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Analyzing the Pharmacokinetic Difference of Vancomycin 24-Hour Infusion Versus Conventional Infusion in Hospitalized Patients: A Pilot Study

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Abstract:

- ***Background:***
Methicillin-Resistant Staphylococcus aureus (MRSA) causes severe infections with high morbidity. Vancomycin remains the recommended therapy, but conventional intermittent infusion (II) requires delayed monitoring and is associated with nephrotoxicity. Continuous infusion (CI) may achieve therapeutic exposure earlier with improved renal safety.

- ***Aim:***
To compare the efficacy, nephrotoxicity, and cost-effectiveness of continuous versus intermittent infusion of vancomycin in patients with MRSA infections.

- ***Methods:***
A retrospective observational study was conducted at Indus Hospital, Karachi, over six months. Patients >14 years with MRSA infection receiving ≥72 hours of vancomycin were included. Participants were randomly allocated to CI (n=22) or II (n=22). Data from hospital records included demographics, dosing, serum creatinine, vancomycin levels, and costs. Outcomes were time to achieve target AUC, change in creatinine, and therapy-related costs.

- ***Results:***
Baseline demographics and creatinine were comparable. CI patients had significantly smaller increases in serum creatinine (0.05 ± 0.20 vs 0.41 ± 0.76 mg/dL; $p<0.05$) and achieved target AUC faster (1.6 ± 1.3 vs 3.3 ± 1.5 days; $p<0.05$). At 48 hours, 81.8% of CI versus 50% of II patients reached target AUC ($p=0.03$). Treatment duration and costs were slightly lower in the CI group, though not statistically significant.

- ***Conclusion:***
Continuous infusion of vancomycin achieved therapeutic exposure earlier with reduced nephrotoxicity and potential cost benefits compared to intermittent infusion. CI may be a safer and more efficient option, particularly in resource-limited settings, though larger prospective studies are required for validation.

Keywords: *Vancomycin, Continuous Infusion, Pharmacokinetics, MRSA, Nephrotoxicity, Cost-Effectiveness.*

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I. INTRODUCTION

Methicillin-Resistant Staphylococcus Aureus (MRSA) is a bacterium that is implicated in causing nosocomial infections that may prove fatal if treated inadequately. MRSA usually causes deep-seated surgical site, skin, soft-tissue and bone infections, but it may also cause pneumonia, meningitis and sepsis, if it reaches blood (1). It is estimated that MRSA is prevalent from 13% to 74% of worldwide reported Staphylococcus infections (2). A study by Zhou et al. found that 17% of all Diabetic Foot Ulcers had MRSA infections (3). World Health Organization claims that MRSA bloodstream infections worldwide have increased from 25% in 2019 to 35% in 2020, while for Pakistan the number has increased from 65% in 2019 to 69% in 2020 (4). A study of MRSA prevalence in Peshawar placed it at 34.8% (5). Methicillin resistance is defined as Minimum Inhibitory Concentration (MIC) of Oxacillin exceeding 4 micrograms/mL and/or detection of a gene called 'mecA' that translates the penicillin-binding protein with lower affinity to bind penicillin drugs (6, 7). The Infectious Diseases Society of America or IDSA recommends using Cotrimoxazole, Clindamycin, Linezolid or Doxycycline for treating MRSA infections in out-patient settings while Vancomycin, Teicoplanin, Clindamycin, Daptomycin, Linezolid, Ceftaroline and Tigecycline are the options for treatment in hospitalized patients (8, 9). Vancomycin is the first line drug for treating MRSA infections in humans. This drug is a glycopeptide drug and is dosed intravenously for systemic MRSA Infections. However, it is known to cause nephrotoxicity and may induce Acute Kidney Injury (AKI), in up to 35% of the cases, if adequate serum levels are not maintained (10). The maintenance of serum levels is cumbersome as it is affected by certain pharmacokinetic factors like total body water, creatinine clearance, glomerular filtration rate, dose of the drug and interval of dosing. As such, Vancomycin requires therapeutic drug monitoring via Area-Under-Curve over MIC or AUC/MIC evaluation, which is calculated with the help of trough and peak serum levels and may also serve as a warning or indicator for AKI, thus, increasing the efficacy of the therapy (11, 12). According to 2009 guidelines by IDSA, the peak and trough concentrations for calculation of AUC are drawn when Vancomycin achieves steady state levels and this is usually after the 3rd dose, so the trough level is drawn at least 30 minutes before the 4th dose and peak level is drawn 1 hour after the completion of the 4th dose (13). This may be problematic because patient may continue to receive low or high dosing for at least 48 hours, therefore, a Continuous Infusion may be beneficial as it requires a single Vancomycin to be drawn at 24th hour with simpler and quicker calculations for AUC (13, 14). Although there have not been any large cohort-based studies evaluating the relative efficacy, there have been some studies that show that Continuous Infusion (CI) of Vancomycin achieves target AUC of 400 – 600 mcg.hr/mL earlier with lower incidences of AKI. A quasi-experimental study showed that critical care patients achieved target AUC more with CI (54.8%) than with conventional Intermittent Infusions (II) given twice a day (25.6%) (14). A systematic review and meta-analysis of 11 studies showed lesser incidence of AKI (odds ratio 0.47) in CI in critical care patients and 2.6 times more likelihood of attaining target AUC (odds ratio 2.63) (15). An observational cohort study by Maarseveen et al. similarly showed that target AUC achievement was higher in CI (48%) versus II (19%) patients with twice higher variation in Vancomycin serum concentrations in the II group (16). As such, it is evident that CI may be more effective and safer than II.

