Higher Pediatric Vancomycin Dosing Trends Toward Improved Therapeutic Trough

August Boeglin, MD, Len Yonemura, PharmD, Marian Melish, MD, and Natascha Ching, MD
Department of Pediatrics, John A. Burns School of Medicine, University of Hawai‘i
Kapi‘olani Medical Center for Women & Children, Honolulu, Hawai‘i

Background

- Vancomycin is commonly used as a first-line drug for treating invasive gram positive bacterial infections.
- Vancomycin is difficult to dose safely due to a narrow therapeutic window.
- Troughs above 20 are associated with adverse effects including Acute Kidney Injury (AKI) and hearing loss.
- Several studies have suggested that the standard initial dose of vancomycin 40-60 mg/kg/day in children frequently produces troughs that are low.
- Our institution began using a higher initial dose of vancomycin in 2016 after medication use evaluation.

Objectives

- To evaluate if a higher initial vancomycin dose resulted in increased therapeutic serum trough levels.
- To monitor if increased vancomycin dosing resulted in increased rates of Acute Kidney Injury.

Methods

- Retrospective review of pediatric patients who received vancomycin from July 2014 to May 2017 (18 months before and 17 months after dosing policy change)
- Data was obtained from the Epic data abstraction and chart review of medical records
- 842 unique courses of vancomycin were evaluated
- 392 vancomycin courses for 340 unique patients were analyzed after excluding infants less than one month old, patients with pre-existing renal failure, and patients with no trough levels obtained
- Vancomycin dosing policy standardized but patients were managed by pharmacy consultation
- Statistical comparisons were performed using Chi-square and Fisher's Exact tests

Results

Table 1: Vancomycin Dosing Protocol

AGE	DOSE
1 month to 12 years	80mg/kg/day divided q6 hours
13 to 18 years	60mg/kg/day divided q8 hours

Table 2: Demographics

Sex	n	%
M	180	52.9%
F	160	47.1%
Total	**340**	**100%**
Age (years)	**n**	**%**
1 month – 12	272	80%
13 to 17	68	20%
Total	**340**	**100%**
Race	**n**	**%**
Pacific Islander	196	57.6%
Asian	82	24.1%
Caucasian	45	13.2%
Hispanic or Latino	6	1.8%
Black	3	0.9%
Native American	1	0.3%
Other or Unknown	7	2.1%
Total	**340**	**100%**

Table 3: Vancomycin Dosing and AKI

Age	Pre-Intervention	Post-Intervention	Change	p-value
1 month to 12 years				
Mean Initial Dose (mg/kg/day)	62.6	73.2	10.6	<0.001
AKI Rate	20.9%	8.1%	-12.8%	0.013
13 to 18 years				
Mean Initial Dose (mg/kg/day)	56.3	54.9	-1.4	0.51
AKI Rate	22.6%	12.0%	-10.6%	0.3

Figure 1: Pre- and Post-Intervention Results (Age 1 month to 12 years)

