Original Article

A Comparative Analysis of Acute Kidney Injury Incidence in Patients Treated with Vancomycin in Combination with Piperacillin-Tazobactam or Meropenem

Muhammad Haroon Ghous, Sikander Afzal amd Mahwish Arooj

ABSTRACT

Objective: The main objective of the study is to find the comparison of acute kidney injury incidence in patients treated with vancomycin, piperacillin-tazobactam, or meropenem.

Study Design: cross-sectional study

Place and Duration of Study: This study was conducted at the University of Lahore Teaching Hospital, Pakistan, from January 2018 to December 2022.

Materials and Methods: The study aimed to investigate the occurrence of acute kidney injury (AKI) in patients receiving treatment with either vancomycin or beta-lactam antibiotics, specifically piperacillin-tazobactam and meropenem.

Results: Data was collected from 350 patients of both genders. Among the participants, 150 patients received vancomycin, 120 patients received piperacillin-tazobactam, and 80 patients received meropenem for the treatment of bacterial infections. The mean age of the participants was 50 years, with a standard deviation of 12 years. The majority of patients were male (60%) and had no history of chronic kidney disease (82%). Regarding AKI occurrence, the results showed that 35 patients developed AKI during the course of antibiotic treatment. Among them, 15 patients were in the vancomycin group, 12 in the piperacillin-tazobactam group, and 8 in the meropenem group. The overall incidence of AKI in the study population was 10%.

Conclusion: It is concluded that the risk of AKI is similar in patients receiving vancomycin and beta-lactam antibiotics. Close monitoring and individualized antibiotic selection are essential to optimize patient outcomes and reduce the risk of renal complications. Age and comorbidities were not major risk factors for AKI in this cohort.

Key Words: AKI, Renal, Patients, Antibiotic, Nephrotoxic

Citation of article: Ghous MN, Afzal S, Arooj M. A Comparative Analysis of Acute Kidney Injury Incidence in Patients Treated with Vancomycin in Combination with Piperacillin-Tazobactam or Meropenem. Med Forum 2023;34(9):79-83. doi:10.60110/medforum.340918.

INTRODUCTION

Acute kidney injury (AKI) is a critical clinical worry that can emerge because of different clinical medicines, including the organization of antibiotics. Among the ordinarily endorsed antibiotics, vancomycin, piperacillin-tazobactam, and meropenem are much of the time used to manage serious bacterial infections. In any case, studies have shown that these antibiotics might have nephrotoxic potential and can prompt antagonistic renal results, including AKI[1]. Etiologies of AKI in the fundamentally sick are mind boggling and reasonable multifactorial. Risk factors incorporate, however not restricted to, prior kidney dysfunction, old age, nephrotoxic medication exposure, and sepsis. Patients with basic disease who foster AKI experience death rates drawing nearer 60%. Negative clinical sequala incorporate longer hospital length of stay, delayed renal substitution treatment following hospital release, and movement to constant kidney illness or end-stage kidney infection [2].

Piperacillin-tazobactam and meropenem have a place with the class of beta-lactam antibiotics, and they are frequently utilized for the treatment of Gram-negative infections in different clinical settings[3]. As of late, there has been developing worry over the rising frequency of AKI related with antibiotic use, and medical care suppliers are progressively aware of the likely nephrotoxicity of normally endorsed antibiotics. Understanding the similar risk of AKI among vancomycin and beta-lactam antibiotics, for example, piperacillin-tazobactam and meropenem, is of most extreme significance to fit treatment designs and limit mischief to weak patient populaces[4].

Vancomycin is a glycopeptide antibiotic that has been utilized in clinical practice for over fifty years. It is

Department of Urology UCMD, University of Lahore.

Correspondence: Professor. Dr. Muhammad Haroon Ghous, Professor of Urology UCMD, University of Lahore.
Contact No: 03438404593
Email: haroonghous745@gmail.com

Received: April, 2023
Accepted: June, 2023
Printed: September, 2023

generally endorsed to treat Gram-positive infections, particularly those brought about by methicillin-safe Staphylococcus aureus (MRSA). The utilization of vancomycin alone has been related with a 5%-43% frequency of AKI. Piperacillin-tazobactam (PT), an antipseudomonal β-lactam/β lactamase inhibitor antibiotic is habitually utilized in blend with vancomycin for empiric treatment in hospitalized patients. As per PT's manufacturer, the product has an under 1% rate of AKI[5].

