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Case Report

Vancomycin Dosing Regimen in Patients with Hyper-Glomerular Filtration Rate: A Case Report

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ABSTRACT

Demonstrate a specific vancomycin regimen for patients with hyper-glomerular filtration rate that was used in clinical practice achieving the therapeutic Area Under the Curve (AUC) without nephrotoxicity incidence. 2020 guidelines recommend using the area under the curve to estimate vancomycin therapeutic concentration rather than using trough due to lower nephrotoxicity risk. However, there is insufficient evidence of the optimized vancomycin dose in patients with augmented renal clearance. In this population, vancomycin dosing is challenging because of the unmeasurable factors in the renal function or pharmacokinetics estimation methods; hence, an individualizing vancomycin dose is required to achieve the therapeutic goals. In our case reports, the optimized vancomycin dose regimen was warranted with augmented renal clearance to treat a suspected methicillin-resistant *Staphylococcus aureus*, by using the AUC-guided dose for the therapeutic concentration estimation. One case received a high vancomycin dose, while the other one was on the standard dose. Additional loading doses were used while continuing their current regimen. Thus, the therapeutic area under the curve was achieved but was close to the lower limit after one dose of additional loading dose without new incidence reports of acute kidney injury hospitalization. In conclusion, optimizing vancomycin dose regimen in patients with augmented renal clearance is still challenging in practice. Using an additional loading dose of vancomycin with continuation of the standard or higher dose of vancomycin, may help in achieving the area under the curve to the recommended therapeutic goal. Further studies are required in these populations.

Keywords: AUC, Hyper-Glomerular Filtration Rate, Pharmacokinetics, Quadriplegia, SCD, Vancomycin.

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INTRODUCTION

Vancomycin is a hydrophilic glycopeptide antibiotic commonly used for the treatment of serious gram-positive infections, particularly Methicillin-Resistant *Staphylococcus aureus* (MRSA) (Abdelmessih *et al*., 2022). It has a wide tissues distribution and is primarily renally eliminated (Adane *et al*., 2015; Aljutayli *et al*., 2020; Rybak *et al*., 2020). Because vancomycin exposure is closely linked to renal function, its pharmacokinetics demonstrate considerable interindividual variability, making dose optimization challenging in clinical practice (Fresquet *et al*., 2025; Marsot *et al*., 2012).

Several patient-specific factors influence vancomycin pharmacokinetics, including body weight, age, and renal clearance (Adane *et al*., 2015; Aljutayli *et al*., 2020). In selected populations, such as patients with Sickle Cell Disease (SCD) or severe neurological injury have Hyper-Glomerular Filtration Rate (HGFR) leading to subtherapeutic drug exposure with standard dosing regimens (Al-Eyadhy and Jelaify, 2022; Tesfamariam *et al*., 2024). Up to 65% of critically ill patients are particularly prevalent in individuals with SCD and patients with severe neurologic injury have HGFR (Eyadhy and Jelaify, 2022; Tesfamariam *et al*., 2024).

Pragmatically, vancomycin efficacy and safety guided by Therapeutic Drug Monitoring (TDM) to achieve the recommended therapeutic concentration for serious MRSA infection (Abdelmessih *et al*., 2022). 2020 guidelines recommend using Area Under the Curve (AUC)-guided vancomycin dosing for serious MRSA infections to optimize efficacy while minimizing nephrotoxicity at goal of AUC at 400-600 mg*h/L for lower risk of toxicity, particularly nephrotoxicity (Abdelmessih *et al*., 2022; Rybak *et al*., 2020; Xiao *et al*., 2022). Moreover, a

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prospective observational study shows that using a weight-based loading dose of vancomycin achieved a therapeutic AUC goal without a significant difference in Acute Kidney Injury (AKI) incidence (Hodiamont *et al.*, 2021).