➢ *Operational Definitions*

- ADR-Adverse Drug Reaction or ADR is any unpredictable noxious effect that occurs due to a drug being administered at therapeutic dosage.
- AKI-Acute Kidney Injury or AKI is the sudden decline in renal function manifested by either increase of Serum Creatinine by 0.3 mg/dL within 48 hours, more than 1.5 times of a known baseline value within 7 days or Urine Volume <0.5 mL/kg/hr for at least 6 hours.
- AUC-Area-Under-Curve or AUC is the concentration of a particular agent in blood plasma measured as a function of time.
- CrCl-Creatinine Clearance is an estimate of renal function which correlates the renal clearance of Creatinine to the Glomerular Filtration Rate of the kidneys and is evaluated using Cockroft-Gault Equation.

➢ *Rationale:*

Conventional Intermittent Infusions (IIs) are known to produce erratic serum levels and give results at least 4 doses (or 48 hours) whereas, a Continuous Infusion (CI) protocol can ensure proper and fixed-rate drug entry into the body with AUC calculations at 24th hour at a single serum level testing. This also reduces the chances of dose accumulation and nephrotoxicity as the CI provides drug at a continuously fixed-rate. Therefore, the rationale and ultimate intended purpose for conducting the study is to check that Vancomycin AUC is achieved earlier and adequately, without nephrotixicity, at at least 24 hours with the continuous infusion in background of at >48 hours to achieve AUC in the intermittent infusion dosing. It will also reduce the direct medicational and laboratory costs.

➢ *Study Objective:*

The primary objective of this study is to observe if continuous infusion of Vancomycin achieves adequate AUC levels faster than intermittent infusion.

Secoondary objective is to compare the trend of Creatinine in both groups.

II. METHODOLOGY

We aimed to conduct a Retrospective Observational Study of patients who received Vancomycin as CI 20-30 mg/kg STAT then 30 – 40 mg/kg/day and up to 60 mg/kg/day according to Creatinine Clearance or II 25 mg/kg STAT then 15 mg/kg IV q12h. The dosing is taken from the consensus guidelines for Vancomycin use (13) and as adopted by the Stanford Healthcare Centre, California, United States of America (17). The study was completed in 6 months after approval from the review board and was conducted on

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patients who were admitted in Indus Hospital and Health Network-Korangi Campus, Karachi.

➢ *Sampling Technique:*

The sample size is calculated on the basis of anticipated mean difference of minimum creatinine clearance of vancomycin of 36±29 ml/min in the continuous infusion group and 22±23 ml/min in the intermittent infusion group. Precision was set at 5% with 95% confidence intervals and the obtained sample size was 110. Considering this as a pilot study a 20% of the total sample will be recruited of 22 participants in each arm. The study sample will be randomly allocated patients in two arms of CI and II respectively (18).

➢ *Eligibility Criteria:*

The included patients were those of age not less than 12 years, those with culture and sensitivity reports (along with their sample sources) positive for MRSA who have received Vancomycin therapy for at least 72 hours.

Those patients who were less than 12 years of age; had any hypersensitivity or contraindications to Vancomycin, and without MRSA in their culture and sensitivity reports were excluded from the study.

