Evaluation of Vancomycin Dosing and Corresponding Drug Concentrations in Pediatric Patients

abstract

OBJECTIVE: To describe the relationships between dosing strategy, age, and vancomycin trough concentrations in pediatric patients.

METHODS: This is a retrospective review of hospitalized pediatric patients between 2 months and 17 years of age treated with intravenous vancomycin from 2008 to 2011. The primary outcome was the number of patients achieving a target trough concentration of 10 to 20 μg/mL in each age group and dosing group. The secondary outcomes were the number of patients in each group to achieve a trough concentration of 15 to 20 μg/mL and the incidence of vancomycin-induced nephrotoxicity.

RESULTS: A total of 102 patients were included in the analysis. Forty-six of 159 evaluated troughs (28.9%) were within the target range of 10 to 20 μg/mL. Dose was found to have a statistically significant effect on the ability to achieve a trough within the target range ($P = .01$). Of the 159 trough concentrations evaluated, only 11 (6.9%) were within the range of 15 to 20 μg/mL. Nephrotoxicity occurred in 7 patients and was not associated with supratherapeutic trough concentration or dose.

CONCLUSIONS: The number of trough concentrations within the target range of 10 to 20 μg/mL was low, and younger patients often needed doses >60 mg/kg per day to achieve a trough concentration in this range. The dose of vancomycin was found to have a statistically significant effect on the ability to achieve a trough concentration within the target range.

AUTHORS

Lauren Maurer Geerlof, PharmD, BCPS, and Jenny Boucher, PharmD, JD, BCPS

Lehigh Valley Health Network, Allentown, Pennsylvania

KEY WORDS

vancomycin, pediatric, infant, child, children, MRSA, methicillin-resistant, pharmacokinetic, trough, antibiotic, *Staphylococcus aureus,* pharmacodynamics, serum concentration

ABBREVIATIONS

AUC: area under the curve
IDSA: Infectious Diseases Society of America
MIC: minimum inhibitory concentration
MRSA: methicillin-resistant *Staphylococcus aureus*
SCr: serum creatinine
VIN: vancomycin-induced nephrotoxicity

Dr Geerlof wrote the first draft of the manuscript and made substantive contributions to the study; Dr Boucher made substantive contributions to the study; and both authors approved the final manuscript as submitted.

www.hospitalpediatrics.org
doi:10.1542/hpeds.2014-0019

Address correspondence to Lauren Maurer Geerlof, PharmD, BCPS, Lehigh Valley Health Network, 1200 South Cedar Crest Boulevard, Inpatient Pharmacy, Allentown, Pennsylvania. E-mail: lauren.geerlof@lvhn.org

HOSPITAL PEDIATRICS (ISSN Numbers: Print, 2154 - 1663; Online, 2154 - 1671).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

Vancomycin is the standard of therapy for empirical treatment of certain bacterial infections and is the treatment of choice for invasive methicillin-resistant *Staphylococcus aureus* (MRSA) infections.[1,2] An increasing number of treatment failures have been reported in recent years, thought to be caused by the emergence of vancomycin-intermediate *S. aureus* and heteroresistant vancomycin-intermediate *S. aureus*, as well as an increase in the median vancomycin minimum inhibitory concentration (MIC). Because of these concerns, research has focused on examining the pharmacokinetic properties of the drug and targeting serum concentrations that improve clinical outcomes. In 2009, expert consensus guidelines recommended that vancomycin trough concentrations be maintained above 10 μg/mL in adult patients to prevent the emergence of resistance.[3] In 2011, the Infectious Diseases Society of America (IDSA) recommended an increase in target trough concentration from 5 to 10 μg/mL to 15 to 20 μg/mL for invasive MRSA infections.[2] This new target was based on pharmacokinetic studies that showed that an area under the curve (AUC) for serum drug concentration versus time

to MIC ratio (AUC/MIC) of ≥400 is associated with treatment efficacy in MRSA infections in adults. A serum trough concentration of 15 to 20 μg/mL (when the MIC of the organism is 1 μg/mL) was determined to correlate with this AUC/MIC target and is more commonly used in the clinical setting.[3]

