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Evaluation of an Empiric Vancomycin Dosing Protocol on Goal Troughs and Acute Kidney Injury in a Neonatal Intensive Care Unit

Allison M. Kenneally, PharmD; Kelsey R. Leonhardt, PharmD; Aric Schadler, PhD; and Karen L. Garlitz, PharmD

OBJECTIVE Review the efficacy and safety of an updated empiric vancomycin dosing protocol in a neonatal intensive care unit (NICU).

METHODS Retrospective chart review including neonates with postmenstrual age (PMA) less than 40 weeks without renal dysfunction who received vancomycin per protocol at a single institution's NICU before and after implementation of an updated dosing protocol. The primary outcome is the proportion of initial therapeutic troughs. Secondary outcomes include average trough, achievement of a therapeutic trough, number of days before attainment of a therapeutic trough, and proportion of acute kidney injury (AKI) during therapy.

RESULTS The 2 groups were similar in gestational age, race, birth weight, PMA, and weight at time of vancomycin initiation. The post-implementation group had a higher proportion of initial therapeutic troughs (33.0% vs 55.1%) and a lower proportion of a subtherapeutic (58.7% vs 43.8%) and supratherapeutic (8.3% vs 1.1%) initial troughs ($p = 0.002$). The median trough was not different (9.20 vs 10.50 mg/L; $p = 0.092$). There was no difference in the proportions of achieving a therapeutic trough throughout therapy (69% vs 76%; $p = 0.235$); however, the post-implementation group achieved a therapeutic trough 1 day earlier (3 vs 2 days; $p < 0.001$). There was no difference in proportions of AKI developing between the pre-implementation vs post-implementation groups (10.1% vs 5.6%; $p = 0.251$).

CONCLUSIONS Implementation of an updated vancomycin dosing protocol yielded a higher percentage of initial therapeutic vancomycin troughs and patients reached the therapeutic range 1 day earlier without increasing the proportion of AKI.

ABBREVIATIONS AKI, acute kidney injury; IDSA, Infectious Disease Society of America; LOS, late-onset sepsis; NICU, neonatal intensive care unit; MRSA, methicillin-resistant *Staphylococcus aureus;* PMA, postmenstrual age; PNA, postnatal age; SCr, serum creatinine; UOP, urine output

KEYWORDS acute kidney injury; critical care; drug monitoring; intensive care units, neonatal; vancomycin

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Introduction

Vancomycin is a commonly prescribed antimicrobial for the treatment of late-onset sepsis (LOS) in neonates, which has a reported incidence between 14% and 41% in neonates, with mortality rates ranging from 13% to 18%.[1–3] Vancomycin targets Gram-positive organisms; in particular it provides coverage of methicillin-resistant *Staphylococcus aureus* (MRSA), coagulase-negative staphylococci, and ampicillin-resistant *Enterococcus* species.[4] Neonates have altered pharmacokinetics compared with other pediatric patients or adults because they have larger volumes of distribution, reduced clearance, and reduced protein binding, leading to difficulties in dosing vancomycin.[5] These changes in pharmacokinetics have led to wide variations in dosing and no clear consensus on the optimal vancomycin dosing regimen.

There are multiple options for dosing vancomycin in the neonatal population, with current dosing recommendations based on the patient's postmenstrual age (PMA), postnatal age (PNA), and serum creatinine (SCr).[6,7] This recommendation for neonates is extrapolated from the 2011 Infectious Disease Society of America (IDSA) recommendations for the treatment of MRSA infections in adults and children, which recommended in adults that serum trough concentrations of 10 to 20 mg/L would be appropriate; more specifically, 15 to 20 mg/L for serious infections and 10 to 15 mg/L for non-serious infections.[8] They also include that the efficacy of targeting trough concentrations of 15 to 20 mg/L in children requires

Figure 1. Vancomycin dosing protocol in pre-implementation and post-implementation groups. Transition between the 2 protocols occurred on January 1, 2020.

