

Vancomycin-induced nephrotoxicity with unusual high serum trough level in a critically ill young patient

Yi Xin Cheng, Chee Ping Chong

Department of Clinical Pharmacy, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia

Address for correspondence:

Dr. Chee Ping Chong,
Department of Clinical Pharmacy, School of Pharmaceutical Sciences, Universiti Sains Malaysia, 11800 Minden, Penang, Malaysia.
E-mail: jjueping@gmail.com

ABSTRACT

Vancomycin-induced nephrotoxicity (VIN) occurs more commonly in the elderly, and the reported serum trough levels seldom exceed 80 mg/L. We present a case of VIN with serum trough levels exceeding 100 mg/L in a critically ill young patient with initially normal kidney function. The patient was admitted to the Intensive Care Unit after a motor vehicle accident. Vancomycin was initiated for methicillin-resistant *Staphylococcus aureus* infection localized in his cerebrospinal fluid. Vancomycin was administered for another 16 days, during which the serum trough levels remained below 10 mg/L, and the renal function tests were normal. After an increment in the vancomycin dose on day 17 from 750 mg every 6 h to 1 g every 6 h, the patient developed acute kidney injury during which his vancomycin trough level was 110.73 mg/L. The acute kidney injury resolved approximately 2 weeks after the discontinuation of vancomycin therapy. The present case highlights that critically ill patients on prolonged vancomycin therapy should be closely monitored, and dose increments should be made cautiously regardless of whether the patient is of young age or has low serum trough levels or normal renal function.

Key words: Acute kidney injury, critically ill, trough level, vancomycin-induced nephrotoxicity

INTRODUCTION

Vancomycin is a glycopeptide antibiotic with a Gram-positive spectrum of activity. It is commonly indicated for the treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) infection.^[1,2] The excretion of vancomycin is via kidney and deterioration in kidney function will leads to high vancomycin blood levels.^[1,2] Nephrotoxicity is a known adverse reaction of vancomycin, commonly occurs in the elderly with the reported serum toxic trough levels seldom exceeding 80 mg/L.^[1-3] We describe a case of reversible vancomycin-induced nephrotoxicity (VIN)

with serum trough level exceeding 100 mg/L in a critically ill young patient with baseline normal kidney function.

CASE REPORT

A 23-year-old, 75 kg male was admitted to the Intensive Care Unit following a motor vehicle accident. He had left frontoparietal cerebral abscess with isolated hydrocephalus. Intravenous vancomycin 1 g every 12 h was initiated for MRSA infection localized in his cerebrospinal fluid (CSF). The patient was

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concurrently treated with tablet N-acetylcysteine 600 mg every 12 h, tablet baclofen 10 mg every 12 h, tablet amlodipine 10 mg once daily, and subcutaneous enoxaparin 40 mg once daily. The vancomycin dose was increased to 750 mg every 6 h on the next day to achieve the desirable serum trough level (15–20 mg/L)^[4] for effective penetration into CSF. However, the therapeutic drug monitoring (TDM) results within the next 15 days showed subtherapeutic trough levels (<10 mg/L) when this patient was maintained on vancomycin 750 mg every 6 h [Figure 1]. The reason for the subtherapeutic trough levels of vancomycin was unclear. On day 10, tablet captopril 25 mg every 8 h was initiated to control the patient's high blood pressure. Captopril was initiated in this critically ill patient as it has a short half-life and any hypotensive event can be corrected shortly upon discontinuation of the therapy. His neutrophil count remained elevated (84.2% on day 13 and 96.6% on day 14) with no significant signs of improvement in his cerebral infection condition. However, the patient did not suffer through sepsis. In view of his normal kidney profile (serum creatinine [Scr] 0.28 mg/dL; blood urea nitrogen [BUN] 4.2 mg/dL; urine output 1.92 ml/kg/day), vancomycin dose was increased to 1 g every 6 h on day 17. The patient's serum potassium levels were in the range of 2.8–3.9 mmol/L between day 10 and day 17.

On day 18, after one dose of 1 g vancomycin, the patient's Scr and BUN increased to 0.90 mg/dL and 10.1 mg/dL, respectively. His serum trough level of vancomycin measured on day 20 was extraordinary high (110.73 mg/L) and therefore vancomycin was stopped. The tablet captopril was discontinued as well as to prevent further deterioration in kidney function. The patient's Scr and BUN continued to rise until they peaked at day 25 (6.64 mg/dL) and day 26 (91.3 mg/dL), respectively. His urine output dropped to 0.62 ml/kg/h on day 20. The acute kidney injury resolved approximately 2 weeks later. After the vancomycin trough level dropped to baseline on day 30, linezolid was initiated for the MRSA infection [Figure 1].