The correlation between AUC/MIC and treatment success has not been adequately studied in children, and there is limited information about what vancomycin trough concentration correlates with an AUC/MIC of ≥400 in this population. Extrapolation of the recommended adult approach to the pediatric population has been made, and recent pharmacokinetic studies are beginning to improve our knowledge of this relationship.[4,5] Genetic and developmental differences in childhood play a large role in our understanding of the optimal dosing approach.[6] Although there is limited evidence in pediatrics to support targeting trough concentrations in the range of 15 to 20 μg/mL, the IDSA recommends an initial dose of 60 mg/kg per day (15 mg/kg per dose every 6 hours) and consideration of a target trough concentration of 15 to 20 μg/mL in pediatric patients being treated for serious or invasive infections such as bacteremia, infective endocarditis, meningitis, pneumonia, severe skin and soft tissue infections, and osteomyelitis.[2] The level of evidence for general application of this dose in pediatric patients was graded B-III, defined as moderate evidence to support the use based on expert opinion, experience, or consensus. Use of this dose for bacteremia or infective endocarditis was graded A-II, defined as good evidence from ≥1 type of study that was not a randomized controlled study.[2]

Traditional dosing of 40 mg/kg per day (10 mg/kg per dose every 6 hours) has been shown in multiple studies to fall short of these target trough concentrations, and doses higher than the IDSA-recommended 60 mg/kg per day are often needed.[7–11] However, for many practitioners, the use of increasing doses raises concern about patient tolerability and safety, especially with regard to vancomycin-induced nephrotoxicity (VIN).[7,8,12–14]

To begin to formulate a dosing approach to reach recommended vancomycin trough targets, more information about the influence of developmental factors in pediatrics would be desirable. This study was designed to gather information about dosing practices at this institution to determine the effect of patient age and vancomycin total daily dose on the ability to achieve a trough concentration in the recommended range. During the time frame examined, there was no institutional protocol or guideline in place, and providers could chose dose and interval based on preference.

A handful of studies in children have attempted to investigate different dosing approaches and the ability to reach a target vancomycin trough concentration or AUC/MIC goal.[15] In our study we attempted to investigate this relationship and explore the potential influence of age on trough concentrations. Because our review spans the time frame before and after publication of the IDSA dosing guidelines recommending the higher vancomycin dosing strategy, we were also interested to see whether prescribing patterns had changed without an official protocol.

METHODS

This was an observational, retrospective, single-center chart review conducted at The Children's Hospital at Lehigh Valley Health Network in Allentown, Pennsylvania. Before study initiation, the study protocol was approved by the institutional review board.

Pediatric patients were included if they were between the ages of 60 days and 17 years, were admitted between July 1, 2007 and June 30, 2011, and were treated with intravenous vancomycin. Patients must have had ≥1 appropriately drawn vancomycin trough concentration reported to be included in the analysis. Patients were excluded if they had rapidly changing renal function at baseline (defined as a serum creatinine [SCr] change of >0.5 mg/dL or of >50% for the 2 consecutive days before initiation of therapy), were on any type of dialysis at initiation of therapy, or had chronic renal insufficiency, or any patient who was <2 years of age at initiation of therapy and was born at <37 weeks' gestation.

Data collected included vancomycin dose, dosing interval, start date, time of administration, date and time of trough draw, number of doses administered before trough draw, reported trough concentration, baseline serum creatinine, maximum SCr and date measured, concomitant nephrotoxic drugs, patient age, weight, and gender.

The appropriateness of each trough concentration was assessed by investigators, and only appropriately drawn trough concentrations were included in this review. A trough was considered appropriately drawn if it was drawn within 1 hour of the next scheduled dose and no earlier than before

the fourth dose, to ensure steady-state concentrations based on the accepted half-life of vancomycin in pediatric patients.[16]

Data were collected for each trough concentration reported. Data were separated based on patient age and total daily dose of vancomycin. Age groups were infant (2–23 months), young child (2–5 years), child (6–12 years), and adolescent (13–17 years). Dosing groups were <45 mg/kg per day, 50 mg/kg per day (doses ranging from 45 to 54 mg/kg per day), 60 mg/kg per day (doses ranging from 55 to 64 mg/kg per day), 70 mg/kg per day (doses ranging from 65 to 74 mg/kg per day), and ≥75 mg/kg per day. To examine the influence of the IDSA guidelines on prescribing patterns, we also evaluated results after separating data before and after guideline publication.

