Vancomycin AUC:MIC-Based Dosing is Associated with Significantly Less Acute Kidney Injury in Patients Admitted to a Burn Intensive Care Unit

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Introduction

- Vancomycin is the drug of choice for methicillin-resistant *Staphylococcus aureus* (MRSA)
- Vancomycin is proven to be nephrotoxic and demonstrates an exposure-response relationship
- Traditionally trough-based dosing >15 mcg/mL were found to have a greater risk of vancomycin associated acute kidney injury (VIKI)
- Trough dosing underestimates true AUC by approximately 25%
- American Society of Health-Systems Pharmacist (ASHP) updated vancomycin dosing guidelines to target AUC 400-600 mcg* h/mL in 2020.
- Bayesian modeling is the gold-standard for pharmacokinetic calculations and AUC:MIC modeling, but models in critically ill and burn patients are limited

Objectives

- To compare the incidence of acute kidney injury (AKI) in patients who were dosed to achieve a target trough 15-20 mcg/mL to those who were dosed to target AUC: MIC 400-600 mcg*h/mL

Methods

- Retrospective cohort study
- Inclusion Criteria:
  - Age ≥ 18 years
  - Admitted to BICU between January 2017 through December 2020
  - Received at least 24 hours of vancomycin therapy
- Exclusion Criteria
  - Receiving renal replacement therapy at the time of vancomycin administration
  - History of chronic kidney disease
- Trapezoidal method was used to calculate AUC
- AKIN criteria was used to determine incidence of AKI

Results

- Two hundred thirty-five subjects who received 317 courses of vancomycin were included.
- One hundred twenty courses were dosed to achieve an AUC goal, and 197 courses were dosed to achieve a trough goal.
- Patients in the AUC group received significantly less vancomycin than in the trough group
- Risk factors for AKI and administration of concomitant nephrotoxins were similar between the two groups

Table 1. Demographic characteristics

	Trough-Based (N=150)	AUC:MIC-Based (N=85)	P-value
Age, years, mean ± SD	46.6 ± 17.7	48.7 ± 18.3	0.199
Male gender, n (%)	105 (70%)	61 (71.7%)	0.775
Admission body weight, kg, mean ± SD	90.9 ± 28.2	91.7 ± 26.5	0.414
ICU LOS, days, mean ± SD	21.2 ± 23.2	20.3 ± 28	0.601
Hospital LOS, days, mean ± SD	36.3 ± 40.9	33.6 ± 36.5	0.699
%TBSA, mean ± SD	24.6 ± 20.5	25.4 ± 16.9	0.401
Admission diagnosis			0.494
Burn, n (%)	97 (64.6%)	48 (56.5%)	
NSTI, n (%)	28 (18.7%)	21 (24.7%)	
Skin disease	16 (10.7%)	7 (8.3%)	
Polytrauma	8 (5.3%)	3 (3.5%)	
Other	6 (4%)	3 (3.5%)	

Table 2. Vancomycin and Concomitant Nephrotoxins

	Trough-Based (N=197)	AUC:MIC-Based (N=120)	P-value
Total daily dose, mg, mean ± SD	3524 ± 1551	3145 ± 1491	0.032
Concomitant nephrotoxins	103 (52.3%)	50 (41.6%)	0.093
Aminoglycoside, n (%)	48 (24.5%)	24 (20.5%)	0.419
Piperacillin/tazobactam, n (%)	52 (26.5%)	18 (15.4%)	0.022
Liposomal amphotericin B, n (%)	3 (1.5%)	8 (6.8%)	0.022
Voriconazole, n (%)	1 (0.5%)	8 (6.8%)	0.002
Acyclovir, n (%)	2 (1%)	1 (0.9%)	1.000
NSAID, n (%)	14 (7.1%)	9 (7.7%)	0.857

Table 3. AKI and Known Risk Factors

	Trough-Based (N=197)	AUC:MIC-Based (N=120)	P-value
AKI, n (%)	40 (20.3%)	12 (10.3%)	0.017
Known risk factor for AKI, n (%)	104 (52.8%)	65 (55.6%)	0.635
History of hypertension, n (%)	66 (33.5%)	32 (26.7%	0.202
Concomitant furosemide, n (%)	39 (19.8%)	35 (29.9%)	0.041
Renal insufficiency, n (%)	25 (12.7%)	25 (21.4%)	0.042

Conclusions

- Using AUC:MIC-based dosing was associated with a decreased incidence of AKI than trough-based dosing in patients admitted to the burn ICU
- AUC:MIC-based dosing was associated with significantly lower total daily doses of vancomycin

References

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Statements

This study was conducted under a protocol reviewed and approved by the USAISR Research Regulatory Department with a HIPAA waiver approved by the US Army Medical Research and Development Command Institutional Review Board and in accordance with the approved protocol.