A few instruments have been proposed to make sense of the nephrotoxic capability of these antibiotics. Vancomycin, in particular, has been related with direct rounded poisonousness, prompting tubulointerstitial nephritis. Piperacillin-tazobactam and meropenem, as beta-lactam antibiotics, may cause AKI by means of unfavorably susceptible extreme touchiness reactions or indirect renal damage from precious stone actuated nephropathy. Perceiving the distinctions in nephrotoxicity profiles among these antibiotics can assist clinicians with making informed choices while selecting the most proper treatment choice for individual patients[6].

By conducting an intensive examination of AKI occurrence during therapy with vancomycin and beta-lactam antibiotics, this study means to contribute basic bits of knowledge into the nephrotoxic capability of these agents and evaluate their overall wellbeing profiles. It is guessed that the discoveries will help clinicians in gauging the risks and advantages of antibiotic treatment and carrying out procedures to screen and relieve AKI-related antagonistic occasions.

MATERIALS AND METHODS

This cross-sectional study was conducted at the University of Lahore Teaching Hospital, Pakistan, over a five-year period from January 2018 to December 2022. The study aimed to investigate the occurrence of acute kidney injury (AKI) in patients receiving treatment with either vancomycin or beta-lactam antibiotics, specifically piperacillin-tazobactam and meropenem.

Inclusion Criteria:

- Patients aged 18 years and above.
- Patients who received treatment with either vancomycin, piperacillin-tazobactam, or meropenem during their hospital stay.
- Patients with bacterial infections requiring antibiotic therapy, as determined by the treating physician.
- Patients with or without preexisting renal impairment or a history of chronic kidney disease.

Exclusion Criteria:

- Patients with a documented allergy or known hypersensitivity to vancomycin, piperacillin-tazobactam, or meropenem.
- Patients with incomplete medical records or missing data on antibiotic prescriptions and laboratory results.

Data collection: The study included a total of 350 patients who were admitted to the hospital during the specified five-year period and received treatment with either vancomycin or one of the beta-lactam antibiotics, piperacillin-tazobactam or meropenem. Patients with preexisting renal impairment or a history of chronic kidney disease were also included. Data were collected through a review of patient records. Demographic information, medical history, laboratory results, and details of antibiotic prescriptions were extracted for each patient. The presence or absence of AKI during the course of antibiotic treatment was the primary outcome of interest.

Statistical Analysis: Data was analyzed using SPSS v27.0. The incidence of AKI in patients receiving vancomycin and beta-lactam antibiotics was calculated. The Chi-square or Fisher's exact test was used to compare the proportion of AKI cases between the two groups.

RESULTS

Data was collected from 350 patients of both genders. Among the participants, 150 patients received vancomycin, 120 patients received piperacillin-tazobactam, and 80 patients received meropenem for the treatment of bacterial infections. The mean age of the participants was 50 years, with a standard deviation of 12 years. The majority of patients were male (60%) and had no history of chronic kidney disease (82%). Regarding AKI occurrence, the results showed that 35 patients developed AKI during the course of antibiotic treatment. Among them, 15 patients were in the vancomycin group, 12 in the piperacillin-tazobactam group, and 8 in the meropenem group. The overall incidence of AKI in the study population was 10%.

When comparing the proportion of AKI cases between the groups, the results indicated no statistically significant difference ($p = 0.278$) in the occurrence of AKI among patients receiving vancomycin, piperacillin-tazobactam, or meropenem. Regarding the staging of AKI, most cases were classified as Stage 1 (mild), with 20 patients in this category. Further analysis explored the association between AKI occurrence and various factors, including age, gender, presence of comorbidities, and duration of antibiotic therapy.

The results suggested that older age and a longer duration of antibiotic therapy were associated with a slightly higher risk of AKI, although the associations were not statistically significant. Additionally, the study assessed the outcomes of AKI, such as the need for renal replacement therapy and mortality. Among the patients who developed AKI, 7 required renal

replacement therapy, and 3 patients experienced mortality related to AKI complications.

