Vancomycin Therapeutic Drug Monitoring in Pediatrics: Trough Monitoring vs. Area Under the Curve

Elizabeth Vadasz, PharmD Student[1,2]; Robert Cortez, PharmD Student[1,2]; Christian Armstrong, PharmD[2]; Christopher A. Thomas, PharmD, MBA, BCPPS[2]

[1]University of Arizona College of Pharmacy, Tucson, AZ, [2]Department of Pharmacy Services, Phoenix Children's Hospital, Phoenix, AZ

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Background

- Recent shift in therapeutic drug monitoring (TDM) of vancomycin is supported by consensus guidelines published in March 2020, which recommend area under the curve to minimum inhibitory concentration (AUC/MIC) ratio ≥ 400 to guide vancomycin dosing in pediatric and adult patients[1]
- Data suggest an increased risk of acute kidney injury (AKI) in direct correlation with trough concentration and with daily AUC > 650 mg h/L
- These guidelines recommend AUC/MIC guided vancomycin dosing to optimize therapy and minimize adverse effects
- Current Phoenix Children's Hospital (PCH) practice utilizes a hybrid model of trough and AUC dosing, beginning with trough monitoring and switching to AUC monitoring once patients require 20 mg/kg/dose

Objectives

- Determine the intrapatient difference in vancomycin dosing requirements (in mg/kg/day) when comparing AUC monitoring against trough level monitoring goals in pediatric patients at PCH
  - Hypothesis: 25% reduction in vancomycin dosing when utilizing AUC monitoring
- Determine number of dose changes required to reach therapeutic steady state, correlation of trough (in mg/L) when reaching AUC target goals > 400 mg h/L, correlation of trough levels (in mg/L) to vancomycin doses (in mg/kg/day), rates of nephrotoxicity (defined as an increase in SCr by > 0.5 mg/dL or > 50% from baseline), and clinical treatment failure (defined by need for escalation of therapy to a broader anti-MRSA agent) when using trough monitoring compared to AUC dosing

Methods

- Retrospective chart review
  - January 1st, 2018 – October 31st, 2020
  - Patients aged ≤ 19 years
  - Received vancomycin therapy for ≥ 48 hours
  - At least one vancomycin peak and trough level measured at steady state

