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Vancomyin Dosing and Serum Trough Levels in Hospitalized Children

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INTRODUCTION

- Vancomycin trough concentrations are the most accurate and practical method for monitoring vancomycin efficacy.[1]
- Vancomycin trough levels >10 mg/L are recommended to prevent the development of antibiotic resistance in adults.
- For complicated or severe infections (e.g. sepsis, pneumonia) serum trough levels 15–20 mg/L are recommended.[1,2]
- The objective of this study was to measure the impact of initial daily dosing on time to adequate trough attainment (defined as ≥10 mg/L) at a tertiary care pediatric hospital across a range of age groups and comorbidities.

METHODS

Study Design and Setting

- Retrospective cohort study .
- Tertiary care children's hospital, January 1, 2010 to December 31,2010.

Participants

- Hospitalized children ≤18 years old who received intravenous vancomycin for ≥72 hours .

Variables

- The primary exposure was initial daily dose of vancomycin in the first 24 hours, categorized as <40, 40-49, 50-59, ≥ 60 mg/kg/day.
- Covariates were measurement of trough at steady state, dose adjustment (≥15% increase in total daily dose in the first 48 hours), use of aminogylcosides, baseline renal insufficiency (serum creatinine level >95%ile)[3], worsening renal function (increase in serum creatinine concentrations by ≥0.50 mg/dL or 50%), use of vasopressors, and a composite age index incorporating birth weight (Table 2).
- The primary outcome was time (hrs) between initial vancomycin dose and first attainment of trough level ≥ 10 mg/L.
- The secondary outcome was time (hrs) between initial vancomycin dose and first attainment of trough level ≥ 15 mg/L for treatment of complicated infections (bacteremia, suspected sepsis, endocarditis, osteomyelitis, meningitis, and pneumonia).

Statistical Analysis

- Cox proportional hazards regression.

RESULTS

- 432 vancomycin courses prescribed to 315 patients were included in the study.
- Most common indications: suspected sepsis or blood stream infection (n=138, 31.9%), isolated fever (n=101, 23.3%), skin or soft tissue infection (n=51, 11.8%), and pneumonia (n=39, 9.0%).
- Most common prescribers: pediatric intensive are (n=121, 28.0%), neonatology (n=75, 17.4%), oncology (n=60, 13.9%), and gastroenterology (n=37, 8.6%).

Table 1. Median Time to Trough Level

Initial daily dose (mg/kg)	Median time to trough 10 mg/L (hrs)		Median time to trough 15 mg/L (hrs)	
<40	(n=156)	46.8	(n=82)	61.7
40-49	(n=137)	37.9	(n=83)	58.6
50-59	(n=44)	34.3	(n=23)	41.5
≥60	(n=23)	24.0	(n=12)	49.2

Table 2. Impact of Initial Daily Dose on Time to Trough ≥10 mg/L, Multivariable Model

Variable	Hazard ratio (CL_{95})	P
Initial daily dose (mg/kg/day)		0.003
<40	Ref	Ref
40-49	1.27 (1.01, 1.61)	0.042
50-59	1.63 (1.15, 2.31)	0.005
≥60	1.89 (1.21, 2.94)	0.004
Steady state		<0.001
Yes	Ref	Ref
No	1.53 (1.20, 1.94)	<0.001
Use of vasopressors		0.006
No	Ref	Ref
Yes	1.48 (1.12, 1.96)	0.006
Baseline renal insufficiency		0.072
No	Ref	Ref
Yes	0.78 (0.59, 1.02)	0.072
Age		0.252
>2000 grams AND ≥7 days	Ref	Ref
>2000 grams and <7 days 1200-2000 grams and <7 days 1200-2000 grams and ≥ 7 days	1.21 (0.83, 1.76)	0.321
<1200 grams AND <7 days <1200 grams AND ≥ 7 days	1.31 (0.90, 1.90)	0.153

RESULTS

Table 3. Characteristics of Vancomycin Courses

Characteristic	Number of courses (%)
Age distribution at first dose of course	
0 ≥ and < 28 days	71 (16.4)
28 days ≥ and < 1 year	114 (26.3)
1 years ≥ and <5 years	90 (20.8)
5 years ≥ and <11 years	77 (17.8)
11 years ≥ and <18 years	80 (18.5)
Hospital location	
NICU	109 (25.2)
PICU	120 (27.7)
Floor	203 (46.9)
Median length of course (hrs)	145.8 IQR 100.2-228.0
Median age at first dose of course (years)	1.8 IQR 0.2-8.4

- 72/432 (16.7%) courses did not attain a serum trough level ≥10 mg/L and 138/268 (51.5%) courses treating complicated infections did not attain a serum trough level ≥15 mg/L.

SUMMARY AND CONCLUSIONS

- A significant proportion of vancomycin courses did not attain a serum trough level >10 mg/L.
- Higher initial daily dosing ≥60 mg/kg/day can lead to serum trough level >10 mg/L nearly twice as fast compared to initial daily dosing <40 mg/kg/day.
- Vancomycin loading doses should be considered for pediatric patients with high likelihood of severe MRSA infection, as even high initial dosing is associated with a 24 hour delay in trough attainment ≥ 10 mg/L.

REFERENCES

[1] Rybak M, AJHP 2009; [2] Liu C; Clin Infect Dis 2011; [3]Soldin SJ, Pediatric Reference Ranges, 1999.

Acknowledgements

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