The primary objective of this study was the number of patients in each age and dosing group who achieve a target vancomycin trough concentration within the range of 10 to 20 μg/mL. The secondary objectives included the number of patients in each age and dosing group who achieve a target trough concentration of 15 to 20 μg/mL and the number of patients with documented VIN, defined as a change in SCr of >0.5 mg/dL or of >50% from baseline on ≥2 consecutive days from initiation of the drug to 72 hours after completion of therapy, a definition used in previous studies.[12] The concomitant use of nephrotoxic drugs (aminoglycosides, nonsteroidal antiinflammatory drugs, loop diuretics, acyclovir, and angiotensin-converting enzyme inhibitors) was noted in the patients meeting the criteria for VIN. A generalized mixed linear model was used to evaluate the overall effect of both age and dose on the ability to achieve a trough concentration in the target range of 10 to 20 μg/mL in this observational study. The model used a multiple degree of freedom χ^2 test. Statistical support was provided by an independent consulting statistician.

RESULTS

Of the 227 medical records evaluated, 102 individual patients met the inclusion criteria and were included in the analysis. The mean age was 6.2 years (range: 6 months–17 years), the mean baseline SCr value was 0.36 mg/dL (range: 0.1–0.9 mg/dL), the mean initial dose was 52.3 ± 7.4 mg/kg per day (range: 19.5–93 mg/kg per day), and 60.8% of patients were male.

A total of 280 troughs were reported, of which 159 were found to be appropriately drawn and were included in this analysis (Fig 1). Of the troughs evaluated, 46 (28.9%) were within the target range of 10 to 20 μg/mL. Some patients included in the analysis had both appropriately and inappropriately drawn concentrations reported. A large number of troughs were excluded for being drawn inappropriately, the majority of which occurred before the implementation of a pharmacist-driven trough timing protocol.

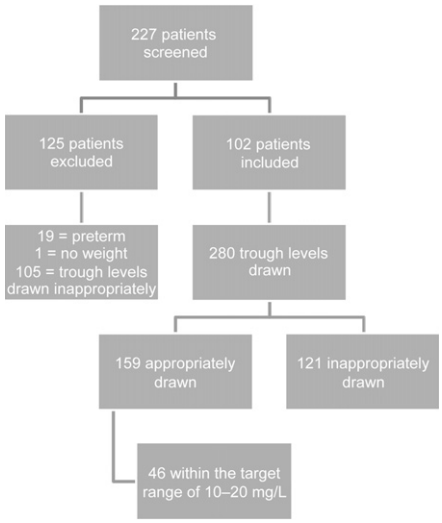

FIGURE 1 Inclusions and exclusions.

Table 1 shows the collected data for both age and dosing group. The influence of patient age on achieving a trough concentration within the recommended range was found to be insignificant ($P = .14$), and the influence of total daily dose was found to be statistically significant ($P = .01$). Of the 159 appropriately drawn troughs, 11 (6.9%) were within the range of 15 to 20 μg/mL, as shown in Table 2.

Interpatient variability led to large differences in dosing and trough concentrations across all age groups. The initial dose ranged from 19.5 to 82 mg/kg per day, and the initial trough concentration ranged from 1.2 to 34.8 μg/mL. As mentioned previously, IDSA guidelines changed dosing recommendations in 2011. Before publication of these guidelines, the average initial dose in our study population was 50.8 mg/kg per day ± 11.5 (range 19.5–82), the average initial trough was 8.2 μg/mL ± 4.6 (range 2.3–34.8), and 21.6% (19/88) of troughs were within the target range. After publication, the average initial dose was 56.8 mg/kg per day ± 7.9 (range 38–75), the average initial trough was 9.6 μg/mL ± 6.2 (range 1.2–33), and 31.25% (10/32) of troughs were within the target range. The most commonly prescribed dosing interval throughout the study period was every 6 hours, followed by every 8 hours.

