

Clinical Considerations for Vancomycin Use in Chronic Kidney Disease

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ABSTRACT

Vancomycin remains vital for treating serious MRSA and other Gram-positive infections, but its use in chronic kidney disease (CKD) patients poses heightened challenges due to altered pharmacokinetics, risk of nephrotoxicity, and dosing complexity. Vancomycin induced nephrotoxicity is multifactorial, with risk factors including high trough concentrations, elevated area under the concentration-time curve (AUC), concurrent use of other nephrotoxic agents, prolonged therapy duration, and pre-existing renal impairment. Clinical manifestations range from mild serum creatinine elevation to acute kidney injury, potentially accelerating CKD progression. Traditional trough-based therapeutic drug monitoring (TDM) methods are increasingly seen as suboptimal.

Keywords: vancomycin, nephrotoxicity, chronic kidney disease, therapeutic drug monitoring.

I. INTRODUCTION

Vancomycin remains a critical antimicrobial for treating serious Methicillin-resistant *Staphylococcus aureus* (MRSA) and other multi drug-resistant Gram-positive infections, particularly in CKD patients where therapeutic options are limited.[1] Achieving the delicate balance between efficacy and safety is essential, as impaired renal clearance in CKD leads to drug accumulation and heightened risk of nephrotoxicity. [2]

In elderly individuals and those with CKD Stage 3-5, elevated vancomycin trough levels have consistently emerged as strong independent predictors of acute kidney injury (AKI). A retrospective cohort of older adults found that levels above 21.5 mg/L (CKD stage 3a) and 16.5 mg/L (CKD Stage 3b-5) corresponded to significantly increased risk of vancomycin-induced nephrotoxicity. [3]

■ Vancomycin can cause nephrotoxicity in up to

10 percent of patients, particularly with prolonged or high dose treatment.

- Regular renal function and drug level monitoring are essential to minimize the risk of kidney damage. Following clinical guidelines for vancomycin dosing and duration can enhance patient safety and therapeutic efficacy.

Implementation of dosing protocols that incorporate TDM has demonstrated meaningful reductions in AKI rates. In CKD patients, these monitoring and dosing challenges are exacerbated by fluctuating renal function, dialysis variability, and frequent comorbidities. This review synthesizes current evidence on vancomycin pharmacokinetics in CKD, compares monitoring strategies (trough vs AUC), explores dose-toxicity relationships.[4]

Pharmacokinetic alterations of vancomycin in CKD

Vancomycin is a glycopeptide antibiotic with hydrophilic properties, a narrow therapeutic index, and predominant renal elimination. In patients with chronic kidney disease (CKD), impaired renal clearance leads to a prolonged half-life of vancomycin and significant accumulation unless appropriate dose adjustments are made. This altered pharmacokinetic profile increases both the risk of nephrotoxicity and the likelihood of subtherapeutic or toxic concentrations without close monitoring.[5]

As renal function declines, the volume of distribution may increase slightly, but the most profound change in vancomycin clearance, which is linearly correlated with creatinine clearance. In patients with end stage renal disease (ESRD), vancomycin clearance becomes highly unpredictable, particularly in those undergoing intermittent hemodialysis.[6]

The introduction of AUC-guided dosing strategies has improved therapeutic precision.

Targeting an area under the concentration-time curve (AUC)/ minimum inhibitory concentration (MIC) of 400-600 mg./L is now recommended over traditional trough- based methods.[7]

Eliminating vancomycin is primarily through renal clearance, exhibiting a half-life of 4-6 hours in adults.[8]

Monitoring of vancomycin

Accurate monitoring of vancomycin exposure is critical in CKD patients due to their heightened risk of nephrotoxicity and altered pharmacokinetics. Traditionally, serum trough concentrations (15-20mg/l) have been used as surrogates for the therapeutic efficacy. Another meta-analysis confirmed that AUC guided monitoring may reduce the incidence of vancomycin-induced AKI versus trough-guided strategies, though mortality benefits remained less conclusive. Regular measurement of vancomycin concentrations, serum creatinine levels, and careful interpretation by healthcare providers balance clinical efficacy and patient safety.[9]

Vancomycin toxicity in CKD Patients.