Yet, there is no validated model for vancomycin dosing in adults with HGFR (Xiao *et al.*, 2022). Hence, monitoring vancomycin concentration and individualizing its dosing for these populations is required. This case reports describe using a different regimen in specific population with HGFR by re-administering a loading dose of vancomycin with a continuing the current standard regimen instead of increasing dose regimen to very high dose, to decrease the risk of AKI incidence and to achieve better therapeutic AUC.

CASE PRESENTATION # 1

Patient Description

A 19-year-old male with a history of homozygous sickle cell anemia, recurrent vaso-occlusive crises, and bilateral shoulder osteonecrosis was admitted for severe back and hip pain consistent with vaso-occlusive crisis. During hospitalization, he developed acute hypoxic respiratory failure secondary to Acute Chest Syndrome (ACS) complicated by multifocal pneumonia requiring Intensive Care Unit (ICU) admission and mechanical ventilation.

The patient's eGFR remained persistently elevated at 150-160 mL/min/1.73 m^2 throughout hospitalization. His total body weight was 102 kg, with an ideal body weight of 73 kg and an adjusted body weight of 84.6 kg.

Clinical Course and Investigations

Two days after admission, the patient developed AKI; however, Serum Creatinine (SrCr) rapidly normalized and remained stable between 0.4 and 0.6 mg/dL thereafter. During the hospitalization, his respiratory status deteriorated, prompting escalation of care. Chest radiography revealed a new left lower lobe opacity with mild cardiomegaly, consistent with ACS.

Microbiologic evaluation demonstrated MRSA colonization via nares swab and MRSA growth in sputum culture, while blood and urine cultures remained negative.

Treatment and Outcome

Empiric vancomycin therapy was initiated. The patient initially received two separate loading doses of 2 g on different days, followed by a scheduled regimen of 1,750 mg every 8 hr.

Following an additional 2 g dose and continuation of the 1,750 mg every 8-hr regimen, therapeutic vancomycin exposure was achieved, with AUC values consistently within the target range of 400-600 mg*h/L, as shown in Table 1. The total daily dose

Table 1: Summary of vancomycin doses and concentrations.

Date	SCr (mg/dL)	Loading dose (g) at (time)	Maintenance dose (g) at (time)	Random concentration (mcg/mL) at (time)	Trough concentration (mcg/mL) at (time)	AUC (mg*h/L)
3-Nov	0.6	.	.	.	.	.
5-Nov	1.5-1.7	.	.	.	.	.
5-Nov	.	2 @16:16	.	.	.	.
6-Nov	.	2 @18:50	.	5 @0430	.	207.6
7-Nov	0.8	.	.	6.6 @08:36	.	253.93
7-Nov	.	.	1 @12:16	.	.	.
7-Nov	.	.	1 @20:20	.	.	.
8-Nov	0.8	.	1 @0354	.	5.9 @11:00	293.09
8-Nov	.	.	1 @11:57	.	.	.
8-Nov	.	.	1.5 @16:55	.	.	.
9-Nov	0.6	.	1.5 @00:43	.	.	.
9-Nov	.	.	1.5 @ 09:00	.	6.9 @16:45	433.85
9-Nov	.	.	1.5 @17:22	.	.	.
10-Nov	0.5	.	1.75 @00:30	.	.	.
10-Nov	.	.	1.75 @16:34	.	11.4 @22:56	506.37
11-Nov	0.5	.	1.75 @01:05			470.62
11-Nov		2 @10:43	1.75 @20:38			
12-Nov	0.4	.	1.75 @04:13		12.3 @10:56	509.83

Table 2: Summary of vancomycin doses and concentrations.

Date	SCr (mg/dL)	Loading dose (g) at (time)	Maintenance dose (g) at (time)	Random concentration (mcg/mL) at (time)	Trough concentration (mcg/mL) at (time)	AUC (mg*h/L)
8-Dec	0.4	.	1 @17:13	.	.	.
9-Dec	0.3	.	1 @04:30	.	.	.
9-Dec	.	.	1 @16:52	.	.	.
10-Dec	0.4	1.25 @17:24	1 @04:35	.	10.5 @03:34	374
11-Dec	0.3	.	1 @05:46	.	.	.
11-Dec	.	.	1 @16:34	.	.	.
12-Dec	0.3	.	1 @05:37	.	12.6 @16:19	411

required was 5,250 mg, corresponding to approximately 52.5 mg/kg/day.

