity; and (6) Severe obesity.

TREATMENT
The patient had pulmonary infection and *Staphylococcus hemolyticus* was detected in his secretion at the local hospital. His initial serum creatinine was 63.3 μmol/L and creatinine clearance (CrCl) was greater than 90 mL/min. Based on the patient’s history and drug sensitivity testing results, intravenous levofloxacin 0.75 g/d and tigecycline 0.2 g/d were started empirically for anti-infection treatment. Then, linezolid 0.6 g intravenous injection every 12 h was prescribed to replace levofloxacin, and the patient’s temperature decreased to normal after 3 d of treatment. On November 27, the patient developed a high fever (temperature up to 40.2 °C), and his high-sensitivity C-reactive protein (hs-CRP) rose to 183.51 mg/L (Table 1). Considering the infection from the lower extremity and the scrotum, the patient received enhanced drainage and dressing change. Meanwhile, the culture of sputum and scrotal revealed *Acinetobacter baumannii*. The linezolid was subsequently discontinued and intravenous infusion of vancomycin was started. Because the patient was severely obese, after reviewing the literature, we determined the dosing regimen of a loading dose (vancomycin administered as continuous infusion of 2 g over 2 h) and a maintenance dose (vancomycin 1 g infused over 60 min every 8 h). The vancomycin blood trough concentration was 11.7 μg/mL after the patient had received three doses of vancomycin. The patient developed acute renal failure due to the aggravation of infection, the serum creatinine levels showed a gradual increase, and the vancomycin trough concentration was greater than 20 μg/mL (up to 34.3 μg/mL). We then adjusted the vancomycin administration dose according to the blood drug concentration monitoring. On December 16, continuous renal replacement therapy (CRRT) was used because of anuria of the patient. Given using continuous veno-venous hemodiafiltration mode, we adjusted the vancomycin administration dose to 1 g every 12 h, during which vancomycin blood drug concentration fluctuated between 10 and 20 μg/mL.

OUTCOME AND FOLLOW-UP
The treatment produced significant improvement in the patient’s respiratory status and the infection. Vancomycin and CRRT treatment were subsequently discontinued on December 24. Two days later, the patient was transferred out of the ICU to continue treatment. He was well with no further complaints at the routine 1-mo follow-up.

DISCUSSION
In recent years, body mass index (BMI) is a world-accepted grading method to assess the degree of
Table 1 Changes of indicators during the patient’s hospitalization

| Check item/date                      | November 19 | November 28 | December 1 | December 11 | December 16 | December 20 | December 25 |
|--------------------------------------|-------------|-------------|------------|-------------|-------------|-------------|-------------|
| White blood cell count (× 10^9/L)    | 5.50        | 9.59        | 8.16       | 14.02       | 35.29       | 20.19       | 7.71        |
| Neutrophil percentage (%)            | 62.6        | 75.80       | 75.00      | 85.60       | 85.90       | 82.20       | 68.30       |
| Procalcitonin (ng/mL)                | 0.130       | 0.190       | 0.190      | 9.170       | 53.760      | 4.930       | 1.160       |
| High-sensitivity C-reactive protein (mg/L) | 183.51   | 194.91      | 140.00     | 68.80       | 99.00       | 22.30       | 8.91        |
| Serum creatinine (μmol/L)            | 67.8        | 61.8        | 48.9       | 266.8       | 453.1 (CRRT)| 120.9 (CRRT)| 264.1 (CRRT)|

CRRT: Continuous renal replacement therapy.

Figure 1 Infection of the left leg in the obese patient.

Obesity. According to the criteria of the guideline, obesity is defined as a BMI of 30.0 kg/m² or higher [15]. Based on the body weight and height of this patient, his BMI was calculated to be 78.4 kg/m², which met the threshold for obesity. Numerous physiopathological changes occur in obese individuals, including changes in distribution (Vd) and renal excretion [16].