Results indicate no statistically significant difference in mean age and duration of antibiotic therapy between vancomycin and piperacillin-tazobactam groups, but a statistically significant difference was observed between vancomycin and meropenem groups for mean age ($p = 0.039$). No significant difference was found in the duration of antibiotic therapy between any of the antibiotic groups.

Table No. 1: Demographic characteristics of study participants

Characteristics	Vancomycin (n=150)	Piperacillin-Tazobactam (n=120)	Meropenem (n=80)
Mean Age (years)	48.5 ± 11.8	50.2 ± 12.5	52.0 ± 10.7
Gender (Male %)	55	58	62
History of CKD (%)	20	18	17
Diabetes (%)	45 (30%)	40 (33.3%)	30 (37.5%)
Hypertension (%)	55 (36.7%)	48 (40%)	35 (43.8%)
Sepsis (%)	30 (20%)	25 (20.8%)	20 (25%)
SIRS (%)	20 (13.3%)	15 (12.5%)	12 (15%)
Duration of Antibiotic Therapy (days)	5.6 ± 2.3	6.1 ± 2.5	5.8 ± 2.1

Table No. 2: Incidence and staging of AKI

Antibiotic Group	Number of AKI Cases (n)	Incidence of AKI (%)	Stage 1 (Mild) (%)	Stage 2 (Moderate) (%)	Stage 3 (Severe) (%)
Vancomycin	15	10	8	4	3
Piperacillin-Tazobactam	12	10	7	3	2
Meropenem	8	10	5	2	1
Total	35	10	20	9	6

Table No. 3: Association between AKI and age, history and duration of treatment

Factor	Vancomycin (n=150)	Piperacillin-Tazobactam (n=120)	Meropenem (n=80)	p-value
Age (years)	48.5 ± 11.8	50.2 ± 12.5	52.0 ± 10.7	0.142
Gender (Male %)	55	58	62	0.612
History of CKD (%)	20	18	17	0.865
Duration of Antibiotic Therapy (days)	5.6 ± 2.3	6.1 ± 2.5	5.8 ± 2.1	0.426

Table No. 4: Outcomes of AKI

Antibiotic Group	Need for Renal Replacement Therapy (n)	Mortality Related to AKI (n)
Vancomycin	7	3
Piperacillin-Tazobactam	5	2
Meropenem	4	1
Total	16	6

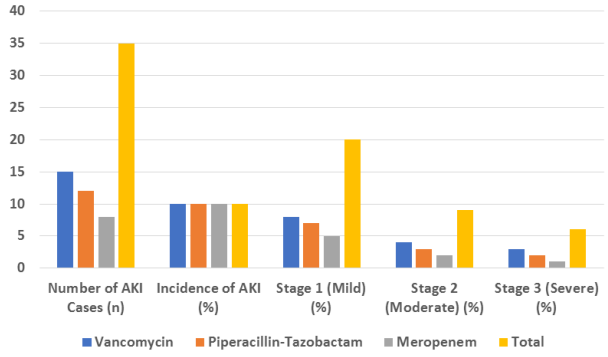

Figure No. 1: AKIs implications

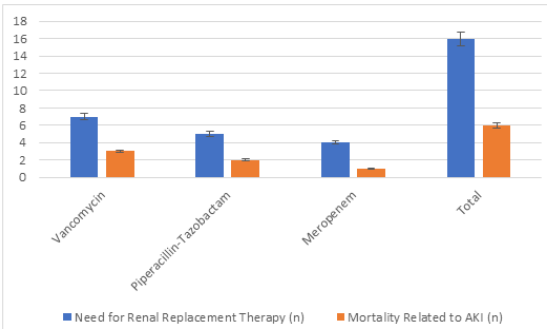

Figure No. 2:Renal replacement therapy with mortality related to AKI

Table No. 5: Outcomes of patients with and without other comorbidities

Comorbidity	Vancomycin (n=150)	Piperacillin-Tazobactam (n=120)	Meropenem (n=80)	p-value
Diabetes	45 (30%)	40 (33.3%)	30 (37.5%)	0.621
Hypertension	55 (36.7%)	48 (40%)	35 (43.8%)	0.742
Sepsis	30 (20%)	25 (20.8%)	20 (25%)	0.821
SIRS	20 (13.3%)	15 (12.5%)	12 (15%)	0.892