➢ *Data Collection and Management:*

Patient data collection was through the Hospital Management Information System or HMIS (ranging from August 2023 till September 2024) and included patient medical registration number, age, height, weight, duration of Vancomycin therapy, serum creatinine at baseline before initiation of Vancomycin and then daily, and Vancomycin serum levels. The outcome variables include AUC (Calculated by Sanford Guide to Antimicrobial Therapy app's Vancomycin AUC Calculator), and mean difference of Cr from baseline in each arm, and cost-effectiveness of therapy in each arm in terms of direct medicinal and laboratory costs for Vancomycin.

III. RESULTS

➢ *Demographics*

The dataset compared two groups of 22 patients each, treated with vancomycin via Continuous Infusion (CI) and Intermittent Infusion (II).

- Age: Patients in the CI group had a mean age of 41.91 years (SD = 21.81), compared to 48.36 years (SD = 21.14) in the II group.
- Weight: The mean weight in the CI group was 55 kg (SD = 17.9), marginally lower than the II group's mean of 60.19 kg (SD = 11.51).
- Height: The CI group showed slightly shorter mean heights 154.59 cm (SD = 25) than the II group 157.77 cm (SD = 15.04).

➢ *Baseline Creatinine:*

The CI group had a baseline Cr of 0.77 mg/dL (SD = 0.36) as compared to the II group which had baseline Cr of 0.75 mg/dL (SD = 0.26).

➢ *Vancomycin Dose:*

The mean vancomycin dose in the CI group was 83.68 mg/hr (SD = 28.70) or 2.008.32 mg/day, while in the II group, it was 906.82 mg/dose (SD = 156.36) or 1813.64 mg/day.

➢ *Mean Difference in Creatinine Levels:*

The CI group exhibited smaller changes in creatinine levels (Mean Difference = 0.05 mg/dL, SD = 0.197) compared to the II group (Mean Difference = 0.41 mg/dL, SD = 0.762) as below in figure 1:

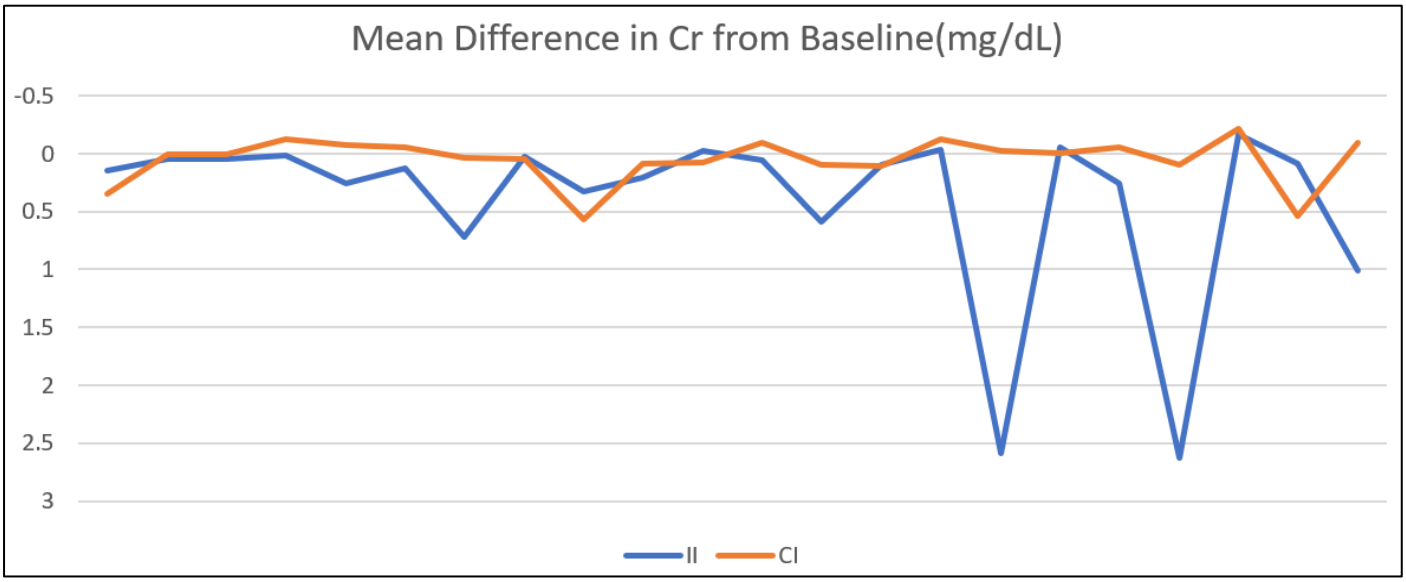

Fig 1 Mean Difference in Creatinine from Baseline

➢ *AUC (Area Under the Curve):*

Figure 2 shows comparison of Vancomycin AUC in both groups. CI provided an AUC range (432 to 1800 mcg.hr/mL) with a higher mean (722.36 mcg.hr/mL; SD = 334.97) compared to II (297 to 1362 mcg.hr/mL; mean = 610 mcg.hr/mL; SD = 258.91). The Coefficients of Variation for