Pre-Implementation		
PMA, wk	PNA, wk	Dose, mg/kg
≤ 28	≤ 2	15 q24h
≤ 28	> 2	15 q18h
29-32	≤ 2	15 q18h
29-32	> 2	15 q12h
≥ 33	≤ 2	15 q12h
≥ 33	> 2	15 q8h

Post-Implementation		
PMA, wk	PNA, wk	Dose, mg/kg
≤ 28	≤ 2	15 q18h
≤ 28	> 2	15 q12h
29-43	≤ 2	15 q12h
29-43	> 2	15 q8h
≥ 44	≤ 2	15 q6h
≥ 44	> 2	

PMA, postmenstrual age; PNA, postnatal age.

additional study but should be considered in serious infections. This vancomycin target of 10 to 20 mg/L was historically used to serve as a surrogate for an AUC/MIC of 400 to 600; however, more recent studies have found that troughs ranging from 7 to 11 mg/L may correlate to an AUC/MIC of >400.[9] This led to the practice in neonates of dosing vancomycin based on a variety of factors, including PMA, PNA, renal function, and collecting a serum trough concentration before the fourth dose to target 10 to 20 mg/L, dependent on severity. The purpose of this study is to evaluate the safety and efficacy of a single institution's neonatal intensive care unit (NICU) vancomycin dosing before and after the implementation of an updated protocol.

Materials and Methods

Patient Population. This study was a retrospective chart review at a single institution's level 4, 70-bed NICU, located within a children's hospital within an adult teaching institution. Patients were identified by performing a search through the electronic medical records looking for vancomycin orders between January 1, 2014, to September 30, 2021. Patients were included if they received intravenous vancomycin per the dosing protocol, had at least 1 vancomycin trough obtained, and were less than 40 weeks PMA upon therapy initiation. Patients were excluded if they had documented renal dysfunction at the time of initiation. Renal dysfunction was defined as urine output (UOP) <1 mL/kg/hr during the last 24-hour period or an active diagnosis of renal dysfunction in the patient problem list. Only the patient's initial vancomycin course was included in the analysis and all subsequent courses were excluded, so each course represents a different patient. At this institution, providers may choose to enter a pharmacist-to-dose order for vancomycin or use the pharmacy-directed order set to order the correct dose of vancomycin per the protocol. Our institution's protocol recommends obtaining a vancomycin serum concentration as a trough before the fourth dose of vancomycin, unless extenuating circumstances arise. The updated vancomycin dosing protocol was implemented on January 1, 2020, and the dosing recommendations for the 2 groups can be found in Figure 1. The pre-implementation group consisted of patients who received an initial course of vancomycin from January 1, 2014, until December 31, 2019. The post-implementation group consisted of patients who received an initial course of vancomycin from January 1, 2020, until September 30, 2021.

Data Collected. Data collected included baseline patient demographics, including gestational age, birth weight, sex, and race. Patient data during vancomycin therapy (including age and weight at time of initiation, UOP, and SCr) and details about dosing of vancomycin throughout therapy (including adherence to the protocol, all serum trough concentrations, duration of treatment, dosing strategies) were obtained. AKIs were determined using the Neonatal Modified KDIGO Criteria for Acute Kidney Injury,[10] and the patient's most severe AKI stage throughout therapy was reported based on collected SCr and UOP. The patient's baseline SCr was defined as the last SCr obtained within 48 hours of vancomycin initiation. A patient was determined to have a stage 1 AKI if their SCr was 1.5 to 1.9 times baseline within 7 days, if their SCr increased by more than 0.3 mg/dL within 48 hours, or if their UOP totaled 0.5 to 1 mL/kg/hr during 24 hours. A patient was determined to have a stage 2 AKI if their SCr was 2.0 to 2.9 times baseline or if their UOP totaled 0.3 to 0.5 mL/kg/hr during 24 hours. And finally, they were determined to have a stage 3 AKI if their SCr was 3 times their baseline, if their SCr was greater than 2.5 mg/dL at any point, if their UOP totaled <0.3 mL/kg/hr during 24 hours, or if they required renal replacement therapy.