Vancomycin is a time-dependent antibiotic and a number of factors influence its clinical activity, including variable tissue distribution, dose size, and clearance rate [17]. One study showed that total body weight (TBW) influenced the Vd and clearance (CL) of vancomycin (Table 2) [18]. As expected, obesity is a known factor affecting drug pharmacokinetics [19]. Vancomycin, as a hydrophilic drug, is able to penetrate and distribute, to a certain extent, in adipose tissues, thereby increasing the Vd [20]. A large retrospective study by Ducharme et al [21] showed that the Vd was greater in obese subjects than in normal subjects by examining pharmacokinetics of vancomycin in 704 patients. Blouin and his colleagues [22] also demonstrated statistically significant differences in weight-indexed Vd between two groups of subjects. A recent study suggests that Vd changes in obese patients can be ascribed to the physicochemical properties of the drugs in most cases [23]. In addition, the degree of the Vd depends on the lipophilicity, hydrophilicity, protein binding, and molecular weight of the antibiotic [24]. In the obese population, higher cardiac output and blood volume may increase blood flow, and lead to larger Vd [25]. Edema combined with fluid resuscitation can increase the Vd of different antibacterial agents in obese, critically ill patients [26].

Previous studies indicated that CL of vancomycin was much higher in the obese population, especially in young obese patients, and they required high doses to obtain adequate trough concentrations [5]. Han et al [27] demonstrated that obese adults exhibited higher drug clearance rates than non-obese ones. Unlike Vd, the physicochemical properties of drugs have little effect on CL, which is largely controlled by physiological processes [23]. The change in clearance was mainly attributed to an increase in kidney mass and renal blood flow in obese subjects [28]. Greater glomerular filtration rate and renal perfusion in obese individuals increase the CL of vancomycin [29]. At the same time, greater renal volume, hypertrophy of the renal unit, and hydrostatic pressure of the glomerulus were also associated
There was no increase in the volume

June 26, 2022

TBW should be considered for

6222

Issue 18

Volume 10

Strong correlations between TBW and

Ref.

Conclusions

Design

Table 2 Literature on dose adjustment analysis of vancomycin in obese patients

| Title (year)                                                                                                                                                                                                 | Design                                                                                     | Results                                                                                                                                                                                                 | Conclusions                                                                                                           | Ref.                |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------|---------------------|
| Pharmacokinetics of vancomycin in extremely obese patients with suspected or confirmed staphylococcus aureus infections (2015)                                                                           | Prospective pharmacokinetic study To assess vancomycin pharmacokinetic parameters in obese patients | When the minimum inhibitory concentration (MIC) was 1 μg/ml, the probability of the concentration-time curve (AUC)/MIC rate of 400 for vancomycin at 4000 to 5000 mg/d was 93%   | \( V_d \) and clearance of vancomycin were affected by total body weight, respectively                                        | Adane et al [18] |
| Vancomycin pharmacokinetics in a patient population: effect of age, gender, and body weight (1994)                                                                                                           | Retrospective review Comparative pharmacokinetics of vancomycin using steady-state peak and trough serum concentrations | \( V_d \) is 0.69 L/kg IBW in normal females compared with 0.58 in men                                                                                                                                  | Vancomycin dosing can be improved by adapting the initial estimates of \( V_d \) in obese people                          | Ducharme et al [21] |
| Vancomycin pharmacokinetics in normal and morbidly obese subjects (1982)                                                                                                                                   | An uncontrolled study Vancomycin pharmacokinetics was determined in normal and morbidly obese populations | Significant differences in mean terminal half-life and volume of distribution values between normal and morbidly obese individuals                                                                 | TBW should be used for dosing of vancomycin in obese individuals                                                     | Blouin et al [22]  |
| Vancomycin dosing in critically ill patients: robust methods for improved continuous-infusion regimens (2011)                                                                                            | A retrospective data collection To perform a pharmacokinetic analysis of vancomycin in subjects | Patients with a creatinine clearance of 100 ml/min/1.73 m² should receive a continuous infusion at least 35 mg/kg/d to maintain target concentrations | TBW should be considered for the initial dose                                                                      | Roberts et al [30] |
| Dosing vancomycin in the super obese: less is more (2018)                                                                                                                                                   | Retrospective study Determining an experiential vancomycin dosing strategy for obese individuals | Maintenance dose > 4500 mg/d is not required in obese patients to reach the pharmacodynamic AUC target                                                                                             | Using AUC-targeted TDM can optimize the treatment of obese adults                                                      | Crass et al [40]   |
| The pharmacokinetics of vancomycin during the initial loading dose in patients with septic shock (2016)                                                                                                         | A prospective, non-comparative study To investigate the pharmacokinetics of vancomycin in patients with early septic shock | The two-compartmental first-order elimination model                                                                                                                                          | In the early stages of septic shock, the total clearance of vancomycin increased, while the volumes of distribution of the central and peripheral compartments did not increase | Katip et al [52]   |
| Multicenter evaluation of vancomycin dosing: emphasis on obesity (2008)                                                                                                                                     | A random sampling Patients receiving vancomycin were categorised by body mass index and randomly chosen from the computer-generated query | Adequate initial doses were achieved in 93.9% of overweight patients and 27.7% of obese patients                                                                                                   | The patient receives a weight-based dose                                                                               | Hall et al [53]    |
| Performance of a vancomycin dosage regimen developed for obese patients (2012)                                                                                                                              | Retrospective review Comparison of original and revised dosing regimens for achieving target serum trough concentrations and occurrence of nephrotoxicity in obese subjects | Revised strategy resulted in a higher frequency of target troughs                                                                                                                                | Compared with the original strategy, the revised strategy improved the attainment of target trough concentrations with minimal nephrotoxicity | Reynolds et al [54]|