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CI is 46.37% as compared to II 42.4%. Moreover, there were 4 cases (18.18%) in II group where the given dose underachieved the AUC (i.e. <400 mcg.hr/mL) as compared to CI where no dose underachieved the AUC (OR 0.0914; 95% CI 0.0046 to 1.8092; p = 0.1162). Similarly, there were 12 (54.54%) cases of AUC overachievement (i.e. >600 mcg.hr/mL) in CI group as compared to 9 (40.9%) in II (OR 1.73; 95% CI 0.5250 to 5.7229; p = 0.3667).

In the CI group, AUC was achieved earlier (Mean = 1.59 days; SD = 1.29) as compared to II group (Mean = 3.27 days; SD = 1.54) which is 50% earlier than II, thus keeping with the original postulate that CI can achieve AUC by 24th hour relative to II which achieves it by 48 hours.

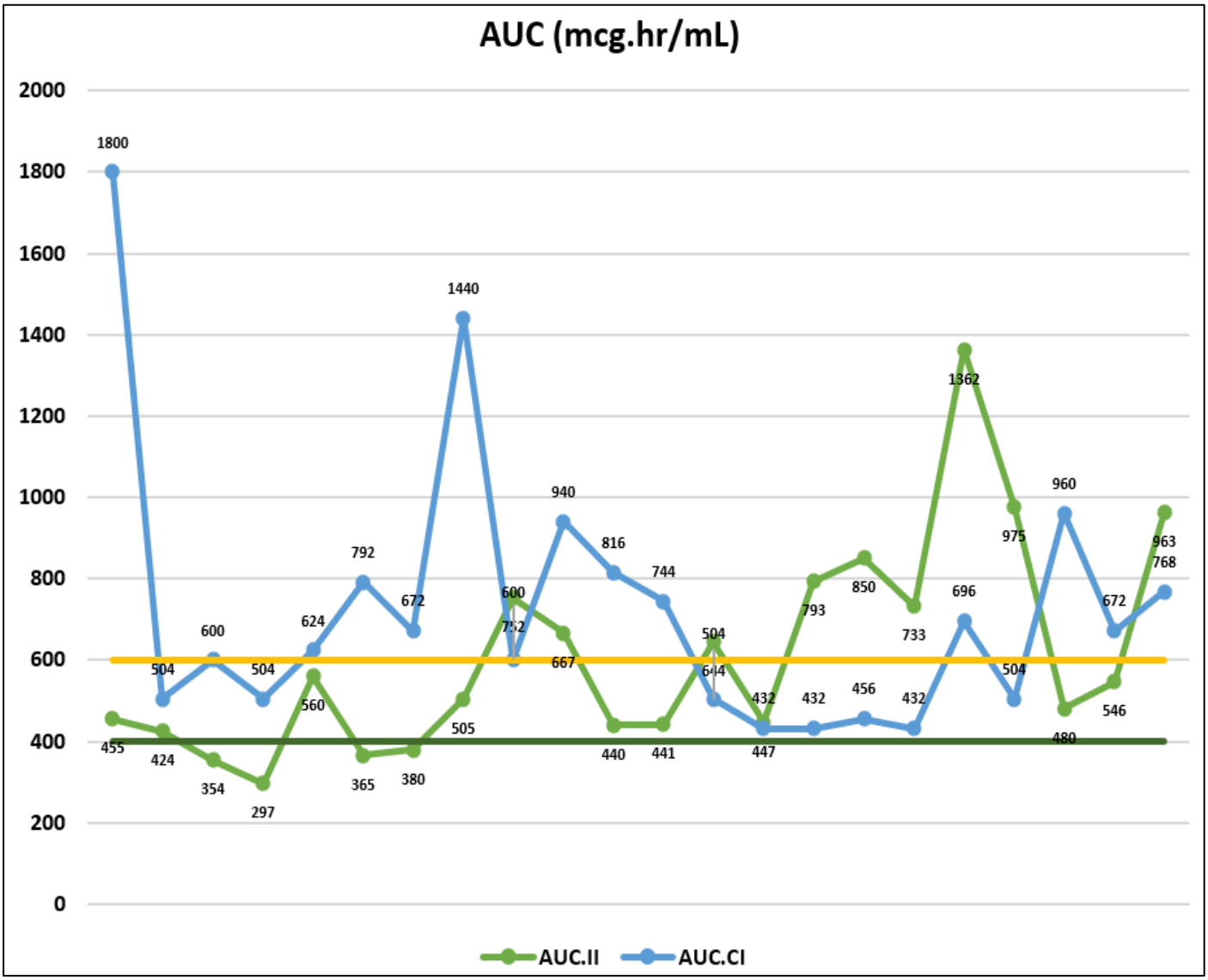

Fig 2 Comparison of Vancomycin AUC Between Groups

➢ *Duration of Therapy:*

Treatment durations ranged from 3 to 28 days for CI, with a mean of 12.45 days (SD = 7.82). For II, durations were longer, ranging from 4 to 30 days, with a mean of 13.27 days (SD = 6.88). The shorter durations in the CI group may reflect faster achievement of therapeutic goals due to stable drug levels but this may not be certain due to retrospective nature of study.

➢ *Treatment Costs:*

CI had a lower mean treatment cost (PKR 52,652.72) than II (PKR 56,234.54). The difference is attributed to fewer and earlier adjustments and reduced test requirements in the CI group.

➢ *Number of Lab Tests and Costs:*

CI tests and costs were significantly lower (Mean = 3.36 tests; SD = 1.78; Mean Cost = PKR 7,554; SD = 4,014) than II group (Mean Tests= 4.36 tests; SD = 2.49; Mean Cost = PKR 9,800; SD = 5,611).

➢ *Independent Samples T-tests:*

Independent Samples T-tests were used to find statistical significance at 5% level of significance. Following are the results in Figure 3:

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Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
									95% Confidence Interval of the Difference	
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
No.of Days	Equal variances assumed	0.551	0.462	-0.368	42	0.714	-0.81818	2.22141	-5.30117	3.66481