Outcomes. The primary outcome was the proportion of initial therapeutic vancomycin troughs, with subtherapeutic defined as a trough of <10 mg/L, therapeutic defined as 10 to 20 mg/L, and supratherapeutic defined as >20 mg/L. Because this study was initiated prior to the publication of the updated vancomycin monitoring guidelines by Rybak et al[11] in 2020, this study defined efficacy based on the therapeutic trough of 10 to 20 mg/L, as per the 2011 IDSA MRSA guidelines, and did not assess AUC/MIC. Secondary outcomes include the average initial trough, proportion of achievement

of a therapeutic trough throughout the course, number of days before attainment of a therapeutic trough, and proportion of AKI throughout the course. A "day" is defined as a calendar day, where vancomycin was initiated on day 1 and each subsequent calendar day is the next day in therapy.

Data Analysis. Statistical analysis was performed using IBM SPSS Statistics Version 27 (IBM Corp, Armonk, NY) and SAS version 9.4 (SAS Institute Inc, Cary, NC). Categoric variables were analyzed using Pearson χ^2 or Fisher exact test, as appropriate. Continuous variables were analyzed using independent samples *t*-test or independent samples difference of medians, as appropriate. Statistical significance was established with an α level of 0.05. Statistically significant variables identified in the bivariate analysis were carried forward into a multivariable logistic model with backwards selection criteria to assess for variables associated with AKI.

Results

There were 384 vancomycin courses in our NICU identified within the selected date range, of which 109 were included in the pre-implementation group and 89 were included in the post-implementation group. All troughs were collected at steady state prior to the fourth or fifth dose of vancomycin. Patients were excluded (n = 186) if: no vancomycin trough was obtained (n = 85; 46%), the initial vancomycin dose did not match the respective protocol (n = 54; 29%), PMA was >40 weeks at time of initiation (n = 28; 15%), or renal dysfunction was documented at the time of initiation (n = 19; 10%).

Baseline demographics can be found in Table 1. The 2 groups were well balanced based on sex, birth weight, race, and PMA and PNA at time of vancomycin initiation. Those in the pre-implementation group had a higher proportion of "other" as the vancomycin indication (22% vs 9%; p = 0.013), which mainly consisted of skin and soft tissue infections. They additionally had a higher use of piperacillin-tazobactam (42% vs 18%; p < 0.001) and a lower use of cefepime (18% vs 37%; p = 0.003). There was no difference among the median duration of therapy (6 vs 5 days; p = 0.575).

As seen in Figure 2, the post-implementation group had a higher proportion of initial therapeutic troughs (33.0% vs

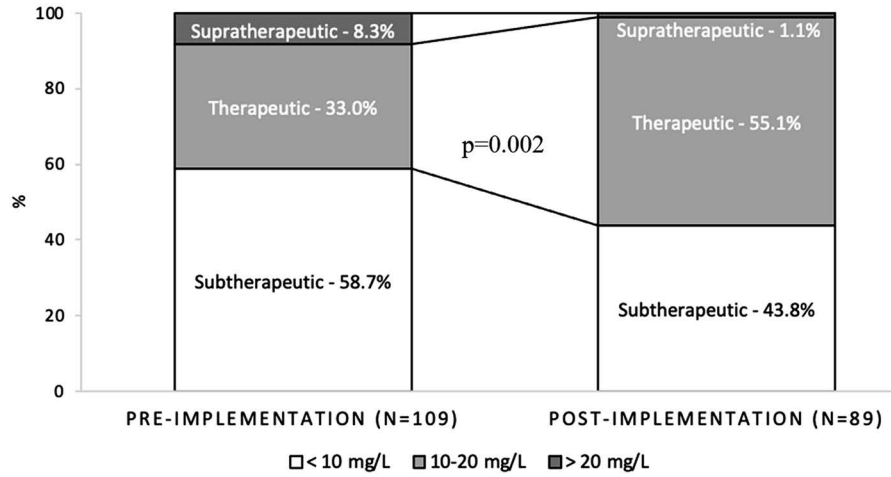
Table 1. Baseline Demographics of Pre-implementation and Post-implementation Groups*