Vancomycin-associated nephrotoxicity remains a significant concern in CKD patients due to altered pharmacokinetics, comorbidities, and longer expected drug exposure. Vancomycin induced acute kidney injury is observed in 5%-40% of treated patients, varying by dose, duration, and co existing risk factors such as CKD and nephrotoxins.[10]

Mechanisms

- Experimental and clinical evidence implicates oxidative stress, mitochondrial dysfunction, proximal tubular cell apoptosis.
- Histologically vancomycin-induced nephrotoxicity may present as acute tubular necrosis, interstitial nephritis, or acute nephropathy, which may be reversible upon discontinuation.[11]

Clinical implications in CKD

- CKD patients frequently have high baseline vulnerability, making them susceptible to cumulative vancomycin exposure even at moderate dosing.
- Combination therapy with other nephrotoxic drugs-especially piperacillin-tazobactam further compounds AKI risk.
- Elevated vancomycin troughs are a convenient

surrogate for AKI risk; however, AUC guided dosing better predicts safety outcomes.[12]

- Pre-existing CKD further predisposes patients to toxicity even at moderate vancomycin exposures, due to impaired clearance and accumulation.
- Most VA-AKI cases in CKD patients are multifactorial, often involving prolonged therapy, nephrotoxic comorbidities, and high baseline comorbidity burden.[13]

RISK FACTORS

1. Patient-specific Factors

- Pre-existing renal impairment (eGFR <60 ML/min/1.73m²) significantly increases vancomycin accumulation and toxicity.
- Obesity alters drug distribution and clearance, leading to inappropriate exposure despite weight-based dosing.
- Comorbidities like diabetes mellitus, heart failure, and sepsis also compound the risk.[14]

2. Age:

Young individuals are at an increased risk of developing nephrotoxicity, possibly due to underdeveloped renal function. However, retrospective studies have also shown that elderly patients might be susceptible, possibly due to age-related decline in kidney function.

3. Vancomycin Exposure Factors

- High vancomycin trough levels (.15-20g/ml) are closely linked to nephrotoxicity.
- Prolonged therapy beyond 7-14days increases cumulative renal exposure.
- High daily doses (4g/day) are independently associated with a higher incidence of AKI.

4. Drug-Drug interactions

Co administration with other nephrotoxic agents such as:

- Piperacillin-tazobactam
- Amino glycosides
- NSAIDs
- Loop diuretics
- Amphotericin B
- These combinations increase the risk of synergistic tubular injury.

5. Critical illness and ICU Admission

- Patients admitted to the ICU often receive higher vancomycin doses due to altered pharmacokinetics.
- They are also exposed to multiple nephrotoxic drugs and may experience hemodynamic instability, which exacerbates the risk.

6. Genetic factors: certain genetic predispositions might elevate the risk of nephrotoxicity, though more research is needed to establish these connections.[15]

CLINICAL MANIFESTATIONS

- Proximal tubule injury: vancomycin can cause injury to the proximal tubule cells in the kidney, leading to impaired reabsorption of electrolytes and other solutes. This can result in proteinuria and glycosuria in young and adult patients.
- Electrolyte imbalances: the damage to the proximal tubule can lead to electrolyte imbalances, causing symptoms like muscle twitching, abnormal heart rhythms, and altered mental status.
- Acute kidney injury: vancomycin-induced AKI is a severe manifestation. This might lead to oliguria, fatigue, edema, and hypertension in adults. In pediatric patients, the symptoms might be less specific, including reduced urine output and poor growth.
- Chronic renal failure: Long- term exposure to vancomycin can cause irreversible damage to renal tissues, leading to chronic renal failure.[16]

ASSOCIATED AGENTS AND EFFECTS

- The concurrent use of vancomycin with other antibiotics, such as piperacillin-tazobactam and aminoglycosides, has complex implications for renal function. When combined with vancomycin, piperacillin-tazobactam has been found to increase the risk of nephrotoxicity, potentially contributing synergistically to renal function.
- Similarly, the combination of vancomycin with aminoglycosides presents a significant challenge. Both these agents are known to be nephrotoxic, and their combined administration can amplify the risk of acute renal failure and renal dysfunction.[17]

Practical dosing recommendations for vancomycin in CKD Patients

Managing vancomycin dosing in patients with chronic disease requires a patient- centered approach that integrates pharmacokinetics, renal function, and therapeutic drug monitoring strategies to avoid toxicity and ensure efficacy.