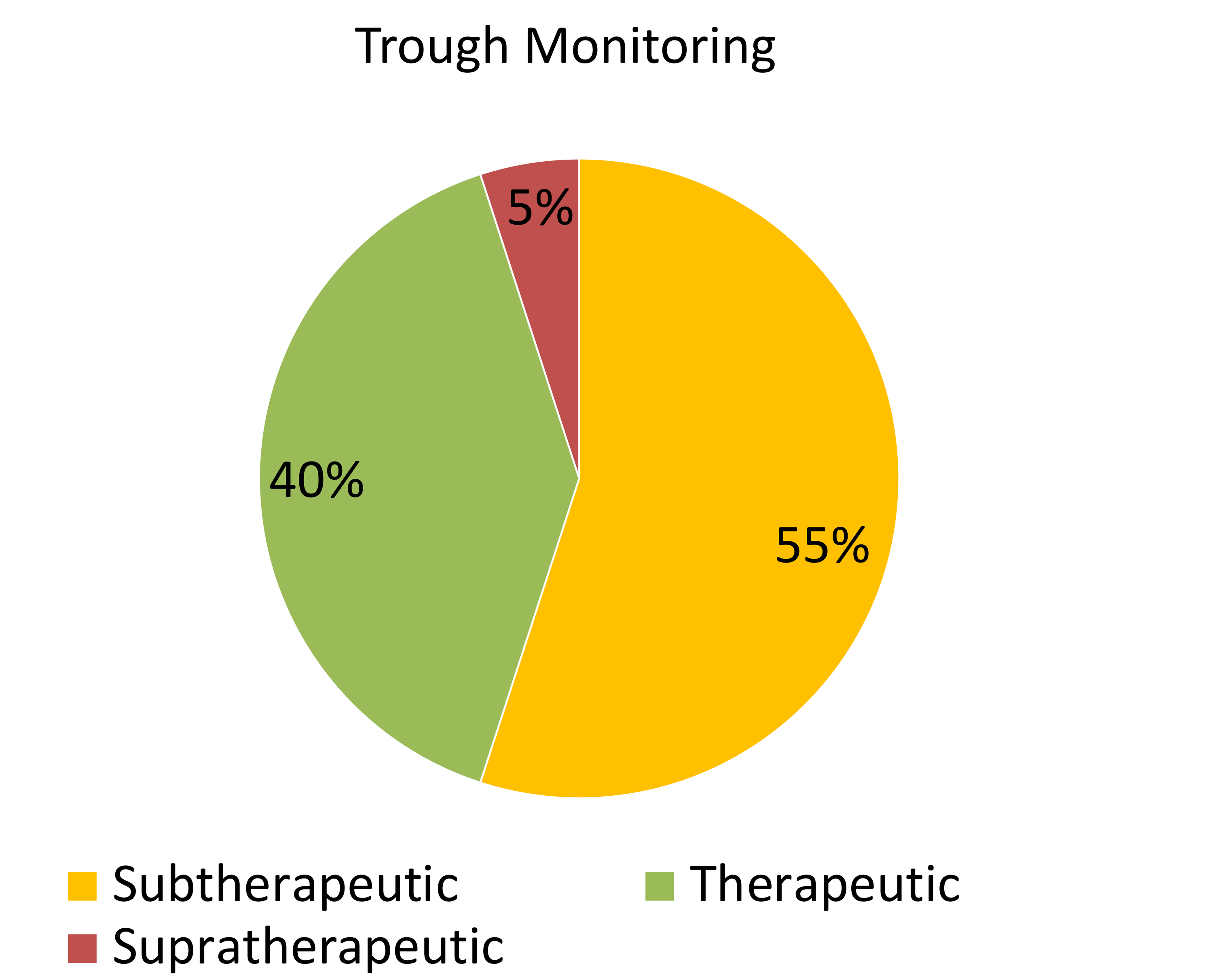
Results (n = 100)

Table 1. Vancomycin Dosing Requirements with Trough vs. AUC Monitoring

	Trough Monitoring	AUC Monitoring
Vancomycin dosing requirements (mg/kg/day)	69.3	60.6
Vancomycin dosing requirements (mg/kg/dose)	17.7	15.5
Trough correlated to AUC 400 mg h/L (mg/L)	10.5	8.4

- Decrease in daily vancomycin dosing requirements by 12.5%
- Average of 2 dose changes required to reach therapeutic steady state on trough monitoring
- No observed difference in rates of nephrotoxicity or treatment failure

Figure 1. Percentage of Therapeutic AUC Utilizing Trough vs. AUC Monitoring



22.5% increase in therapeutic target range of AUC 400-600 mg h/L

Conclusion and Discussion

- Vancomycin dosing requirements appear to be 12.5% lower in these pediatric patients when comparing AUC against trough level monitoring
- AUC monitoring led to a 15% increase in supratherapeutic levels, suggesting potential to further reduce vancomycin exposure while meeting therapeutic needs
- Adoption of AUC monitoring could decrease vancomycin exposure, ensure patients are maintained on a therapeutic regimen, and potentially minimize cost with fewer required trough levels and dose changes
- Early intervention by a pharmacist may aid empiric dosing and AUC monitoring when patients are started on vancomycin

1. Rybak MJ, Le J, Lodise TP, et al. Therapeutic monitoring of vancomycin for serious methicillin-resistant *Staphylococcus aureus* infections: a revised consensus guideline and review of the American Society of Health-System Pharmacists, the Infectious Diseases Society by America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists. *Am J Health-Syst Pharm* 2020; 77: 835–64.