	Equal variances not assumed			-0.368	41.326	0.715	-0.81818	2.22141	-5.30334	3.66698
Mean Diff Cr	Equal variances assumed	8.552	0.006	-2.109	42	0.041	-0.35409	0.16787	-0.69286	-0.01532
	Equal variances not assumed			-2.109	23.812	0.046	-0.35409	0.16787	-0.70070	-0.00748
AUC	Equal variances assumed	0.124	0.726	1.238	42	0.222	111.77273	90.26211	-70.38358	293.92903
	Equal variances not assumed			1.238	39.492	0.223	111.77273	90.26211	-70.72694	294.27240
AUC Day	Equal variances assumed	2.252	0.141	-3.905	42	0.000	-1.68182	0.43065	-2.55090	-0.81273
	Equal variances not assumed			-3.905	40.744	0.000	-1.68182	0.43065	-2.55170	-0.81194
Vanc Cost	Equal variances assumed	1.393	0.245	-0.366	42	0.716	-3581.81818	9778.88218	-23316.40139	16152.76503
	Equal variances not assumed			-0.366	39.774	0.716	-3581.81818	9778.88218	-23349.17068	16185.53432
No. of Tests	Equal variances assumed	2.908	0.096	-1.527	42	0.134	-1.00000	0.65495	-2.32175	0.32175
	Equal variances not assumed			-1.527	38.034	0.135	-1.00000	0.65495	-2.32585	0.32585
Test Cost	Equal variances assumed	2.908	0.096	-1.527	42	0.134	-2246.00000	1471.02708	-5214.65284	722.65284
	Equal variances not assumed			-1.527	38.034	0.135	-2246.00000	1471.02708	-5223.85232	731.85232

Fig 3 Independent Samples T-test

This shows that the only variables with statistical significance are Mean Difference in Creatinine and Number of Days to achieve target AUC. This means that CI group had a lesser chance of increasing Cr from baseline (Mean Difference = 0.05 ± 0.197 mg/dL vs 0.41 ± 0.762 mg/dL; $p<0.05$) and would therefore, be significantly less nephrotoxic as compared to the II mode of therapy. Similarly, since AUC was achieved by CI group prior to the II group (Mean = 1.59 ± 1.29 days vs 3.27 ± 1.54 days), CI group was statistically significant to achieve AUC target within 48 hours ($p<0.05$). However, the CI group was not found to be statistically significant in terms of therapy and lab tests costs as well as number of lab tests ordered. Although, all these variables show arithmetically, that CI is better than II in terms of cost-effectiveness and lesser number of lab tests ordered. Perhaps, low sample-size is the reason behind this insignificance.