DISCUSSION

We reported a young patient developing VIN after 16 days of therapy as compared to the previous case series,^[1-3] which mostly involved the elderly with early onset on day 3 or day 4 of the therapy. The Naranjo *et al.* adverse drug reaction probability scale^[5] indicated a probable (score of 5) relationship between the patient's acute kidney injury and vancomycin

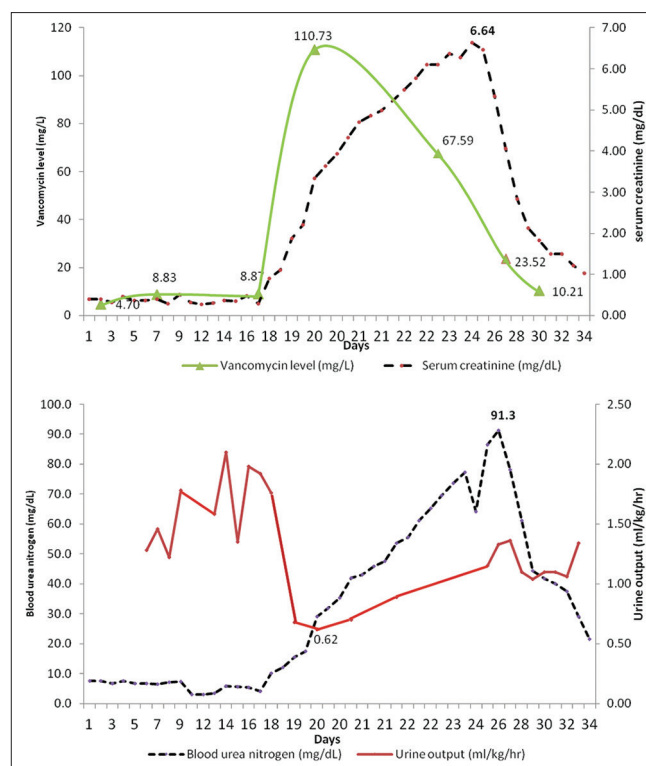


Figure 1: Evolution of serum vancomycin trough concentration, serum creatinine, blood urea nitrogen, and urine output

therapy. Although our patient had risk factors for VIN such as critically ill, severe head trauma, and on prolonged vancomycin therapy (>14 days),^[6] he had advantages of young age without preexisting kidney disease and low serum trough level throughout the therapy. The VIN in this case raises the concern that patients on prolonged vancomycin treatment should be closely monitored regardless of young age, low serum level, and normal kidney function.

We also noticed a huge raise in vancomycin dose when we reanalyzed the dosing regimen based on patient's actual body weight. He was started with 26.67 mg/kg/day (1 g every 12 h) of vancomycin for a day then raised to 40.00 mg/kg/day (750 mg every 6 h). After 15 days of subtherapeutic level, the dose was raised to 53.33 mg/kg/day (1 g every 6 h), and he developed nephrotoxicity immediately just after one high dose. Therefore, clinicians should be cautious in vancomycin dose increment to avoid nephrotoxicity, particularly for patients on long-term therapy.

Previous experimental studies revealed that VIN is due to oxidative stress which leads to tubular injury.^[7] Kidney impairment in association with vancomycin is identified when Scr increases more than 0.5 mg/dL or 50% from baseline (whichever is greater),^[4] as observed in our patient besides the BUN elevation.

These call for immediate vancomycin discontinuation or dose adjustment based on TDM results.^[4] The patient's captopril therapy may have increased the risk of nephrotoxicity as angiotensin converting enzyme inhibitors can decrease the glomerular capillary hydrostatic pressure.^[8] The cumulative effect of vancomycin and captopril therapy on the patient's kidney may have contributed to the acute kidney injury in this case. As renal Doppler examination was not performed in the patient to screen for renal artery stenosis, the possibility of captopril-induced acute kidney injury could not be excluded. Nevertheless, as the drastic kidney impairment was happened after the increment in the vancomycin dose, this finding suggested that the captopril therapy may not been the main contributing agent to the development of kidney impairment. Indeed, previous reported cases suggested that VIN is dose dependent.^[3] Close serum vancomycin monitoring is necessary when Scr and BUN are found to be on the rising trend to allow early detection of nephrotoxicity and therefore prompt dose adjustment. Apart from intermittent administration, continuous infusion of vancomycin is an alternative choice to significantly lower the risk of nephrotoxicity without compromising the efficacy.^[9]

CONCLUSION

Critically ill patients on prolonged vancomycin therapy should be closely monitored and cautious in dose increment regardless of young age, low serum trough levels, and normal kidney function throughout the treatment period.

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Conflicts of interest

There are no conflicts of interest.

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