	Pre-implementation (n = 109)	Post-implementation (n = 89)	p value
PMA (wk,day), median (IQR)	32w4d (29w2d–37w5d)	32w4d (28w6d–37w6d)	0.775
PNA, median (IQR), days	14 (7–30)	14 (6–28)	0.874
Male, n (%)	74 (68)	56 (63)	0.464
Race, n (%)			
White	99 (91)	75 (84)	n/a
African American	8 (7)	10 (11)	
Hispanic	1 (1)	0 (0)	
Asian	1 (1)	1 (1)	
Unknown	0 (0)	3 (4)	
Weight at time of vancomycin initiation, median (IQR), kg	1.07 (0.77–2.49)	1.03 (0.74–2.70)	0.775
Vancomycin indication, n (%)			
Early-onset sepsis	16 (15)	14 (16)	0.837
Late-onset sepsis	66 (61)	63 (71)	0.133
Necrotizing enterocolitis	12 (11)	8 (9)	0.639
Pneumonia	9 (8)	5 (6)	0.471
Other	24 (22)	8 (9)	0.013
Concomitant antimicrobials, n (%)			
Ampicillin	10 (9)	8 (9)	0.964
Gentamicin	32 (29)	33 (37)	0.250
Cefepime	20 (18)	33 (37)	0.003
Nafcillin	2 (2)	1 (1)	0.684
Piperacillin-tazobactam	46 (42)	16 (18)	<0.001
Acyclovir	14 (13)	9 (10)	0.551
Fluconazole	6 (6)	6 (7)	0.717
Other	29 (27)	20 (22)	0.503
None	15 (14)	6 (7)	0.111

n/a, not applicable; PMA, postmenstrual age; PNA, postnatal age

* For the definition of pre-implementation and post-implementation, please see Figure 1.

Figure 2. Primary outcome of initial proportion of therapeutic, subtherapeutic, and supratherapeutic vancomycin troughs in pre-implementation and post-implementation groups.



55.1%) and a lower proportion of initial subtherapeutic (58.7% vs 43.8%) and initial supratherapeutic troughs (8.3% vs 1.1%), p = 0.002. Secondary outcomes can be found in Table 2. Despite the higher vancomycin dosing recommended in the post-implementation group, there was no difference among the median initial vancomycin trough (9.20 vs 10.50; p = 0.092). There was no difference in the proportions of achieving a therapeutic trough throughout the course (69% vs 76%; p = 0.235); however, the post-implementation group achieved a therapeutic trough 1 day earlier (3 vs 2 days; p < 0.001). There was no difference in the proportion of initial therapeutic trough based on the patient's PMA and PNA dosing category during the course (p = 0.235).

The 2 groups had a similar baseline UOP (3.2 vs 3.4 mL/kg/hr; p = 0.192) and similar lowest UOP during

Table 2. Secondary Outcomes for Pre-implementation and Post-implementation Groups

	Pre-implementation (n = 109)	Post-implementation (n = 89)	p value
Initial vancomycin trough, median (IQR), mg/L	9.20 (5.90–13.30)	10.50 (7.70–13.75)	0.092
Duration of vancomycin therapy, median (IQR), days	6 (4–9)	5 (4–8.5)	0.575
Attainment of therapeutic trough during therapy, n (%)	75 (69)	68 (76)	0.235
Days to attainment of therapeutic vancomycin trough, median (IQR)	3 (2–4)	2 (1–3)	<0.001
Baseline SCr, median (IQR), mg/dL	0.51 (0.36–0.73)	0.42 (0.27–0.57)	0.042
Baseline UOP, median (IQR), mL/kg/hr	3.2 (2.4–4.2)	3.4 (2.4–4.2)	0.192
Highest SCr during therapy, median (IQR), mg/dL	0.59 (0.39–0.84)	0.46 (0.30–0.67)	0.004
Lowest UOP during therapy, mean ± SD, mL/kg/hr	2.5 ± 1.1	2.7 ± 1.1	0.413
AKI development, n (%)			
No	98 (89.9)	84 (94.4)	0.251
Yes	11 (10.1)	5 (5.6)	
AKI by stage, n (%)			
Stage 1	6 (5.5)	5 (5.6)	n/a
Stage 2	2 (1.8)	0 (0)	
Stage 3	3 (2.8)	0 (0)	
Day of AKI development, median (IQR)	3.0 (2.0–4.0)	3.0 (2.0–7.0)	1.000

