Trough-based vs AUC:MIC based Monitoring of Vancomycin: Impact on Nephrotoxicity and Efficacy at PIH Health Good Samaritan Hospital

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Introduction

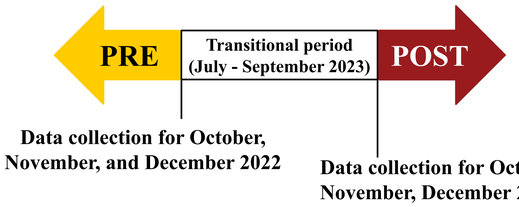
- Vancomycin is a tricyclic glycopeptide antibiotic widely used to treat and prevent bacterial infections caused by gram-positive bacteria.
- Vancomycin is known to cause acute kidney injury (AKI), especially when used concomitantly with other nephrotoxic antimicrobials.
- Therapeutic drug monitoring has been effective in mitigating vancomycin-induced toxicities.
- PIH Health Good Samaritan Hospital (PHGSH) recently revised vancomycin dosing protocol from target goal trough to AUC:MIC approach.

Objective

- To compare the incidence of vancomycin-induced AKI between the two vancomycin-dosing methods:
  - **Pre-implementation**: dosing based on attainment of target goal trough
  - **Post-implementation**: dosing based on attainment of target AUC:MIC
- To evaluate the incidence of AKI in patients on concurrent vancomycin and piperacillin-tazobactam
- To evaluate and compare both methods in achieving therapeutic goal AUC:MIC of 400-600 mg*hr/L

Methods

- **Study design:**
  - Retrospective Cohort Study
- **Number of patients:**
  - Pre-implementation: N = 112 patients
  - Post-implementation: N = 58 patients
- **Inclusion:**
  - All patients 18+ years old and on vancomycin IV
- **Exclusion:**
  - On vancomycin for 3 days or less
  - On Hemodialysis, Continuous Ambulatory Peritoneal Dialysis or Continuous Renal Replacement Therapy
  - Patient without measured vancomycin steady-state trough levels



Demographics

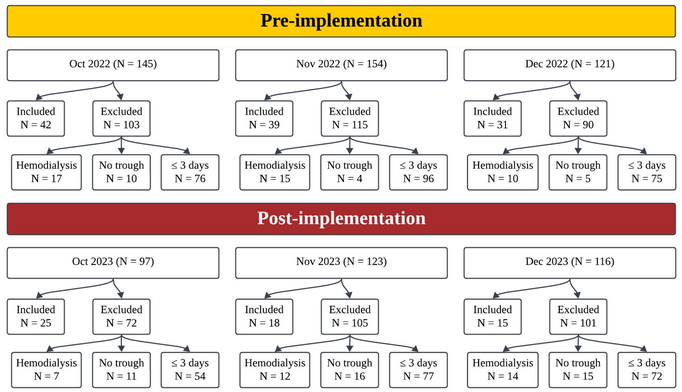


Figure 1. Patient Selection

Table 1. Patient Characteristics at Baseline

Characteristics	Pre-implementation (N=112)	Post-implementation (N=58)
Age (years)	58 (18-89)	56 (26-86)
Male	77 (68.8%)	38 (65.5%)
Indication		
SSTI with or without Abscess	45 (40.2%)	21 (36.2%)
Sepsis	25 (22.3%)	16 (27.6%)
Pneumonia	16 (14.3%)	9 (15.5%)
Osteomyelitis	14 (12.5%)	8 (13.8%)
CNS Infection	5 (4.5%)	2 (3.4%)
Intra-abdominal Infection	3 (2.7%)	1 (1.7%)
Septic Arthritis	3 (2.7%)	0 (0%)
Urinary Tract Infection	1 (0.9%)	1 (1.7%)
BMI		
< 18.5 kg/m^2	4 (3.6%)	8 (13.8%)
18.5 - 24.9 kg/m^2	47 (42%)	21 (36.2%)
25 - 29.9 kg/m^2	29 (25.9%)	15 (25.9%)
≥ 30 kg/m^2	32 (28.6%)	14 (24.1%)

Results

Table 2. Vancomycin AUC:MIC Pre and Post Implementation

	Pre-implementation	Post-implementation
AUC < 400	41 (36.6%)	20 (34.5%)
AUC 400 - 600	49 (43.8%)	27 (46.5%)
AUC > 600	22 (19.6%)	11 (19%)

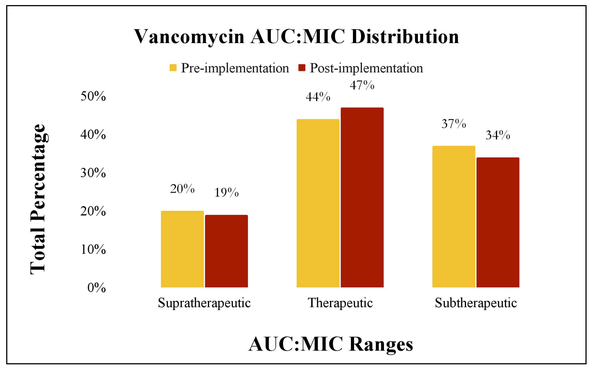


Figure 2. Comparison of vancomycin AUC:MIC between the two methods. Post-implementation group had a slightly higher number of patients in the therapeutic goal range (46.5% vs 43.8%).