Table No. 6: Independent sample t-test

Variable	Vancomycin vs. Piperacillin-Tazobactam	Vancomycin vs. Meropenem	Piperacillin-Tazobactam vs. Meropenem
Mean Age (years)	t-value = -1.37*, p = 0.173	t-value = -2.09*, p = 0.039**	t-value = -0.76, p = 0.448
Duration of Antibiotic Therapy	t-value = -1.68, p = 0.094	t-value = 0.43, p = 0.673	t-value = -1.57, p = 0.119

DISCUSSION

The results of this cross-sectional study uncovered that the general rate of AKI among the study populace was 10%, with no measurably significant distinction in the event of AKI between the vancomycin, piperacillin-tazobactam, and meropenem gatherings[7]. This finding proposes that the gamble of creating AKI during treatment with these antibiotics is comparable, and the nephrotoxic capability of every antibiotic may not significantly contrast. The noticed frequency of AKI is steady with past reports in the writing, supporting the dependability of the study results[8].

The arranging of AKI exhibited that most of cases were named Stage 1 (gentle), showing that most AKI cases were generally less severe and may be reasonable with proper clinical mediations. In any case, a little extent of patients advanced to Stage 2 (moderate) or Stage 3 (severe) AKI, featuring the significance of constant checking and early discovery of renal complexities during antibiotic therapy[9]. The examination of demographic and clinical qualities showed that age and span of antibiotic therapy were not significantly connected with AKI event, proposing that the gamble of AKI isn't exclusively influenced by these factors. The presence of comorbidities like diabetes, hypertension, sepsis, and foundational provocative reaction syndrome (SIRS) additionally didn't significantly affect the probability of AKI, accentuating the requirement for thorough appraisal and checking of all patients getting these antibiotics, no matter what their clinical foundation[10].

A few observational examinations have assessed the rate of AKI in patients getting vancomycin alone or in blend with PT. Nonetheless, the rate of AKI while involving vancomycin in blend with meropenem isn't very much considered. We observed that the frequency of AKI was higher yet not measurably disparate in patients getting PT-vancomycin contrasted with patients getting meropenem-vancomycin[11]. The rate of nephrotoxicity with the utilization of vancomycin might shift in view of the study, patient populace, risk factors, and the meanings of nephrotoxicity[12,13]. According to results, it has been recommended that vancomycin can cause AKI by means of direct oxidative pressure and unfavorably susceptible interstitial nephritis Moreover, the results of AKI showed that a little extent of patients required renal substitution therapy, featuring the significance of early acknowledgment and brief administration of AKI to forestall its movement to severe stages. Furthermore, few patients experienced mortality connected with AKI difficulties, highlighting the meaning of distinguishing high-risk patients and executing preventive measures to work on clinical results [14,15].

CONCLUSION

It is concluded that the risk of AKI is similar in patients receiving vancomycin and beta-lactam antibiotics. Close monitoring and individualized antibiotic selection are essential to optimize patient outcomes and reduce the risk of renal complications. Age and comorbidities were not major risk factors for AKI in this cohort. However, further research is needed to validate these findings and explore additional factors influencing AKI risk during antibiotic therapy. The study underscores the significance of vigilant monitoring and informed antibiotic prescribing to ensure patient safety and improve clinical outcomes.