IV. DISCUSSION

The findings of our study provides initial observations regarding achievement of therapeutic target, the clinical outcomes, renal safety, and cost-effectiveness of continuous infusion (CI) versus intermittent infusion (II) of vancomycin in the treatment of methicillin-resistant Staphylococcus aureus (MRSA) infections. The results suggest that CI may offer significant advantages over II in these aspects, though further research is needed to validate these results.

➢ *Outcomes:*

The finding that a higher proportion of CI group patients achieved the therapeutic target at 48 hours as compared to II group patients with fewer sub therapeutic episodes is paralleled in previous studies (14). The shorter mean duration of therapy observed in the CI group (12 days) compared to the II group (13 days) may reflect the more stable pharmacokinetic profile of CI, although it is not significant. Continuous infusion maintains constant therapeutic vancomycin serum concentrations, avoiding the sub therapeutic trough levels and toxic peak levels that are associated with II (13). This early achievement and maintenance of constant therapeutic target can potentially lead to early bacterial culture clearance and clinical improvement. However, as this study was retrospective in nature, the impact of confounding factors such as differences in baseline infection severity, comorbidities, and clinical management cannot be omitted. These results support previous studies that suggest CI may facilitate faster therapeutic target attainment, but additional prospective trials are necessary to confirm this benefit (19, 20).

➢ *Renal Safety:*

Renal safety is a key concern in vancomycin therapy, as nephrotoxicity is a well-documented adverse effect. In our study, CI demonstrated a superior renal safetloy profile, with minimal changes in serum creatinine levels as compared to II. The reduction in nephrotoxicity is due to the avoidance of

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high peak drug concentrations, which is risk factor for renal injury in II (21, 22). Similar results have been reported in previous studies, where CI was associated with lower acute kidney injury compared to II (23). However, larger prospective studies are needed to confirm this safety benefits of CI.

➢ *Cost Analysis:*

The direct cost analysis revealed a low cost advantage of CI over II on the basis of cost of vancomycin vials used during treatment laboratory test cost, although not statistically significant. Still, the mean treatment cost for CI (PKR 52,652) was substantially lower than that for II (PKR 56,234) as there were less number of vancomycin vials used in CI patient group. Second cost difference is related to reduced laboratory test requirements and fewer dose adjustments in the CI group. The test costs were significantly lower for CI (mean = PKR 7,554) compared to II (mean = PKR 9,800), likely reflecting less frequent therapeutic drug monitoring due to the stable pharmacokinetic profile of CI. These findings are connected with prior research demonstrating the cost-saving potential of CI in terms of reduced laboratory and healthcare resource utilization (24, 25). In resource-limited settings, this cost advantage could make CI a particularly attractive option.

V. STUDY LIMITATIONS

Despite the encouraging findings, there are some limitations of this study. First, the retrospective design of this study limits the ability to make causal conclusions. Second, the small sample size (n = 44) reduces the statistical power and generalizability of the results to larger patient populations. Third, key clinical data such as infection severity, microbiological clearance, and adherence to therapeutic drug monitoring protocols were not assessed, limiting the depth of the analysis. Lastly, potential confounding factors, such as the use of concomitant nephrotoxic medications and variations in patient management, may also have affected the outcomes.

➢ *Clinical Impact:*

The results of this study suggest that CI of vancomycin has the potential to improve clinical outcomes, reduce nephrotoxicity, and lower treatment costs compared to II. These benefits are particularly related in those patients in which renal safety is of high priority due comorbidities and concomitant nephrotoxic drugs. Additionally, all previous studies were in critical care units of health care setting but this study reveal that CI can be implemented in areas other than critical care unit. However, given the limitations of this study, the findings should be interpreted cautiously.