Initial loading dose

Recommended: 20-25mg/kg (based on total weight), irrespective of renal function. Pharmacokinetic monitoring and dose adjustment in CKD

- Frequent adjustments based on estimated glomerular filtration rate or measured creatinine clearance are essential.
- Bayesian dosing software can predict AUC early and individualize therapy, particularly helpful in CKD patients where vancomycin clearance is unpredictable.
- Avoidance of concomitant nephrotoxins
- Use of piperacillin-tazobactam, loop diuretics, NSAIDs, or amino glycosides should be minimized or avoided.
- When unavoidable, monitoring frequency should be increased, and shorter vancomycin courses should be considered.[18]

Shorter Duration

- Shorter courses (5-7 days) are often equally effective and reduce nephrotoxicity risk, especially in non- complicated MRSA bloodstream infections.
- AUC – based dosing is safer and more accurate than trough monitoring. Target: AUC/MIC= 400-600mg.h/L. [19]
- Renal function must be monitored frequently and dynamically.
- Shorten duration of therapy when appropriate.
- Dialysis-specific Considerations: Dosing after each dialysis session
- Monitor levels before next session to guide next dose.[20]

VANCOMYCIN PREVENTION

NEPHROTOXICITY

- Preventing vancomycin- associated nephrotoxicity requires an intricate, multifaceted approach that emphasizes understanding the specific risk factors of patients.

- Ensure adequate hydration to maintain renal perfusion, especially in hospitalized or critically ill patients.
- Regular evaluation of eGFR or CrCl is necessary to adjust maintenance doses.
- Implementing individualized doses should be based on the patient's weight, renal function, and severity of infection. Regular therapeutic monitoring of serum concentrations and biomarkers should be done during administration. This promotes precise dose adjustments.[21]
- The judicious use of vancomycin must be patient-centered, emphasizing evidence-based strategies. Healthcare professionals must commit to staying current with scientific literature.
- These collective efforts ensure the maximization of vancomycin's therapeutic benefits while minimizing the risk of nephrotoxicity.[22]

II. CONCLUSION

Preventing vancomycin nephrotoxicity in CKD requires a multi-pronged approach-careful dose selection, avoidance of harmful drug combinations, modern monitoring techniques, and patient specific adjustments. Early implementation of AUC-guided therapy and stewardship principles are essential in reducing avoidable kidney injury.

REFERENCES

- [1]. Ramirez-Osorio JF, Velez-Hernandez JE, Nathalia Fernandez-Castaño, Rojas-Hernandez DF, Jaimes F. Impact of Vancomycin trough levels monitoring on uncomplicated methicillin-resistant *Staphylococcus aureus* bacteremia in chronic kidney disease on hemodialysis, retrospective cohort. *BMC Infectious Diseases*. 2024 Jun 25;24(1).
- [2]. Baiocco GG, Greiner S, Rosa MB, Flores CD, Barros HMT. Impact of implementing a vancomycin protocol to reduce kidney toxicity: A comparative study. *Frontiers in Pharmacology*. 2023 Sep 28;14.
- [3]. Dai N, Jiang C, Wang Y. Relationship between vancomycin-induced nephrotoxicity and vancomycin trough concentration in older adults. *Indian Journal of Pharmacology* [Internet]. 2023 May 1 [cited 2025 Aug 15];55(3):155–61
- [4]. Vezina B. Safeguarding the Kidneys: A Comprehensive Guide to Vancomycin Nephrotoxicity Prevention • Dose Merx [Internet]. DoseMeRx. 2023. Available from: <https://dosemerx.com/vancomycin/articles/guide-to-vancomycin-nephrotoxicity-prevention>
- [5]. Colin PJ, Allegaert K, Thomson AH, Touw DJ, Dolton M, de Hoog M, et al. Vancomycin Pharmacokinetics Throughout Life: Results from a Pooled Population Analysis and Evaluation of Current Dosing Recommendations. *Clinical Pharmacokinetics*. 2019 Jan 17;58(6):767–80.
- [6]. Srour N, Lopez C, Succar L, Nguyen P. Vancomycin dosing in high-intensity continuous renal replacement therapy: A retrospective cohort study. *Pharmacotherapy*. 2023 Jul 26;43(10):1015–23.
- [7]. Finch NA, Zasowski EJ, Murray KP, Mynatt RP, Zhao JJ, Yost R, et al. A Quasi-Experiment to Study the Impact of Vancomycin Area under the Concentration-Time Curve-Guided Dosing on Vancomycin-Associated Nephrotoxicity. *Antimicrobial Agents and Chemotherapy* [Internet]. 2017 Sep 18;61(12). Available from: <https://aac.asm.org/content/aac/61/12/e01293>
- [8]. Patel S, Preuss CV, Bernice F. Vancomycin [Internet]. Nih.gov. Stat Pearls Publishing;2024. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK459263/>
- [9]. Tsutsuura M, Moriyama H, Kojima N, Mizukami Y, Tashiro S, Osa S, et al. The monitoring of vancomycin: a systematic review and meta-analyses of area under the concentration-time curve-guided dosing and trough-guided dosing. *BMC Infectious Diseases*. 2021 Feb 6;21(1).
- [10]. Carreno JJ, Kenney RM, Divine G, Vazquez JA, Davis SL. Randomized Controlled Trial to Determine the Efficacy of Early Switch from Vancomycin-to-Vancomycin Alternatives as a Strategy to Prevent Nephrotoxicity in Patients with Multiple Risk Factors for Adverse Renal Outcomes(STOP-NT). *Annals of Pharmacotherapy*. 2016 Nov 13;51(3):185–93.
- [11]. Vora S. Acute Renal Failure Due to