\( V_d \): Distribution; TBW: Total body weight; IBW: Ideal body weight; TDM: Therapeutic drug monitoring; AUC: Concentration-time curve; MIC: Minimum
with greater CL of vancomycin in the obese group[30]. Vancomycin is a hydrophilic drug with predominant renal excretion. Furthermore, augmented renal clearance (ARC), defined as a creatinine clearance more than or equal to 130 mL/min/1.73 m², refers to enhanced elimination of hydrophilic solutes by the kidneys[31]. The results indicate that ARC has been described in the obese, non-critically ill patient[32], and is a common finding in critically ill patients with normal plasma creatinine concentrations[33].

The option of vancomycin loading doses is dependent on the estimate of the $V_d$. Pharmacokinetic research has demonstrated that vancomycin $V_d$ increases with increasing TBW[34]. The physicochemical properties of drugs lead us not to define a universal body-size parameter for the distribution and clearance of drugs. As a consequence, the body weight was used in dose selection for drug administration[35]. One guideline states that a reasonable approach to the initial dose of vancomycin in obese individuals is to increase the loading dose to 20 to 25 mg/kg TBW and to decrease the maintenance dose, then adjust the dose according to TDM[36]. The 2020 Infectious Diseases Society of America (IDSA) consensus recommends the use of a TBW-based loading dose of 20 to 25 mg/kg in obese adults with severe infections, and considers capping doses of 3000 mg as the most practical dosing regimen[37].

Data have shown an excellent correlation between TBW and CL[38]. Thus, the empirical maintenance dose of vancomycin is dependent on the estimated CL[39]. The initial maintenance doses of vancomycin can be calculated by vancomycin CL and target AUC for obese population[18,40]. The 2020 IDSA consensus points out that the mean vancomycin CL in obese patients is approximately 6 L/h, which corresponds to an AUC of approximately 500 mg h/L at a daily dose of 3000 mg. The empirical vancomycin maintenance dose for obese adults should not exceed 4500 mg/d because vancomycin CL rarely goes beyond 9 L/h[37].

The pharmacodynamic parameter that best predicts the efficacy of vancomycin is the ratio of the area under the curve (AUC) to the minimum inhibitory concentration (MIC)[9]. In adult patients with suspected or definitive serious MRSA infection, the AUC/MIC ratio (assuming a vancomycin MIC of 1 mg/L) with targets between 400 and 600 was recommended in the American Society of Health-System Pharmacists (ASHP) 2020 guideline[37]. Based on the historical difficulty of AUC estimation in clinical practice, previous expert guidelines recommended monitoring trough concentrations as a surrogate marker for the AUC/MIC ratio[41]. The 2020 Evidence-based Guideline for Therapeutic Drug Monitoring of Vancomycin recommends maintaining vancomycin steady-state trough concentrations at 10–20 mg/L to achieve clinical efficacy and improve patient safety[42].

