Vancomycin Therapeutic Drug Monitoring: How to Hit the Curve

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Background

- Vancomycin therapeutic drug monitoring (TDM) guidelines now recommend the use of area under the curve over minimum inhibitory concentration (AUC/MIC) based versus traditional trough-based dosing
- AUC/MIC should be maintained between 400-600 mg·h/L
- Guidelines recommend two vancomycin serum levels, with at least 1 trough, or Bayesian modeling be used to most accurately estimate AUC (A-II)

Study Objectives

Primary : Assess trough level correlation to AUC/MIC based dosing using different pharmacokinetic calculators
Secondary:
1. Compare different pharmacokinetic calculators (Bayesian and non-Bayesian)
2. Evaluate proportion of patients with avoidable dose adjustments

Study Design

- Single-center, retrospective analysis, N=55
- Extrapolated trough levels were used to estimate AUC using three online calculators
- Calculator 1 (C1) utilized Bayesian modeling
- Calculators 2 and 3 (C2 and C3) utilized traditional pharmacokinetic equations

Patients who received intravenous vancomycin for any indication in 2019

Inclusion Criteria
- ≥ 18 years old
- On IV vancomycin for ≥48 hours
- Trough drawn at steady state

Exclusion Criteria
- Unstable renal function
- Undergoing renal replacement therapy

Results

Trough Analysis	Subtherapeutic			Therapeutic						Supratherapeutic		
	(<10 μ/mL)			(10-15 μ/mL)			(15-20 μ/mL)			(>20 μ/mL)		
	N=9			N=24			N=19			N=3		
AUC/MIC Estimate (mg·h/L)*	<400	400-600	>600	<400	400-600	>600	<400	400-600	>600	<400	400-600	>600
Calculator n (%)												
C1	3 (33)	5 (56)	1 (11)	1 (4)	11 (46)	12 (50)	0	0	19 (100)	0	0	3 (100)
C2	7 (78)	1 (11)	1 (11)	3 (13)	20 (83)	1 (4)	0	6 (32)	13 (68)	0	0	3 (100)
C3	6 (67)	3 (33)	0	5 (21)	18 (75)	1 (4)	0	15 (79)	4 (21)	0	1 (33)	2 (66)

*A vancomycin MIC of 1 mcg/mL was assumed for all calculations. No patients had a culture growing *Staphylococcus aureus* with a vancomycin MIC >1 mcg/mL

Trough vs. AUC/MIC Distribution

C1 R² = 0.5166   C2 R² = 0.6772   C3 R² = 0.4516
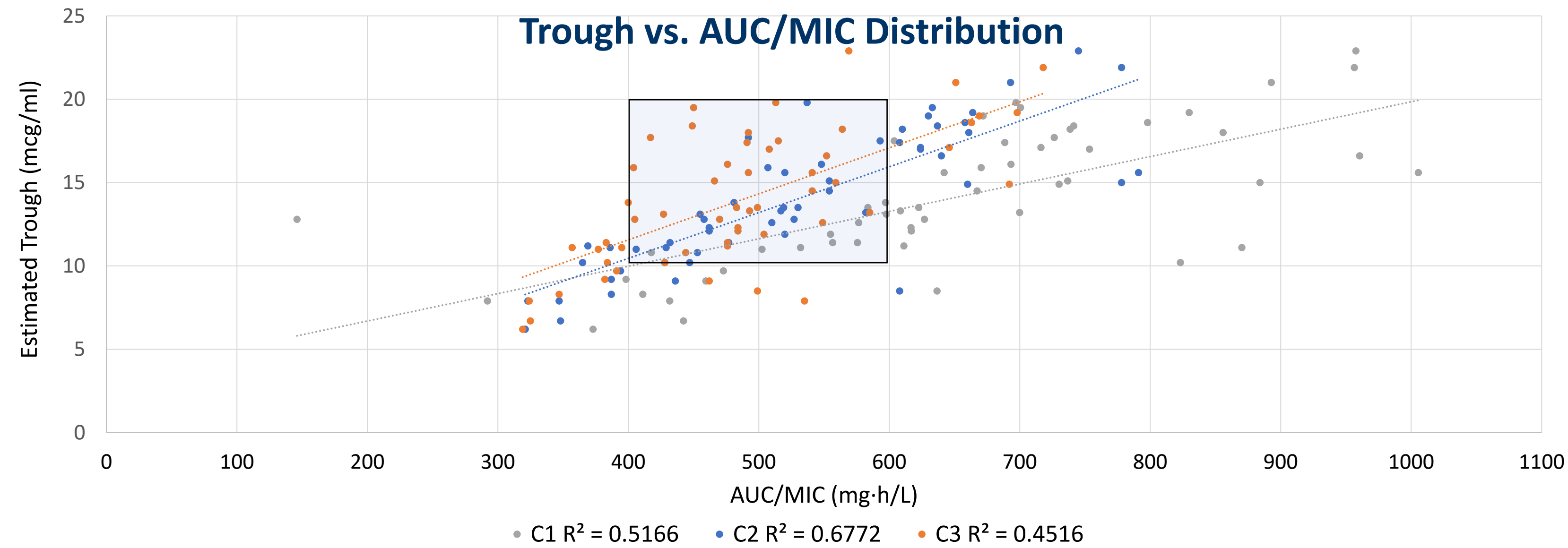
Dose Adjustments	N (%)
0	17 (31)
1	31 (56)
2	3(5)
3	1 (2)
4	3 (5)