- Vancomycin Toxicity in the Setting of Unmonitored Vancomycin Infusion. Baylor University Medical Center Proceedings. 2016 Oct;29(4):412–3.
- [13]. Filippone E, Kraft W, Farber J. The Nephrotoxicity of Vancomycin. *Clinical Pharmacology & Therapeutics* [Internet]. 2017 Jun 5;102(3):459–69. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5579760/>
- [14]. Nachiappa Ganesh R, Edwards A, El Zaatari Z, Gaber L, Barrios R, Truong LD. Vancomycin nephrotoxicity: A comprehensive clinico-pathological study. *PloS One* [Internet]. 2024 [cited 2024 Apr 16];19(3):e0295136. Available from: <https://pubmed.ncbi.nlm.nih.gov/38452051/>
- [15]. Kim JY, Yee J, Yoon HY, Han JM, Gwak HS. Risk factors for vancomycin-associated acute kidney injury: A systematic review and meta-analysis. *British Journal of Clinical Pharmacology*. 2022 Jun 15;
- [16]. Bagshaw SM, George C, Bellomo R. Early acute kidney injury and sepsis: a multicenter evaluation. *Critical Care* [Internet]. 2008;12(2):R47. Available from: <http://ccforum.com/content/12/2/R47>
- [17]. Elyasi S, Khalili H, Dashti-Khavidaki S, Mohammadpour A. Vancomycin-induced nephrotoxicity: mechanism, incidence, risk factors and special populations. A literature review. *European Journal of Clinical Pharmacology* [Internet]. 2012 Mar 13;68(9):1243–55. Available from: <https://link.springer.com/article/10.1007%2Fs00228-012-1259-9>
- [18]. Rybak MJ, Le J, Lodise TP, Levine DP, Bradley JS, Liu C, et al. 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. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America* [Internet]. 2020 Jul 13; Available from: <https://pubmed.ncbi.nlm.nih.gov/32658968/>
- [19]. Tanuja Y, Shahrzad Z, Kwabena AN, Pooneh A. Incidence and risk factors of vancomycin-associated acute kidney injury in a single center: Retrospective study. *Journal of Clinical Nephrology*. 2021 Mar 8;5(1):010–6.
- [20]. Neely MN, Youn G, Jones B, Jelliffe RW, Drusano GL, Rodvold KA, et al. Are Vancomycin Trough Concentrations Adequate for Optimal Dosing? Antimicrobial Agents and Chemotherapy [Internet]. 2013 Oct 28;58(1):309–16. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3910745/>
- [21]. 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. *Antimicrobial Agents and Chemotherapy*. 2012 Nov 19;57(2):734–44.
- [22]. Nyman HA, Agarwal A, Senekjian HO, Leypoldt JK, Cheung AK. Removal of vancomycin administered during dialysis by a high-flux dialyzer. *Hemodialysis International*. 2018 Jan 30;22(3):383–7.
- [23]. Tantranont N, Luque Y, Hsiao M, Haute C, Gaber L, Barrios R, et al. Vancomycin-Associated Tubular Casts and Vancomycin Nephrotoxicity. *Kidney International Reports*. 2021 Jul;6(7):1912–22.