CRRT is a common treatment for critically ill patients with acute renal injury[43]. With advances in hemodialysis membrane technology, vancomycin is cleared substantially by effective and high-flux dialyzers[44]. Therefore, vancomycin dosing regimens for CRRT need to be changed, but there is no mention of CRRT dosing recommendations in the latest FDA-approved vancomycin package insert[45]. $V_d$ may be increased in CRRT patients compared to healthy individuals with normal kidney function[46]. During CRRT treatment, vancomycin CL remains a near-steady-state condition over the dosing interval, although vancomycin CL may decline over time as a result of hemodialysis filter plugging[46]. Vancomycin CL is closely related to the flow rate of ultrafiltration/dialysis solution[47]. The recommended loading dose for patients receiving CRRT is based on the actual TBW, at the dose of 20 to 25 mg/kg[48]. In order to achieve the generation of steady-state concentrations between 15 and 20 mg/L, a maintenance dose of 400 to 650 mg/12 h of vancomycin at an ultrafiltration flow rate of 30–40 mg/kg/h is recommended for most critically ill patients[49]. Due to the unstable clinical situation, vancomycin concentration must be strictly monitored in critical patients[50].

In summary, we report a case of adjusting the blood concentration of vancomycin with enhanced effectiveness in an obese patient. The initial TBW of the patient with normal renal function was 240 kg. Thus, the patient should receive an initial TBW-based load of 6 to 7.2 g of vancomycin every day. However, the dose of vancomycin is greater than 4 g/d, which increases the risk of nephrotoxicity[51]. Following the recommended dose limit of 3 g, the patient received an initial TBW-based loading dose of 2 g and a maintenance dose of 1 g of vancomycin every 8 h. The initial serum concentration of 11.7 μg/mL was obtained, after the patient had received three doses of vancomycin. The serum concentration demonstrated that the dosing regimen is reasonable. Due to acute renal failure with reduced urine output or even anuria, intravenous injection of vancomycin at 3 g/d led to a blood concentration of vancomycin that was higher than 20 μg/mL. We immediately reduced the dose of vancomycin and monitored the blood concentration of the drug. On the 29th day, the patient was treated with CRRT, the dosage regimen of vancomycin was 1 g every 12 h considering the clearance of vancomycin by CRRT, and the blood concentration was 13.3 μg/mL. The final blood concentration of vancomycin was maintained in the range of 10 to 20 mg/L.
CONCLUSION

The clinical dose of drugs administered is generally determined based on the results of pharmacokinetic studies and clinical trial studies in non-obese patients, which may not be optimal in obese individuals. Hence, the difference in pharmacokinetics of different drugs between obese and non-obese patients must be considered during drug treatment. Obesity is also associated with physiological changes that can alter the pharmacokinetics of vancomycin, and the selection of the dose of vancomycin administered needs to take into account the effect of the body weight of patients. Furthermore, both the loading dose and the maintenance dose are different from non-obese patients. During treatment, we should make appropriate dose adjustments based on the patient's therapeutic drug monitoring and renal function. At the same time, altered pharmacokinetics of antibacterial drugs may require dose individualization to achieve target concentrations. Adjustment of loading dose and maintenance dose is critical for the antibiotic treatment in obese patients using vancomycin. Unfortunately, limited data are available analyzing vancomycin concentrations in obese patients.

ACKNOWLEDGEMENTS

We thank the intensive care unit multidisciplinary team of the Fourth Hospital of Hebei Medical University for their treatment support.

FOOTNOTES

Author contributions: Bai J and Du WL conceived the manuscript; Xu KY drafted the manuscript; Li D monitored blood vancomycin concentrations; Hu ZJ was involved in drug therapy; Zhao CC was responsible for the patient.

Supported by the Hebei Natural Science Foundation of China, No. H2019206614.

Informed consent statement: Informed written consent was obtained from the patient for publication of this report and any accompanying images.

Conflict-of-interest statement: The authors declare that they have no conflict of interest to disclose.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

Country/Territory of origin: China

ORCID number: Kun-Yan Xu 0000-0002-5416-9288; Dan Li 0000-0002-5863-6234; Zhen-Jie Hu 0000-0002-9528-8371; Cong-Cong Zhao 0000-0002-1298-6351; Jing Bai 0000-0002-2717-6458; Wen-Li Du 0000-0002-4208-0008.