As shown in Table 3, patients <6 years of age needed doses above the IDSA-recommended pediatric dose of 60 mg/kg per day to achieve a trough

TABLE 1 Number of Troughs Within Target Range (10–20 μg/mL)

Dose (mg/kg per day)	2–23 mo (%)	2–5 y (%)	6–12 y (%)	13–17 y (%)	Total (%)
<45	1/10 (10)	1/11 (9.1)	3/12 (25)	4/12 (33.3)	9/45 (20)
50	1/4 (25)	0/9 (0)	1/4 (25)	0/2 (0)	2/19 (10.5)
60	2/10 (20)	4/25 (16)	8/21 (38.1)	6/7 (85.7)	20/63 (31.7)
70	1/3 (33.3)	5/11 (45.5)	2/7 (28.6)	—	8/21 (38.1)
>75	2/2 (100)	3/4 (75)	2/4 (50)	0/1 (0)	7/11 (63.6)
Total	7/29 (24.1)	13/60 (21.7)	16/48 (33.3)	10/22 (45.5)	46/159 (28.9)

concentration within the target range of 10 to 20 μg/mL. The average daily dose when the trough was within the target range of 10 to 20 μg/mL was 69.7 mg/kg per day in the 2- to 23-month group and 66.5 mg/kg per day in the 2- to 5-year age group. Patients in the 2- to 5-year age group had the lowest average trough concentrations, and the adolescent group had lower doses and higher trough concentrations than other age groups. There were 5 (3%) supratherapeutic troughs (>20 μg/mL) in this study population (range: 24–78.8 μg/mL).

Nephrotoxicity occurred in 7 (6.9%) patients in the study population, as shown in Table 4. Six of the 7 patients were receiving concomitant nephrotoxic medications. Nephrotoxicity was not associated with supratherapeutic trough concentrations or large doses per body weight.

DISCUSSION

Deficits still exist in our knowledge of vancomycin pharmacokinetic and pharmacodynamic properties related to treatment of MRSA infections in children.[16] The "vancomycin MIC creep" is an area of interest with respect to whether traditional dosing strategies are adequately treating these dangerous and often life-threatening infections. Supporting this concern is a study that found that the majority of the MICs among community-acquired MRSA strains isolated over a 4-year period in pediatric patients were 1.5 to 2 μg/mL.[17,18]

Our data support the results of previous studies and show how prescribing patterns have changed at our institution since the publication of the IDSA recommendation in 2011. In our study population, although the number of troughs within the target range was higher after publication of the guidelines, more than half of all pediatric patients treated with vancomycin are unable to achieve an initial trough above 10 μg/mL. In our study population, doses of between 59 and 69 mg/kg per day were needed to achieve a target trough concentration >10 μg/mL in younger patients.

TABLE 2 Number of Troughs Within the Range of 15–20 μg/mL

Dose (mg/kg per day)	2–23 mo (%)	2–5 y (%)	6–12 y (%)	13–17 y (%)	Total (%)
<45	0/10 (0)	1/11 (9.1)	1/12 (8.3)	3/12 (25)	5/45 (11.1)
50	0/4 (0)	0/9 (0)	0/4 (0)	0/2 (0)	0/19 (0)
60	0/10 (0)	0/25 (0)	1/21 (4.8)	2/7 (28.6)	3/63 (4.8)
70	0/3 (0)	1/11 (9.1)	0/7 (0)	—	1/21 (4.8)
>75	0/2 (0)	0/4 (0)	2/4 (50)	0/1 (0)	2/11 (18.2)
Total	0/29 (0)	2/60 (3.3)	4/48 (8.3)	5/22 (22.7)	11/159 (6.9)

Evidence is mounting that the previous dosing strategy of 40 mg/kg per day, although still listed as a dosing option in some pediatric references, may be lagging behind what recent data suggests may be needed to pharmacokinetically optimize vancomycin treatment.[16,19] However, the targeting of higher trough concentration is controversial because the correlation between target vancomycin trough concentrations and clinical efficacy has not been shown in pediatric patients. There are currently no well-designed prospective clinical trials to establish this correlation, so we are left to rely on the pharmacokinetic properties of the drug and properties of the organisms being treated, such as *Staphylococcus aureus,* to guide treatment.