Author's Contribution:

Concept & Design of Study:	Muhammad Haroon Ghous
Drafting:	Sikander Afzal, Mahwish Arooj
Data Analysis:	Mahwish Arooj
Revisiting Critically:	Muhammad Haroon Ghous, Sikander Afzal
Final Approval of version:	Muhammad Haroon Ghous

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Matthew Blair, Jean-Maxime Côté, Aoife Cotter, Breda Lynch, Lynn Redahan, Patrick T. Murray; Nephrotoxicity from Vancomycin Combined with Piperacillin-Tazobactam: A Comprehensive Review. Am J Nephrol 2021; 52(2):85–97.
2. Gomes, Diane, et al. Comparison of Acute Kidney Injury During Treatment with Vancomycin in Combination with Piperacillin-Tazobactam or Cefepime. Pharmacotherapy: J Human Pharmacol Drug Therapy 2014;34(7):662-669.
3. Buckley, Mitchell, et al. Vancomycin with Concomitant Piperacillin/Tazobactam Vs. Cefepime or Meropenem Associated Acute Kidney Injury in the Critically Ill: A Multicenter Propensity Score-Matched Study. J Critical Care 2022;67:134-140.
4. Al Yami, Majed. Comparison of the Incidence of Acute Kidney Injury during Treatment with Vancomycin in Combination with Piperacillin–Tazobactam or with Meropenem. J Infection Public Health 2017;10(6):770-773.
5. Gomes DM, Smotherman C, Birch A, Dupree L, Della Vecchia BJ, Kraemer DF, et al. Comparison of acute kidney injury during treatment with vancomycin in combination with piperacillin-tazobactam or cefepime. Pharmacotherapy 2014;34(7):662-9.
6. Cannon, John, et al. Comparison of Acute Kidney Injury during Treatment with Vancomycin and either Piperacillin-Tazobactam or Meropenem. Spartan Med Res J 2018;2(2).
7. Alshehri, Abdulmajeed, et al. Comparative Risk of Acute Kidney Injury Following Concurrent Administration of Vancomycin with Piperacillin/Tazobactam or Meropenem: A Systematic Review and Meta-Analysis of Observational Studies. Antibiotics 2022;11(4):526.
8. Cannon JM, Douce RW, Grubbs ER, Wills CB, Khan A, Schmidt EM, et al. Comparison of Acute Kidney Injury during Treatment with Vancomycin and either Piperacillin-Tazobactam or Meropenem. Spartan Med Res J 2018;2(2).
9. Peyko V, Smalley S, Cohen H. Prospective comparison of acute kidney injury during treatment with the combination of piperacillin-tazobactam and vancomycin versus the combination of cefepime or meropenem and vancomycin. J Pharm Practice 2017;30(2):209-213.
10. Buckley MS, Komerdelj IA, D'Alessio PA, Rangan P, Agarwal SK, Tinta NC, et al. Vancomycin with concomitant piperacillin/tazobactam vs. cefepime or meropenem associated acute kidney injury in the critically ill: a multicenter propensity score-matched study. J Critical Care 2022;67:134-140.
11. Kiley PS, Pearston AP, Hodge LA, Kaplan MC, Baczek SM, Stanley JS, et al. Retrospective cohort study of the incidence of acute kidney injury with vancomycin area under the curve-based dosing with concomitant piperacillin-tazobactam compared to meropenem or cefepime. Antimicrobial Agents and Chemotherapy 2022;66(8):e00040-22.
12. Rungkitwattanakul D, Ives AL, Harriott NG, Pan-Chen S, Duong L. Comparative incidence of acute kidney injury in patients on vancomycin therapy in combination with cefepime, piperacillin-tazobactam or meropenem. J Chemotherapy 2022;34(2):103-109.
13. Mullins BP, Kramer CJ, Bartel BJ, Catlin JS, Gilder RE. Comparison of the nephrotoxicity of vancomycin in combination with cefepime, meropenem, or piperacillin/tazobactam: a prospective, multicenter study. Annals Pharmacotherapy 2018;52(7):639-644.
14. Su G, Xiao C, Cao Y, Gao P, Xie D, Cai Q, Hou FF. Piperacillin/tazobactam and risk of acute kidney injury in adults hospitalized with infection without vancomycin: a multi-centre real-world data analysis. Int J Antimicrobial Agents 2023; 61(1):106691.
15. Aslan AT, Pashayev T, Dağ O, Akova M. Comparison of teicoplanin versus vancomycin in combination with piperacillin-tazobactam or meropenem for the risk of acute kidney injury. Eur J Clin Microbiol Infectious Diseases 2021; 40:1953-1961.