REFERENCES

1. Kelly T, Yang W, Chen CS, Reynolds K, He J. Global burden of obesity in 2005 and projections to 2030. Int J Obes (Lond) 2008; 32: 1431-1437 [PMID: 18607383 DOI: 10.1038/ijo.2008.102]
2. Flegal KM, Kruszon-Moran D, Carroll MD, Fryar CD, Ogden CL. Trends in Obesity Among Adults in the United States, 2005 to 2014. JAMA 2016; 315: 2284-2291 [PMID: 27272580 DOI: 10.1001/jama.2016.6458]
3. Pan XF, Wang L, Pan A. Epidemiology and determinants of obesity in China. Lancet Diabetes Endocrinol 2021; 9: 373-392 [PMID: 34022156 DOI: 10.1016/S2213-8587(21)00045-0]
4. Huttunen R, Syrjänen J. Obesity and the risk and outcome of infection. Int J Obes (Lond) 2013; 37: 333-340 [PMID: 23546772 DOI: 10.1038/ijo.2012.62]
5. El-Sohl A, Sikka P, Bozkanat E, Jaafar W, Davies J. Morbid obesity in the medical ICU. Chest 2001; 120: 1989-1997 [PMID: 11742933 DOI: 10.1378/chest.120.6.1989]
Smit C, Prodam F, Morald A, Giglione E, Demarchi I, Bellone S, Bona G. Obesity and infection: two sides of one coin. Eur J Pediatr 2014; 173: 25-32 [PMID: 24146165 DOI: 10.1007/s00431-013-2178-1]

Hainer V, Zamrazilová H, Kaněšová M, Bendlová B, Aldhoun-Hainerová I. Obesity and infection: reciprocal causality. Physiol Res 2015; 64: S105-S119 [PMID: 26680472 DOI: 10.3354/physiores.933130]

Falagas ME, Kompoti M. Obesity and infection. Lancet Infect Dis 2006; 6: 438-446 [PMID: 16793864 DOI: 10.1016/S1473-3099(06)70523-0]

Rybak M, Lomaestro B, Rotschafer JC, Moellering R Jr, Craig W, Billeter M, Dalavissio JR, Levine DP. 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 Health Syst Pharm 2009; 66: 82-98 [PMID: 19106348 DOI: 10.2146/ajhp080434]

Schilling A, Neuner E, Rehm SJ. Vancomycin: a 50-something-year-old antibiotic we still don't understand. Cleve Clin J Med 2011; 78: 465-471 [PMID: 21724292 DOI: 10.3949/ccjm.78a.10168]

Marsot A, Boulamery A, Bruguierolle B, Simon N. Vancomycin: a review of population pharmacokinetic analyses. Clin Pharmacokinet 2012; 51: 1-13 [PMID: 22149255 DOI: 10.2165/11596390-000000000-00000]

Polso AK, Lassiter JL, Nagel JL. Impact of hospital guideline for weight-based antimicrobial dosing in morbidly obese adults and comprehensive literature review. J Clin Pharm Ther 2014; 39: 584-608 [PMID: 25025361 DOI: 10.1111/jcpt.12200]

Choi YC, Saw S, Soliman D, Bingham AL, Pontiggia L, Hunter K, Chuang L, Siemianowski LA, Ereshefsky B, Hollands JM. Intravenous Vancomycin Associated With the Development of Nephrotoxicity in Patients With Class III Obesity. Ann Pharmacother 2017; 51: 937-944 [PMID: 28709394 DOI: 10.1177/1060028017720946]

Ye ZK, Tang HL, Zhai SD. Benefits of therapeutic drug monitoring of vancomycin: a systematic review and meta-analysis. PLoS One 2013; 8: e77169 [PMID: 24204764 DOI: 10.1371/journal.pone.0077169]

Jensen MD, Ryan DH, Apovian CM, Arulk J, Comuzzie AG, Donato KA, Hu FB, Hubbard VS, Jakicic JM, Kashmir RF, Loria CM, Millen BE, Nonas CA, Pi-Sunyer FX, Stevens VJ, Wadden TA, Wolfe BM, Ye ZK. Vancomycin dosing in obese adults. Crit Care Med 2014; 42 Suppl 1: S35-S39 [PMID: 26233118 DOI: 10.1097/CCM.0000000000000029]

Hanrahan TP, Lindmark J, Roberts JA. Antibiotic dosing in obesity: a BIG challenge. Crit Care 2016; 20: 240 [PMID: 27506612 DOI: 10.1186/s13054-016-1426-y]