Avoidable dose adjustments*	N (%)
C1	*11 (29)*
C2	15 (39)
C3	24 (63)

*Dose adjustments when trough correlated to AUC/MIC target (400-600mg*h/L)

Trough Timing	N (%)
>3 hours early	6 (11)
2-3 hours early	5 (9)
1-2 hours early	17 (31)
<1 hour early	7 (13)
On Time	10 (18)
<1 hour late	5 (9)
1-2 hours late	2 (4)
2-3 hours late	3 (5)

Age	Years
Mean	62.9
Median	64
Range	28 - 92
Creatine Clearance	**mL/min**
25th Percentile	76.64
Median	92
75th Percentile	114

Weight	Kg
25th Percentile	67.09
Median	81.85
75th Percentile	96.63
IBW:ABW Ratio	**N (%)**
>1.5	11 (20)
1-1.5	34 (62)
<1	9 (16)

Conclusion

- A weak relationship between AUC/MIC and steady state troughs was found
- Therapeutic troughs often correlated to an AUC/MIC greater than 400-600 mg·h/L
- All troughs between 15-20µg/ml demonstrated excess vancomycin exposure when using Bayesian modeling (C1)
- Utilizing AUC/MIC estimates for vancomycin may limit excess drug exposure
- More than 25% of trough-based dose adjustments were unnecessary with AUC/MIC estimations

Next Steps

- Conduct a prospective study comparing two level and single level AUC/MIC conversions
- Assessing nephrotoxicity post implementation of AUC based dosing

References

1. Craig W. State-of-the-Art Clinical Article: Pharmacokinetic/Pharmacodynamic Parameters: Rationale for Antibacterial Dosing of Mice and Men. Clinical Infectious Diseases. 1998;26(1):1-10. doi:10.1086/516284
2. Deryke C. Alexander D. Optimizing Vancomycin Dosing through Pharmacodynamic Assessment Targeting Area under the Concentration-Time Curve/Minimum Inhibitory Concentration. Hosp Pharm. 2009;44(9):751-765. doi:10.1310/hpj4409-751
3. Kane S. Vancomycin Calculator - ClinCalc.com. Clincalc.com. https://clincalc.com/Vancomycin/Beta.aspx#OneCompartment. Published 2020. Accessed July 15, 2020.
4. Rybak M, Le J, Lodise T et al. Therapeutic Monitoring of Vancomycin for Serious Methicillin-resistant Staphylococcus aureus Infections: A Revised Consensus Guideline. Clinical Infectious Diseases. 2020. doi:10.1093/cid/ciaa303

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