No evidence of nephrotoxicity was observed during therapy, as serum creatinine remained stable. The patient's respiratory status improved; he was successfully extubated, and vancomycin therapy was completed without adverse renal effects.

CASE PRESENTATION # 2

Patient Description

A 69-year-old female with past medical history of hypothyroidism, hypertension and hyperlipidemia. At the time of admission, eGFR was 80 mL/min; Total Body Weight (TBW) was 75.1 kg, Ideal Body Weight (IBW) was 50.1 kg, and Adjusted Body Weight (ABW) was 60.1 kg.

Clinical Course and Investigations

The patient initially presented with progressive bilateral upper and lower extremity weakness and paresthesia. Given the ascending pattern of symptoms, Guillain-Barre syndrome was strongly suspected, and neurology recommended therapeutic plasma exchange.

During hospitalization, the patient developed worsening respiratory function, with a decline in Negative Inspiratory Force (NIF) from 39 to -28 cm H_2O by hospital day 4, necessitating transfer to the intensive care unit. Her neurologic status progressed to flaccid quadriplegia, ultimately requiring endotracheal intubation and mechanical ventilation.

On hospital day 15, chest computed tomography angiography demonstrated bilateral lower lobe consolidations, and laboratory studies revealed leukocytosis, raising concern for ventilator-associated pneumonia. Vancomycin was initiated. Admission of blood cultures and MRSA nasal screening were negative. Respiratory cultures grew *Staphylococcus epidermidis*, and urine cultures yielded *Escherichia coli*, which were interpreted in the clinical context to distinguish colonization from infection.

Renal function remained stable throughout hospitalization, with serum creatinine ranging from 0.2 to 0.8 mg/dL and remaining between 0.2 and 0.4 mg/dL during vancomycin therapy, without evidence of acute kidney injury.

Treatment and Outcome

The patient was initiated on a scheduled dose of 1000 mg every 12 hr due to SCr of 0.4 mg/dL and CrCL of 127.8 mL/min. The following day, the patient experienced flaccid quadriplegia, and a vancomycin trough was obtained prior to the fourth dose. The trough was determined to be subtherapeutic at 10.5 mcg/mL, corresponding to an AUC of 374 mg*h/L, and the SCr remained stable at that time. Accordingly, the patient subsequently received another loading dose of 1250 mg and resumed the maintenance regimen of 1000 mg every 12 hr. A repeat trough was collected after receiving this loading dose and two doses of the scheduled regimen. The second trough measured 12.6 mcg/mL, corresponding to a therapeutic AUC of 411 mg*h/L. At that time, the patient's SCr further decreased to 0.3 mg/dL. The patient received two additional doses of the scheduled maintenance regimen prior to discontinuation of therapy. On the day of discontinuation, the patient's SCr further decreased to 0.2 mg/dL and without getting another vancomycin trough, as shown in Table 2.

DISCUSSION

In our case reports, AUC was used to evaluate vancomycin therapeutic concentration. Previously, the recommended concertation for serious MRSA infection was 15-20 mcg/mL (Abdelmessih *et al.*, 2022). However, compared with trough-based monitoring, AUC-guided approaches provide a more accurate representation of drug exposure (Lodise and Drusano, 2021). Multiple studies have demonstrated improved safety outcomes with AUC-guided monitoring; a previous prospective trial reported lower rates of Vancomycin-Associated Acute Kidney Injury (VA-AKI) with Bayesian AUC-guided dosing. Further, a recent meta-analysis confirmed a significantly reduced risk of

AKI compared with trough-based strategies (Abdelmessih *et al.*, 2022; Neely *et al.*, 2018).