New information is becoming available, including pharmacokinetic predictor models published to examine the AUC/MIC relationship in children. In 1 study, doses of 40 to 60 mg/kg per day predicted adequate AUC/MIC values for MRSA MICs of 0.5 μg/mL, and doses of 60 mg/kg per day predicted an AUC/MIC goal of >400 in most patients when the MIC was 1 μg/mL. Neither of the dosing strategies would be expected to reach the AUC/MIC target with an MIC of 2 μg/mL in the predictor models.[8]

A recent pharmacokinetic study by Frymoyer et al[4] was designed to determine the trough concentration that would predict an AUC/MIC >400 in pediatric patients. This analysis evaluated 3 different dosing regimens: 15 mg/kg per dose every 6 hours, 20 mg/kg per dose every 8 hours, and 15 mg/kg per dose every 8 hours. The trough concentrations predictive of an AUC/MIC >400 were 7 to 10 μg/mL, 6 to 8 μg/mL, and 8 to 10 μg/mL, respectively. In

TABLE 3 Age-Related Differences in Dose and Trough Concentrations

Category	2–23 mo (n = 29)	2–5 y (n = 60)	6–12 y (n = 48)	13–17 y (n = 22)
Average trough concentration μg/mL	10.3 ± 13.8	7.3 ± 3.0	9.6 ± 5.0	12.8 ± 7.2
No. troughs within target range of 10–20 μg/mL, (%)	7 (24.1)	13 (21.7)	16 (33.3)	10 (45.5)
Average daily dose (mg/kg per day)	57.3 ± 10.3	57.2 ± 11.8	57.1 ± 13.7	47.8 ± 11.5
Average daily dose when trough <10 μg/mL	52.9 ± 9.6	54.6 ± 10.5	55.9 ± 13.5	44.0 ± 13.6
Average daily dose when trough 10–20 μg/mL	69.7 ± 14.7	66.5 ± 12.0	59.4 ± 14.2	51.3 ± 9.6

agreement with our study, results showed that children were unlikely to achieve a trough concentration of ≥10 μg/mL with dosing of 45 mg/kg per day divided every 8 hours. Interestingly, authors concluded that doses >60 mg/kg per day are unnecessary in most pediatric patients, and target trough concentrations of 7 to 10 μg/mL with IDSA-recommended dosing are reliable to achieve a goal AUC/MIC >400 in organisms with an MIC ≤1 μg/mL. However, when organisms with an MIC of 2 μg/mL were evaluated, only 1% to 17% of children achieved an AUC/MIC >400, even with a trough concentration of 15 to 20 μg/mL.

Another study in pediatric patients found that an initial dose of 60 mg/kg per day was less likely to result in a low initial vancomycin trough concentration of <5 μg/mL (P < .001) without causing more supratherapeutic levels (P = .9). However, only 37% of patients in this "high dose" group achieved an initial target trough concentration of 10 to 20 μg/mL.[10] Several other studies in pediatric patients have reported difficulty in reaching recommended target vancomycin trough concentrations with dosing <60 mg/kg per day.[7–11] Eiland et al[7] used predictive equations to determine that doses of 70 to 85 mg/kg per day would be needed to meet target trough concentrations of 10 to 15 μg/mL. Glover et al[11] concluded that doses >40 mg/kg per day were needed to attain trough concentrations between 5 and 10 μg/mL. Authors recommended an initial dose of 60 mg/kg per day.

Other studies have investigated the peak and trough concentrations attained with various dosing interval strategies.[20,21] These studies have found that to avoid undesirably high peak levels, the best approach would be to provide the daily dose divided every 6 hours, which is in line with the dosing approach recommendations from IDSA.[3,20,21] Benner et al[21] found that for groups receiving 10 mg/kg every 8 hours, the mean trough concentration was below the target range (<5 μg/mL) more frequently compared with the groups dosed at 15 mg/kg per dose and 20 mg/kg per dose every 6, 8, or 12 hours (P < .001).