Table 3. Vancomycin AUC:MIC Outside Goal Range in Post-implementation

	Number of Patients AUC:MIC ≤ 350	Number of Patients AUC:MIC ≥ 650
Obese	2	0
Undetermined reason	4	0
Drawn inappropriately	4	1
Acute renal failure	0	3
CKD	0	1
Sepsis	0	2

Table 4. Incidence of AKI Pre and Post Implementation

Outcomes	
Vancomycin	
Pre-implementation	10/112 (**8.9 %**)
Post-implementation	4/58 (**6.9 %**)
Concurrent piperacillin-tazobactam	
Pre-implementation	7/54 (**13 %**)
Post-implementation	2/33 (**6.1** %)

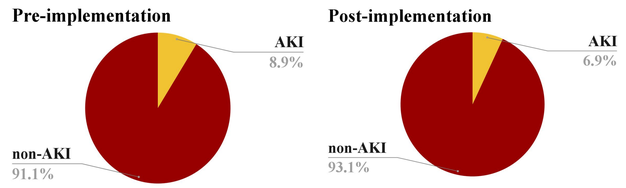


Figure 3. Vancomycin-induced AKI trended lower with AUC:MIC approach vs trough-based method (6.9% vs 8.9%)

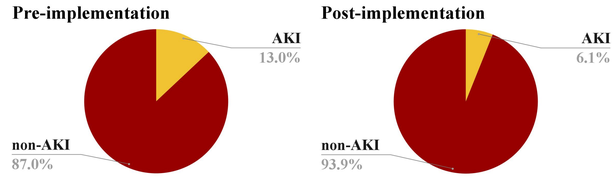


Figure 4. Concurrent vancomycin and piperacillin-tazobactam AKI trended lower with AUC:MIC approach vs trough-based method (6.1% vs 13%)

Discussion

Despite the small sample size, our study demonstrated a trend towards better attainment of the therapeutic goal of achieving an AUC:MIC ratio of 400-600 mg*hr/L, along with a reduced incidence of AKI compared to traditional trough-based dosing methods. AUC:MIC dosing method yielded a higher percentage of patients achieving therapeutic goal (47% of patients post-implementation vs 44% pre-implementation) while showing lower percentage of subtherapeutic levels. Moreover, the post-implementation group did not show higher incidences of supratherapeutic levels.

It is worth noting there were 10 patients in the post-implementation group in the AUC:MIC 350-399 mg*hr/L range. Some studies suggest that AUC:MIC range of 350-399 mg*hr/L may provide positive therapeutic outcomes for certain indications, such as skin and soft tissue infections. Although these patients did not achieve defined therapeutic AUC goals, they did show clinical resolution, thus adding to overall positive results of our study.

Our study showed that AUC:MIC guided dosing, using protocol approved pharmacokinetic calculators, was associated with a decreased AKI incidence in the post-implementation group (6.9% vs 8.9%). This strategy also yielded a lower AKI incidence in those on concurrent vancomycin and piperacillin-tazobactam (6.1% vs 13%).

Patients that fell outside therapeutic range of AUC:MIC 400-600 mg*hr/L were analyzed. Findings indicate that several factors, including obesity, improper trough sampling, chronic kidney disease (CKD), and sepsis, may have contributed to the outlier AUC levels.

Several limitations were identified, including pharmacists' familiarity with the new dosing method, variations in data collection methods among students, manual review of patient profiles, inappropriate collection of vancomycin trough levels, and unpredictable pharmacokinetic parameters in obese patients.

Conclusion

The findings of our study emphasize the benefits of AUC:MIC guided dosing over traditional trough-based dosing, with a higher proportion of patients achieving therapeutic AUC:MIC levels and a reduced occurrence of vancomycin-induced AKI. Notably, decreased incidence of AKI was recognized in the group of patients receiving concurrent administration of vancomycin and piperacillin-tazobactam.

Our findings support using vancomycin AUC:MIC guided dosing protocols to improve safety and efficacy in our clinical setting. While larger clinical trials are needed to validate these results, within the context of PHGSH, AUC:MIC monitoring appears to yield better clinical outcomes.

Acknowledgement

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Citations

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