Additional risk factors for VA-AKI that may contribute to the vancomycin dosing; include critical illness, elevated body weight, pre-existing renal dysfunction, and concurrent nephrotoxic medications (Altowayan *et al.*, 2023; Almeida *et al.*, 2019; Kim *et al.*, 2022). Maintenance of therapeutic AUC values likely contributed to the favorable renal outcome observed in this case (Robinson *et al.*, 2023).

Despite the general standard dose regimen of vancomycin of 15-20 mg/kg every 8-12 hr, there is no standard dose regimen for paraplegic patients or patients with HGFR (Lee, 2014; Sahraei *et al.*, 2022). In our case report for the SCD patient, despite this high-dose regimen, early vancomycin trough concentration and calculated AUC values were subtherapeutic, consistent with accelerated drug clearance in the setting of AR (Eyadhy and Jelaify, 2022; Tesfamariam *et al.*, 2024). A previous study shows that chronic anemia and increased renal blood flow contribute to glomerular hyperfiltration, resulting in enhanced elimination of renally cleared medications (Eyadhy and Jelaify, 2022). HGFR is commonly defined as an estimated Glomerular Filtration Rate (eGFR) exceeding 130 mL/min/1.73 m^2 and it is associated with subtherapeutic levels for some medications such as vancomycin (Tesfamariam *et al.*, 2024).

A previous study demonstrates that children with SCD and ACS exhibited significantly lower vancomycin trough concentrations and AUC values compared with non-SCD controls, even after dose adjustment. A negative correlation between CrCL and vancomycin AUC further supports the role of hyperfiltration in reduced drug exposure (Eyadhy and Jelaify, 2022; Sahraei *et al.*, 2022).

Moreover, a previous study shows that severe neurologic injury patients, such as paraplegic or quadriplegic patients, there are different mechanisms that lead to the HGFR such as the higher rate of metabolism (Cook and Hatton-Kolpek, 2019). Furthermore, a previous study shows lower vancomycin trough in the HGFR group compared with the normal renal function group who underwent neurosurgery (Chen *et al.*, 2020). However, the methods used for predicting eGFR and CrCL in paraplegic population do not include a paraplegic factor which may lead to a false HGFR (Lee, 2014).

On the other hand, even the more loading vancomycin doses were used in these two patients; no new AKI incidence occurred at the achieved goal of therapeutic AUC of 400-600 mg*h/L. This observation aligns with evidence suggesting that nephrotoxicity risk increases primarily when AUC values exceed 600-700 mg*h/L (Lodise and Drusano, 2021; Rybak *et al.*, 2020). A previous systematic review and meta-analysis shows that higher trough concentrations are associated with increased nephrotoxicity risk, emphasizing the advantage of AUC-based monitoring (van Hal *et al.*, 2013).

CONCLUSION

These two case reports illustrate the profound effect of HGFR on vancomycin pharmacokinetics in adults with sickle cell disease and quadriplegia. Standard dosing strategies may result in subtherapeutic exposure, placing patients at risk for treatment failure. Aggressive dose individualization and re-administering of loading dose with a continuing standard dose regimen of vancomycin might be associated with achieving the therapeutic goal of AUC without reporting new incidence of AKI in those two patients. Further prospective studies are needed to develop validated dosing regimen of vancomycin in patients with HGFR.

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ABBREVIATIONS

ABW: Adjusted Body Weight; **ACS:** Acute Chest Syndrome; **AKI:** Acute Kidney Injury; **AUC:** Area Under the Curve; **CrCL:** Creatinine Clearance; **eGFR:** Estimated Glomerular Filtration Rate; **HGFR:** Hyper-Glomerular Filtration Rate; **IBW:** Ideal Body Weight; **ICU:** Intensive Care Unit; **MRSA:** Methicillin Resistant Staphylococcus aureus; **NIF:** Negative Inspiratory Force; **SCD:** Sickle Cell Disease; **SCr:** Serum Creatinine; **TBW:** Total Body Weight; **TDM:** Therapeutic Drug Monitoring; **VA-AKI:** Vancomycin-Induced Acute Kidney Injury.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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