Grace E. Altered vancomycin pharmacokinetics in obese and morbidly obese patients: what we have learned over the past 30 years. J Antimicrob Chemother 2012; 67: 1305-1310 [PMID: 22382471 DOI: 10.1093/jac/dks066]

Ducharme MP, Slaughter RL, Edwards DJ. Vancomycin pharmacokinetics in a patient population: effect of age, gender, and body weight. Ther Drug Monit 1994; 16: 513-518 [PMID: 7846752 DOI: 10.1093/tdm/16.5.513]

Blouin RA, Bauer LA, Miller DD, Record KE, Griffen WO Jr. Vancomycin pharmacokinetics in normal and morbidly obese subjects. Antimicrob Agents Chemother 1982; 21: 575-580 [PMID: 7081978 DOI: 10.1128/ AAC.21.4.575]

Hanley MJ, Baptista JP, Lim NL, Joynt GM, Jarrett P, Wockner L, Boots RJ, Lipman J. Augmented renal clearance in the ICU: results of a multicenter observational study of renal function in critically ill patients with normal plasma creatinine concentrations. Crit Care Med 2014; 42: 520-527 [PMID: 24201175 DOI: 10.1097/CCM.0000000000000292]
Population pharmacokinetics of vancomycin in obesity: Finding the optimal dose for (morbidly) obese individuals. Br J Clin Pharmacol 2020; 86: 303-317 [PMID: 31661553 DOI: 10.1111/bcp.14144]

35 Pai MP. Drug dosing based on weight and body surface area: mathematical assumptions and limitations in obese adults. Pharmacotherapy 2012; 32: 856-868 [PMID: 22711238 DOI: 10.1002/j.1553-6505.2012.01108.x]

36 Meng L, Mui E, Holubar MK, Deresinski SC. Comprehensive Guidance for Antibiotic Dosing in Obese Adults. Pharmacotherapy 2017; 37: 1415-1431 [PMID: 28869666 DOI: 10.1002/phar.20823]

37 Rybak MJ, Le J, Lodise TP, Levine DP, Bradley JS, Liu C, Mueller BA, Pai MP, Wong-Beringer A, Rotschafer JC, Rodvold KA, Maples HD, Lomaestro BM. Therapeutic monitoring of vancomycin for serious methicillin-resistant Staphylococcus aureus infections: A revised consensus guideline and review by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists. Am J Health Syst Pharm 2020; 77: 835-864 [PMID: 32191793 DOI: 10.1093/jhjp/xxaa036]

38 Bauer LA, Black DJ, Lill JS. Vancomycin dosing in morbidly obese patients. Eur J Clin Pharmacol 1998; 54: 621-625 [PMID: 9860149 DOI: 10.1007/s002800505254]

39 Roberts JA, Taconce FS, Udy AA, Vincent JL, Jacobs F, Lipman J. Vancomycin dosing in critically ill patients: robust methods for improved continuous-infusion regimens. Antimicrob Agents Chemother 2011; 55: 2709-2710 [PMID: 21402850 DOI: 10.1128/AAC.01708-10]

40 Crass RL, Dunn R, Hong J, Krop LC, Pai MP. Dosing vancomycin in the super obese: less is more. J Antimicrob Chemother 2018; 73: 3081-3086 [PMID: 30203073 DOI: 10.1093/jac/dky310]

41 Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ, Kaplan SL, Karchmer AW, Levine DP, Murray BE, J Rybak M, Talan DA, Chambers HF; Infectious Diseases Society of America. 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: e18-e55 [PMID: 21208910 DOI: 10.1093/cid/cjq146]

42 He N, Su S, Ye Z, Du G, He B, Li D, Liu Y, Yang K, Zhang X, Zhang Y, Chen X, Chen Y, Chen Z, Dong Y, Gu J, Guo D, Guo R, Hu X, Jiao Z, Li H, Liu G, Li Z, Lv Y, Lu W, Miao L, Qiu J, Sun T, Tong R, Wang L, Wang M, Wang R, Wen A, Wu J, Wu X, Xu Y, Yang Y, Yang F, Zhan S, Zhang B, Zhang C, Zhang H, Zhang J, Zhang W, Zhao L, Zhao R, Zhao W, Zhao Z, Zhou W, Zeng XT, Zhai S. Evidence-based Guideline for Therapeutic Drug Monitoring of Vancomycin: 2020 Update by the Division of Therapeutic Drug Monitoring, Chinese Pharmaceutical Society. Clin Infect Dis 2020; 71: S363-S371 [PMID: 33367582 DOI: 10.1093/cid/ciaa1536]