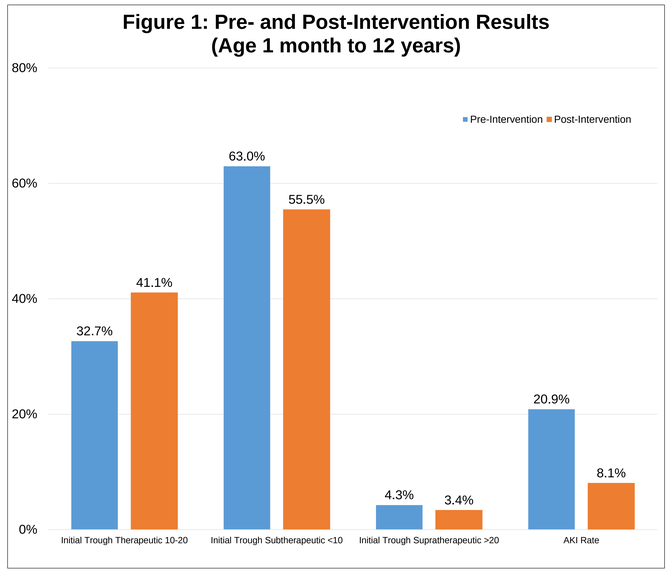
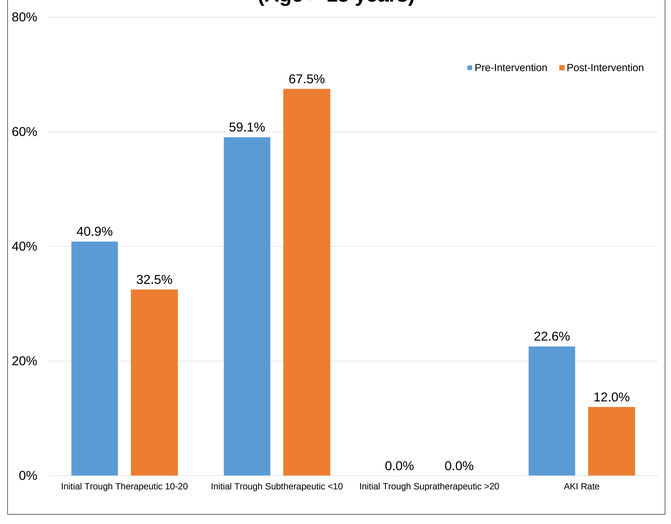


Figure 2: Pre- and Post-Intervention Results (Age > 13 years)



Conclusions

- A higher vancomycin dosing was only achieved in children under 12 years of age.
- Higher vancomycin dosing led to a trend of achieving therapeutic troughs in younger children under 12 years of age.
- An increased rate of AKI was not found with this higher dosing in both age groups.
- Supratherapeutic troughs > 20 were not found with higher dosing in either age groups.
- It remains difficult to achieve a therapeutic dose of vancomycin.
- Further study is warranted to determine optimal vancomycin dosing in pediatric patients.

References

- Abdel Hadi O, et al. Vancomycin pharmacokinetics and predicted dosage requirements in pediatric cancer patients. J Oncol Pharm Pract. 2016 Jun;22(3):448-53.
- Arfa P, et al. A Prospective Study to Assess Vancomycin Serum Concentrations in Pediatric Patients with Current Dosing Guidelines. Iran J Pharm Res. 2016 Winter;15(1):341-6.
- Akcan-Arikan A, et al. Modified RIFLE criteria in critically ill children with acute kidney injury. Kidney International 2007 71:1028-1035.
- Frymoyer A, et al. Association between Vancomycin Trough Concentration and Area under the Concentration-Time Curve in Neonates. AAC Nov 2014 Vol 58 No 11:6454-6461.
- Hwang D, et al. Vancomycin dosing and target attainment in children. J Microbiol Immunol Infect. 2017 Aug;50(4):494-499.
- Kellum JA, et al. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Journal of the International Society of Nephrology. 2012 Mar;2(1):19-23.
- Le J, et al. Improved Vancomycin Dosing in Children Using Area Under the Curve Exposure. PIDJ April 2013;Vol 32 No 4, e155-163.
- Orr H, et al. Assessment of Initial Vancomycin Dosing in Pediatric Oncology Patients. Children (Basel). 2017;Aug 28;4(9). Pii.E79.
- Rybak M, et al. Therapeutic monitoring of vancomycin in adult patients: a consensus review of the American Society of Health-System Pharmacists, the Infectious Diseases Society of American, and the Society of Infectious Diseases Pharmacists. Am J Health-Syst Pharm. 2009;66:82-98.
- Rybak M, et al. Vancomycin Therapeutic Guidelines: A Summary of Consensus Recommendations from the Infectious Diseases Society of America, the American Society of Health-System Pharmacists, and the Society of Infectious Diseases Pharmacists. Clinical Infectious Diseases, 2009;49:325–327.

Correspondence to Natascha Ching, MD at chingnat@hawaii.edu

Presented at ID Week October 3-7, 2018, San Francisco, CA