AKI, acute kidney injury; n/a, not applicable

therapy (2.5 vs 2.7; p = 0.413). The pre-implementation group had a higher baseline SCr (0.51 vs 0.42; p = 0.042) and higher peak SCr during therapy (0.59 vs 0.46; p = 0.004). There was no difference in the proportions of development of AKI (10.1% vs 5.6%; p = 0.251); however, those in the pre-implementation group had a higher proportion of stage 2 and 3 AKIs. Of those who did develop AKI, the median (IQR) onset of AKI was day 3 (days 2–6) of therapy for all patients. Most patients who developed AKI were initiated on vancomycin for LOS (50.0%), followed by necrotizing enterocolitis (37.5%) and early-onset sepsis (25.0%). Of the 16 patients who developed AKI, 14 patients received at least 1 dose of a concomitant nephrotoxic antimicrobial during their vancomycin therapy; 8 of those patients received piperacillin-tazobactam, 4 received gentamicin, and 2 received both piperacillin-tazobactam and gentamicin. Only 2 patients developed AKI without an additional nephrotoxic antimicrobial during therapy. The 4 significant variables identified in the bivariate analysis (pre- vs post-implementation, concomitant cefepime, concomitant piperacillin-tazobactam, and "other" indication) were carried forward to complete a multivariate logistic regression for the development of an AKI. It was determined that the OR for a patient who received concomitant piperacillin-tazobactam was 3.18 times more likely to develop an AKI (95% CI, 1.11–8.84; Supplemental Table). In the presence of significant variables identified in the bivariate analysis, this was the only variable found to be a significant driver in explaining an increase in the proportion of AKI.

Discussion

During the implementation of a new protocol using larger total daily doses of vancomycin in preterm infants, a higher proportion of patients achieved an initial therapeutic serum trough concentration and a lower proportion achieved a subtherapeutic or supratherapeutic trough. After updating the vancomycin protocol, neonates received a total daily dose of vancomycin ranging from 20 to 60 mg/kg/day based on their PMA and PNA, which aligns with current literature on the dose required to achieve a trough concentration of 10 to 20 mg/L.[6,7,12,13] There was no difference in the median initial trough value or the proportion of attainment of therapeutic trough throughout the vancomycin course, but those in the post-implementation group did reach a therapeutic trough 1 day earlier than those in the pre-implementation group. This likely represents that the larger total daily dose in the post-implementation group was more appropriate for these patients to reach a goal vancomycin serum trough concentration of 10 to 20 mg/L. Additionally, there were no significant differences in the proportion of initial therapeutic troughs based on the patient's PMA and PNA dosing category, indicating that there was not a group of patients where the newly implemented protocol performed better or worse than the previous protocol.

In the same month as the implementation of the new vancomycin dosing protocol, vancomycin was also added as a preferred empiric antibiotic to the institution's LOS workup, which may account for the similar number of patients enrolled in the post-implementation group despite the shorter time period.