➢ *Future Directions:*

To expand on the results of this pilot study, prospective randomized controlled trials are needed to confirm the efficacy, safety, and cost-effectiveness of CI in MRSA infections. These studies should include larger and more diverse patient populations, close monitoring of clinical and microbiological outcomes, and detailed assessments of renal function and long-term health consequences. A broader economic analyses that incorporate indirect costs, such as hospitalization, all laboratory tests cost and adverse event management, would strengthen the use of vancomycin CI as a standard practice.

VI. CONCLUSION

In conclusion, this study suggests that CI of vancomycin may offer clinical and economic advantages over II in the treatment of MRSA infections, particularly with respect to renal safety, consistent therapeutic concentration, and cost effectiveness. However, the limitations of this study highlight the need for further research to validate these findings. Until robust evidence becomes available, clinicians should weigh the potential benefits of CI against individual patient needs and institutional resources.

➢ *Statements and Declaration*

- *Funding*

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

- *Competing Interests*

The authors have no relevant financial or non-financial interests to disclose.

- *Author Contributions*

S.S. and M.H.H. wrote the main manuscript text and prepared figures. All authors reviewed the manuscript.

- *Data Availability*

All data supporting the findings of this study are available within the paper.

- *Ethics Approval*

The Indus Hospital and Health Network-Institutional Review Board has reviewed the study referenced as IHHN_IRB_2024_05_010 and determined that, as currently described, it is exempt from ongoing IRB review, per the following exemption category: EXEMPTION: (4): Secondary research for which consent is not required and involves the re-use of data and specimens that were or will be collected for non-research purposes or from research studies other than the proposed research study.

- *Consent to Participate*

Informed consent was obtained from all individual participants included in the study.

- *Consent to Publish*

The authors affirm that human research participants provided informed consent for publication of the data.

REFERENCES

[1]. Siddiqui AH, Koirala J. Methicillin-Resistant Staphylococcus aureus. [Updated 2023 Apr 2]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls

Publishing; 2024–. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482221/
[2]. Hassoun A, Linden PK, Friedman B. Incidence, prevalence, and management of MRSA bacteremia across patient populations—a review of recent developments in MRSA management and treatment. Crit Care. 2017;21(1):211. doi:10.1186/s13054-017-1801-3
[3]. Zhou S, Hu X, Wang Y, Fei W, Sheng Y, Que H. The global prevalence of methicillin-resistant Staphylococcus aureus in patients with diabetic foot ulcers: a systematic review and meta-analysis. Diabetes Metab Syndr Obes. 2024;17:563–74. doi:10.2147/DMSO.S446911
[4]. World Health Organization. Proportion of bloodstream infection due to methicillin-resistant Staphylococcus aureus (MRSA) (%) [Internet]. 2024 [cited 2024 Apr 14]. Available from: https://data.who.int/indicators/i/5DD9606
[5]. Ullah A, Qasim M, Rahman H, Khan J, Haroon M, Muhammad N, et al. High frequency of methicillin-resistant Staphylococcus aureus in Peshawar Region of Pakistan. Springerplus. 2016;5:600. doi:10.1186/s40064-016-2277-3
[6]. Wang G, Hindler JF, Ward KW, Bruckner DA. Increased vancomycin MICs for Staphylococcus aureus clinical isolates from a university hospital during a 5-year period. J Clin Microbiol. 2006;44(10):3883–6. doi:10.1128/JCM.01388-06
[7]. Kumar VA, Steffy K, Chatterjee M, Sugumar M, Dinesh KR, Manoharan A, et al. Detection of oxacillin-susceptible mecA-positive Staphylococcus aureus isolates by use of chromogenic medium MRSA ID. J Clin Microbiol. 2013;51(1):318–9. doi:10.1128/JCM.01040-12
[8]. Mahjabeen F, Saha U, Mostafa MN, Siddique F, Ahsan E, Fathma S, et al. An update on treatment options for methicillin-resistant Staphylococcus aureus (MRSA) bacteremia: a systematic review. Cureus. 2022;14(11):e31486. doi:10.7759/cureus.31486
[9]. Choo EJ, Chambers HF. Treatment of methicillin-resistant Staphylococcus aureus bacteremia. Infect Chemother. 2016;48(4):267–73. doi:10.3947/ic.2016.48.4.267
[10]. Rose W, Volk C, Dilworth TP, Sakoulas G. Approaching 65 years: is it time to consider retirement of vancomycin for treating methicillin-resistant Staphylococcus aureus endovascular infections? Open Forum Infect Dis. 2022;9(5):ofac137. doi:10.1093/ofid/ofac137
[11]. Kim B, Hwang S, Heo E, Kim HS, Jung J, Kim ES, et al. Evaluation of vancomycin TDM strategies: prediction and prevention of kidney injuries based on vancomycin TDM results. J Korean Med Sci. 2023;38(14):e101. doi:10.3346/jkms.2023.38.e101
[12]. Al-Maqbali JS, Shukri ZA, Sabahi NA, Al-Riyami I, Al Alawi AM. Vancomycin therapeutic drug monitoring (TDM) and its association with clinical outcomes: a retrospective cohort. J Infect Public Health. 2022;15(5):589–93. doi:10.1016/j.jiph.2022.04.007
[13]. 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. Am J Health Syst Pharm. 2020;77(11):835–64. doi:10.1093/ajhp/zxaa036
[14]. Maluangnon C, Tongyoo S, Permpikul C. Continuous vancomycin infusion versus intermittent infusion in critically ill patients. Infect Drug Resist. 2022;15:7751–60. doi:10.2147/IDR.S395385
[15]. Flannery AH, Bissell BD, Bastin MT, Morris PE, Neyra JA. Continuous versus intermittent infusion of vancomycin and the risk of acute kidney injury in critically ill adults: a systematic review and meta-analysis. Crit Care Med. 2020;48(6):912–8. doi:10.1097/CCM.0000000000004326
[16]. van Maarseveen EM, Gipmans S, Vasbinder E, Petjak M, van Zanten AR. Switching from intermittent to continuous infusion of vancomycin in critically ill patients: toward a more robust exposure. Ther Drug Monit. 2016;38(3):398–401. doi:10.1097/FTD.0000000000000295
[17]. Stanford Health Care. Vancomycin dosing guide [Internet]. Stanford: Stanford Medicine; c2024 [cited 2024 Apr 14]. Available from: https://med.stanford.edu/content/dam/sm/bugsanddrugs/documents/antimicrobial-dosing-protocols/SHC%20Vancomycin%20Dosing%20Guide.pdf
[18]. Hutschala D, Kinstner C, Skhirdladze K, Thalhammer F, Müller M, Tschernko E. Influence of vancomycin on renal function in critically ill patients after cardiac surgery: continuous versus intermittent infusion. Anesthesiology. 2009;111(2):356–65. doi:10.1097/ALN.0b013e3181ae6151
[19]. Barbour A, Schmidt S, Rout WR, Ben-David D, Burkhardt O, Derendorf H. Soft tissue penetration of vancomycin in diabetic patients with bacterial foot infections. Int J Antimicrob Agents. 2009;34(5):480–5. doi:10.1016/j.ijantimicag.2009.06.019
[20]. Wysocki M, Delatour F, Faurisson F, Rauss A, Pean Y, Misset B, et al. Continuous infusion of vancomycin in severe staphylococcal infections: a pilot study. Antimicrob Agents Chemother. 2001;45(9):2465–7. doi:10.1128/AAC.45.9.2465-2467.2001
[21]. Adane ED, Herald M, Pfaller MA, Diekema DJ, Doern GV, Karre T, et al. Pharmacodynamic targets and continuous infusion of vancomycin in critically ill patients: a retrospective study. Ther Drug Monit. 2015;37(5):607–13. doi:10.1097/FTD.0000000000000187
[22]. Elyasi S, Khalili H, Dashti-Khavidaki S, Mohammadpour A. Vancomycin-induced nephrotoxicity: mechanism, incidence, risk factors and special populations. Eur J Clin Pharmacol. 2012;68(9):1243–55. doi:10.1007/s00228-012-1259-9
[23]. Lodise TP, Patel N, Lomaestro B, Rodvold KA, Drusano GL. Relationship between initial vancomycin concentration-time profile and nephrotoxicity among

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/25sep333

hospitalized patients. Clin Infect Dis. 2009;49(4):507–14. doi:10.1086/600884

[24]. Wallace KL, Neyra JA, Kanji Z, Bissell BD, Flannery AH. Cost-effectiveness of continuous infusion versus intermittent infusion of vancomycin in critically ill patients. Crit Care Med. 2019;47(5):e405–11. doi:10.1097/CCM.0000000000003712

[25]. Gill J, Ko J, Schilling AL. Economic evaluation of continuous infusion vancomycin for serious infections. Am J Health Syst Pharm. 2016;73(2):e25–31. doi:10.2146/ajhp140798