Another recent pharmacokinetic study by Le et al[5] found that an initial dose of ~45 mg/kg per day resulted in a mean AUC of 449 ± 216 μg-hr/mL and minimum trough concentration of 12 ± 8 μg/mL, and an initial dose of 70 mg/kg per day resulted in a mean AUC of 699 ± 333 μg-hr/mL and minimum trough concentration of 19 ± 13 μg/mL. Authors recommended an empirical dose of 60 mg/kg per day for patients ≥2 years old and 70 mg/kg per day divided every 6 hours for patients between 3 months and 2 years of age, or MICs ≥1.5 μg/mL. These results and those of multiple other studies, including our own, have shown that younger children, specifically those <5 years of age, consistently have the lowest serum trough concentrations of all pediatric age groups.[22] In our study, patients in the 2- to 5-year age group had an average trough concentration of 7.3 μg/mL and an average daily dose of 57.2 mg/kg per day, compared with patients in the 6- to 12-year-old group, who had an average trough concentration of 9.6 μg/mL with a similar average daily dose of 57.1 mg/kg per day.

Another area of interest is the influence of higher dosing targets on the incidence of nephrotoxicity. The incidence of VIN in our study was similar to that of other trials in pediatric patients.[12–14] Although 7 patients met the criteria of our prespecified definition of nephrotoxicity, only 2 patients had an increase in SCr of ≥0.5 mg/dL. Six of the 7 patients were receiving drugs with nephrotoxic potential in addition to vancomycin.

TABLE 4 Nephrotoxicity

Age	Dose (mg/kg per day)	Trough (μg/mL)	Baseline SCr (mg/dL)	Maximum SCr (mg/dL)	% Change	Concomitant Nephrotoxic Drugs?
10 mo	40	6.6	0.1	0.2	100	No
11 mo	58	6.2	0.2	0.3	50	Yes, furosemide
5 y	52	6.1	0.3	0.8	166.7	Yes, furosemide
5 y	58	5	0.2	0.4	100	Yes, gentamicin
8 y	40	8.9	0.4	0.6	50	Yes, gentamicin
8 y	43	7.7	0.3	1.1	266.7	Yes, furosemide
15 y	55	21	0.4	0.6	50	Yes, gentamicin

The strengths of this study include that the patients were separated based on age and dosing strategy. Renal clearance of vancomycin varies by age, and separating patients by age allowed us to observe trends. Also, the troughs were assessed for appropriate timing, and only appropriately drawn trough concentrations were included. Limitations of the study include that only a single institution was sampled, there was a small sample size, some patients were sampled multiple times, and a retrospective study design was used. Dividing the small sample size into multiple groups weakened the statistical power to detect relationships. We also did not separate patients by severity of illness or disease state, which could have influenced volume of distribution and therefore trough concentrations.

CONCLUSIONS

Less than a third of trough concentrations in our study population were within the target range of 10 to 20 μg/mL, and doses ≥60 mg/kg per day were often needed when that trough range was desired, especially for younger patients. An initial dose of 60 mg/kg per day for patients ≤12 years of age is reasonable and in our study population was not associated with an increase in nephrotoxicity or supratherapeutic trough concentrations.