Our study is comparable to other published literature on vancomycin dosing to achieve a goal trough of 10 to 20 mg/L. Chung et al[14] retrospectively reviewed neonates who were initiated on vancomycin, most of whom (86.6%) were dosed according to the NeoFax (2015)/Harriet Lane (20th edition) algorithm, where patients received 10 to 15 mg/kg/dose every 6 to 18 hours based on their PMA and PNA. Their results showed that 60.7% of patients who were dosed according to the algorithm had an initial therapeutic trough defined as 10 to 20 mg/L, and those who were initiated at a larger dose (15 mg/kg/dose vs 10 mg/kg/dose) were more likely to attain therapeutic concentrations (OR, 11.22; 95% CI, 3.96–31.81). This study is overall comparable to our study with regard to dosing and proportion of initial therapeutic trough in the post-implementation group (60.7% vs 55.1%). Radu et al[15] also evaluated a revised vancomycin dosing protocol for neonates on the achievement of a target vancomycin trough of 10 to 20 mg/L. Patients received 15 mg/kg/dose every 8 to 24 hours based on their PNA and weight, which was increased from their original dosing regimen that recommended 15 to 45 mg/kg/day, and had a similar proportion of therapeutic trough at 55.1% as our study in the post-implementation group. Finally, Vandendriessche et al[16] reviewed neonates who received vancomycin for LOS. Vancomycin dosing changed from being originally based on PMA and SCr, for which they would receive 15 mg/kg/dose every 8 to 24 hours, and changed to dosing based on PMA and PNA, for which they would receive 10 mg/kg/dose every 8 to 18 hours. Both dosing regimens provide a smaller total daily vancomycin dose than in our study, and they correlated with a lower trough (7.8 and 5.8 mg/L in each dosing regimen, respectively) and higher proportion of subtherapeutic trough (66.3% and 76.3% in each dosing regimen, respectively) than in our study's post-implementation group (43.8%).

In our study, both groups of patients most commonly received vancomycin for LOS, followed by early-onset sepsis and necrotizing enterocolitis. Vancomycin has a clear therapeutic place in the management of LOS, but it is not a common empiric antibiotic for early-onset sepsis or necrotizing enterocolitis.[17,18] Culture data were not obtained during our study, so it is unknown if vancomycin was added on for these patients after a positive blood culture that would indicate vancomycin is required (i.e., MRSA, coagulase-negative *Staphylococcus*, etc). Patients in both groups received a similar duration of

vancomycin, indicating that the patients likely received a 5- to 7-day course for rule-out LOS management or for the treatment of a coagulase-negative bacteremia.

One concern with increasing the total daily dose of vancomycin for our patients was the possibility of an increased rate of adverse effects of vancomycin, most notably AKIs.[4] This study, however, found no difference in the rate of AKI in the pre- vs post-implementation group. This result could be expected, because the median trough was not different between the 2 groups in the study, and previous literature has found an increasing rate of vancomycin-induced nephrotoxicity with troughs ≥15 mg/L.[19,20] One difficulty with determining the rate of AKI in the neonatal population is the lack of consensus regarding the best AKI scoring tool.[21] Neonates, especially within the first few days of life, do not have accurate SCr because their SCr during this time is reflective of the maternal SCr.[22] Another potential marker of AKI would be the neonate's UOP, with the daily UOP goal of >1 mL/kg/hr; however, the logistics of this may be difficult if the patient does not have a Foley catheter, because weighing diapers may be inaccurate. The Neonatal Modified KDIGO Criteria for AKI is emerging as a preferred method for detecting and scoring the severity of AKI in the neonatal population because it incorporates both the neonate's SCr, UOP, and need for renal replacement therapy, so it is thought to be more accurate.[14–16]

One interesting finding from this study was that the patients in the pre-implementation group trended towards a higher rate and severity of AKIs, but this was not statically significant. There are a few theories that could explain this higher rate and severity of AKIs when the patients received a smaller total daily dose of vancomycin. First, patients in the pre-implementation group had a higher baseline SCr. Second, patients in the pre-implementation group had a higher usage of piperacillin-tazobactam and a lower use of cefepime, and our study found that patients who received concomitant piperacillin-tazobactam were more likely to develop an AKI. Multiple studies in adult and pediatric patients have documented the risk of AKI with vancomycin and piperacillin-tazobactam because both are known to have additive nephrotoxicity.[23–25] There is limited literature, however, surrounding the risk of nephrotoxicity with vancomycin and piperacillin-tazobactam in the neonatal population. Bartlett et al[26] reported the incidence of AKI in neonates, also using the Neonatal Modified KDIGO Criteria for AKI, who were receiving vancomycin at a median dose of 30 mg/kg/day with either piperacillin-tazobactam or cefepime. They reported an overall low rate of AKI (3% vs 5%; p = 1.000) that was not different among the 2 groups but may be due to the low overall number of included patients. Our study reported a slightly higher rate of AKIs compared with Bartlett et al, which may be attributed to the larger doses of vancomycin received by patients in our study. Literature also documents the risk of AKI in neonates who received vancomycin and gentamicin, because Linder et al[27] found that 3 of 35 patients (8.6%) who received vancomycin and gentamicin experienced nephrotoxicity. Overall, our study may suggest that the concomitant use of a nephrotoxic agent, either piperacillin-tazobactam or gentamicin, may increase the risk of subsequent AKI, but further research is needed to confirm this finding.