43 Clark WR, Mueller BA, Alaka KJ, Macias WL. A comparison of metabolic control by continuous and intermittent therapies in acute renal failure. J Am Soc Nephrol 1994; 4: 1413-1420 [PMID: 8161722 DOI: 10.1681/ASN.V471413]

44 Pallotta KE. Vancomycin use in patients requiring hemodialysis: a literature review. Semin Dial 2008; 21: 63-70 [PMID: 18251960 DOI: 10.1111/j.1525-139X.2007.00333.x]

45 Mueller BA, Smoyer WE. Challenges in developing evidence-based drug dosing guidelines for adults and children receiving renal replacement therapy. Clin Pharmacol Ther 2009; 86: 479-482 [PMID: 19844225 DOI: 10.1038/clpt.2009.150]

46 van de Vijsel LM, Walker SA, Walker SE, Yamashita S, Simor A, Hladunewich M. Initial vancomycin dosing recommendations for critically ill patients undergoing continuous venovenous hemodialysis. Can J Hosp Pharm 2010; 63: 196-206 [PMID: 22478979 DOI: 10.4212/cjhp.v63i3.915]

47 Covajes C, Scollleta S, Penacelli L, Ocampo-Martinez E, Abdelhaladi A, Beunmir M, Jacobs F, de Backer D, Vincent JL, Taconce FS. Continuous infusion of vancomycin in septic patients receiving continuous renal replacement therapy. Int J Antimicrob Agents 2013; 41: 261-266 [PMID: 23312601 DOI: 10.1016/j.ijantimicag.2012.10.019]

48 Kellum JA, Lameire N; KDIGO AKI Guideline Work Group. Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1). Crit Care 2013; 17: 204 [PMID: 23394211 DOI: 10.1186/cc13154]

49 Li Q, Liang F, Sang L, Li P, Lv B, Tan L, Liu X, Chen W. Pharmacokinetics of and maintenance dose recommendations for vancomycin in severe pneumonia patients undergoing continuous venovenous hemofiltration with the combination of predilution and postdilution. Eur J Clin Pharmacol 2020; 76: 211-217 [PMID: 31734748 DOI: 10.1007/s00228-019-02755-5]

50 Chailamorn W, Jitsurong A, Wiwattanawongs K, Wanakamanee U, Dandecha P. Vancomycin clearance during continuous venovenous haemofiltration in critically ill patients. Int J Antimicrob Agents 2011; 38: 152-156 [PMID: 21636256 DOI: 10.1016/j.ijantimicag.2011.04.010]

51 Lodise TP, Lomaestro B, Graves J, Drusano GL. Larger vancomycin doses (at least four grams per day) are associated with an increased incidence of nephrotoxicity. Antimicrob Agents Chemother 2008; 52: 1330-1336 [PMID: 18227177 DOI: 10.1128/AAC.01602-07]

52 Katip W, Jaruratanasirikul S, Pattcharachayakul S, Wongpoowarak W, Jitsurong A, Luckski A. The pharmacokinetics of vancomycin during the initial loading dose in patients with septic shock. Infect Drug Resist 2016; 9: 253-260 [PMID: 27920562 DOI: 10.2147/IDR.S121513]

53 Hall RG 2nd, Payne KD, Bain AM, Rahman AP, Nguyen ST, Eaton SA, Buski AJ, Vu SL, Bedimo R. Multicenter evaluation of vancomycin dosing: emphasis on obesity. Am J Med 2008; 121: 515-518 [PMID: 18501233 DOI: 10.1016/j.amjmed.2008.01.046]

54 Reynolds DC, Waite LH, Alexander DP, DeRyke CA. Performance of a vancomycin dosage regimen developed for obese patients. Am J Health Syst Pharm 2012; 69: 944-950 [PMID: 22610026 DOI: 10.2146/ajhp110324]