REFERENCES

1. Kaplan SL. Methicillin-resistant *Staphylococcus aureus* in children: treatment of invasive infections. 2011. Available at: www.uptodate.com/contents/treatment-of-invasive-methicillin-resistant-staphylococcus-aureus-infection-in-children?view=print
2. Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infection in adults and children. *Clin Infect Dis*. 2011;52(3):1–38.
3. Rybak M, Lomaestro B, Rotschafer JC, 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 America, and the Society of Infectious Diseases Pharmacists. *Am J Health Syst Pharm*. 2009;66(1):82–98.
4. Frymoyer A, Guglielmo J, Hersh AL. Desired vancomycin trough serum concentration for treating invasive methicillin-resistant staphylococcal infections. *Pediatr Infect Dis J*. doi:10.1093/jpids/pis083.
5. Le J, Bradley JS, Murray W, et al. Improved vancomycin dosing in children using area under the curve exposure. *Pediatr Infect Dis J*. 2013;32(4):e155–e163.
6. Anderson GD, Lynn AM. Optimizing pediatric dosing: a developmental pharmacologic approach. *Pharmacotherapy*. 2009;29(6):680–690.
7. Eiland LS, English TM, Eiland EH III. Assessment of vancomycin dosing and subsequent serum concentrations in pediatric patients. *Ann Pharmacother*. 2011;45(5):582–589.
8. Frymoyer A, Hersh AL, Benet LZ, Guglielmo BJ. Current recommended dosing of vancomycin for children with invasive methicillin-resistant *Staphylococcus aureus* infections is inadequate. *Pediatr Infect Dis J*. 2009;28(5):398–402.
9. Broome L, So TY. An evaluation of initial vancomycin dosing in infants, children, and adolescents. *Int J Pediatr*. 2011;2011:470364.
10. Frymoyer A, Guglielmo BJ, Wilson SD, Scarpace SB, Benet LZ, Hersh AL. Impact of hospital-wide change in empiric pediatric vancomycin dosing and associate therapeutic concentrations. *Pharmacotherapy*. 2011;31(9):871–876.
11. Glover ML, Cole E, Wolfsdorf J. Vancomycin dosage requirements among pediatric intensive care unit patients with normal renal function. *J Crit Care*. 2000;15(1):1–4.
12. McKamy S, Hernandez E, Jahng M, Moriwaki T, Deveikis A, Le J. Incidence and risk factors influencing the development of vancomycin nephrotoxicity in children. *J Pediatr*. 2011;158(3):422–426.
13. Kim DI, Im MS, Choi JH, Lee J, Choi EH, Lee HJ. Therapeutic monitoring of vancomycin according to initial dosing regimen in pediatric patients. *Korean J Pediatr*. 2010;53(12):1000–1005.
14. Cies JJ, Shankar V. Nephrotoxicity in patients with vancomycin trough concentrations of 15–20 μg/ml in a pediatric intensive care unit. *Pharmacotherapy*. 2013;33(4):392–400.
15. Cole TS, Riordan A. Vancomycin dosing in children: what is the question? *Arch Dis Child*. 2013;98(12):994–997.
16. Taketomo CK, Hodding JH, Kraus DM. Vancomycin. In: *Pediatric and Neonatal Dosage Handbook*. 19th ed. Hudson, OH: Lexi-comp, Inc; 2012:1715.
17. Gordon CL, Thompson C, Carapetis JR, Turnidge J, Kilburn C, Currie BJ. Trough concentrations of vancomycin: adult therapeutic targets are not appropriate for children. *Pediatr Infect Dis J*. 2012;31(12):1269–1271.
18. Jimenez-Truque N, Thomsen I, Saye E, Creech CB. Should higher vancomycin trough levels be targeted for invasive community-acquired methicillin-resistant *Staphylococcus aureus* infections in children? *Pediatr Infect Dis J*. 2010;29(4):368–370.
19. Tschudy MM, Arcara KM. Vancomycin. In: Johns Hopkins Hospital, Arcara K, Tschudy M. *The Harriet Lane Handbook*. 19th ed. Philadelphia, PA: Elsevier Mosby; 2012:974.
20. Nassar L, Hadad S, Gefen A, et al. Prospective evaluation of the dosing regimen of vancomycin in children of different weight categories. *Curr Drug Saf*. 2012;7(5):375–381.
21. Benner KW, Worthington MA, Kimberlin DW, Hill K, Buckley K, Tofil NM. Correlation of vancomycin dosing to serum concentrations in pediatric patients: a retrospective database review. *J Pediatr Pharmacol Ther*. 2009;14(2):86–93.
22. Madigan T, Sieve RM, Graner KK, Banerjee R. The effect of age and weight on vancomycin serum trough concentrations in pediatric patients. *Pharmacotherapy*. 2013;33(12):1264–1272.

Evaluation of Vancomycin Dosing and Corresponding Drug Concentrations in Pediatric Patients

Lauren Maurer Geerlof and Jenny Boucher

Hospital Pediatrics 2014;4;342
DOI: 10.1542/hpeds.2014-0019

Evaluation of Vancomycin Dosing and Corresponding Drug Concentrations in Pediatric Patients

Lauren Maurer Geerlof and Jenny Boucher

Hospital Pediatrics 2014;4;342
DOI: 10.1542/hpeds.2014-0019