Because the IDSA MRSA guidelines were published in 2011, there has been increasing literature in the adult population that supports the use of AUC/MIC monitoring to target a goal AUC/MIC of 400 to 600 to optimize efficacy and reduce rates of AKI, but there has been limited literature supporting AUC/MIC monitoring in the neonatal population. In 2020, the American Society of Health-System Pharmacists, in conjunction with IDSA and the Society for Infectious Disease Pharmacists and Pediatric Infectious Disease Society, released guidelines on the therapeutic monitoring of vancomycin for serious MRSA infections.[11] In these guidelines, they recommend vancomycin doses to achieve an AUC/MIC of >400 for MRSA infections, instead of trough-directed monitoring alone. There are no studies that directly compare the safety and efficacy of vancomycin dosed based on troughs alone vs AUC/MIC monitoring in neonates, but this recommendation is instead based on extrapolation from adult data showing a decreased rate of AKI while maintaining efficacy end points. One complicating factor for neonates is there is no goal AUC/MIC for infections caused by coagulase-negative staphylococci as there is for MRSA. Since these guidelines, there has been an increase in dosing vancomycin based on a targeted AUC/MIC of >400, rather than with trough-directed monitoring alone. Because this study was initiated prior to these updated guidelines, AUC/MIC monitoring was not used.

Overall, our study demonstrated that the implementation of an updated vancomycin dosing protocol that recommended a larger total daily dose of vancomycin resulted in a higher proportion of initial therapeutic vancomycin trough, reduced the time to a therapeutic trough by 1 day, and did not change the proportion of AKIs. This is a positive result for our patient population because this may increase the effectiveness of our vancomycin therapy without increasing the risk of adverse effects from therapy. This study does have multiple limitations. First, blood cultures were not collected for this study, so the authors could not determine the efficacy of vancomycin based upon the clearance of blood cultures. Second, this study was retrospective in nature, so patients were not randomized to the 2 different treatment regimens, and outside factors, such as concomitant antimicrobials, could represent confounding factors. Similarly, patient acuity of illness was not evaluated in this study and could have affected the findings. Third, given the increase in frequency of

vancomycin doses in the updated protocol, the troughs obtained prior to the fourth dose of vancomycin could have been obtained sooner and thus skewed the number of days before attainment of a therapeutic trough in favor of the post-implementation group. Finally, since the initiation of this study further research has emerged that supports AUC/MIC monitoring in neonates, which was not included in this study.

Conclusion

Implementation of an updated vancomycin dosing protocol that recommended larger dosing of vancomycin resulted in a higher proportion of initial therapeutic vancomycin trough and reduced the time to therapeutic trough by 1 day. The rates of AKI were rare but did not change with the larger recommended vancomycin dosing. Of the patients who developed AKI, most also received a concomitant nephrotoxic agent.

Article Information

Affiliations. Department of Pharmacy (AMK, KRL, KLG), University of Kentucky Healthcare, Lexington, KY; Department of Pediatrics (AS), Kentucky Children's Hospital, Lexington, KY.

Correspondence. Allison M Kenneally, PharmD; akenneally@iuhealth.org

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Ethical Approval and Informed Consent. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and have been approved by the appropriate committees at our institution. Given the nature of this study, institutional review board/ethics committee review and informed consent were not required.

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