Original Work

Attainment of Area Under the Curve Targets and Incidence of Nephrotoxicity Utilizing Local Pharmacokinetic Vancomycin Dosing Guidelines

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Abstract

Objective: Current vancomycin monitoring guidelines recognize area under the curve (AUC) to minimum inhibitory concentration (MIC) ratio as the target efficacy parameter for vancomycin. Despite the historical use of trough-only dosing as a surrogate marker for the AUC/MIC ratio, recent studies have challenged this strategy's efficacy and safety. The objective of this study is to determine the extent to which vancomycin dosing and monitoring achieves target AUC levels and avoids nephrotoxicity. Secondary outcomes include incidence of clinical failure.

Methods: While receiving vancomycin therapy, adult patients were dosed and monitored according to current practice, with one additional vancomycin concentration drawn per dose-adjustment period to calculate the AUC. For the primary outcomes, percent of AUC levels within the established goal range of 400-600 mg h/L was calculated. Percent of patients who developed nephrotoxicity within 21 days of vancomycin initiation, or until the termination of their inpatient stay, was calculated. For the secondary outcomes, escalation to other methicillin-resistant Staphylococcus aureus active agents was measured.

Results: Of 46 AUC values calculated, 39.1% of values were in the target range of 400-600 mg h/L. There were notable variations between trough levels obtained and the calculated AUC. Of 43 patients, 16.3% developed nephrotoxicity. When limited to nephrotoxicity likely attributable to vancomycin, the incidence was lower at 6.98%. One patient required escalation of therapy to an alternate agent.

Conclusion: Trough levels obtained during this study did not accurately predict AUC values calculated, and incidence of nephrotoxicity was confounded by concomitant nephrotoxic agents.

Area under the curve (AUC) to minimum inhibitory concentration (MIC) ratio, or AUC/MIC, is currently recognized as the target efficacy parameter for the dosing of vancomycin.[1] An AUC/MIC specifically ≥ 400 is the recommended efficacy goal. Due to the difficulty of calculating the AUC/MIC ratio, the 2009 vancomycin monitoring guidelines (from the American Society of Health-System Pharmacists, Infectious Diseases Society of America, and Society of Infectious Diseases Pharmacists) promoted trough monitoring as a surrogate marker for this AUC/MIC target. These guidelines recommended trough concentration targets of > 10 mg/L or, for complicated infections, 15-20 mg/L. This goal range will provide an AUC/MIC of ≥ 400 in most patients if the MIC ≤1 mg/L.

Despite widespread use of trough-only dosing to achieve target levels of 10-20 mg/L, recent studies have challenged this dosing strategy's efficacy and safety. Evidence is lacking to support the correlation of higher vancomycin trough levels with clinical efficacy. Hale et al found no difference in attainment of target AUC ≥ 400 between patients with trough levels of 10-14.9 mg/L, or > 20 mg/L compared to those with trough levels 15-20 mg/L.[2] However, many studies have found increased rates of nephrotoxicity with higher trough levels.[2-4] Neely et al demonstrated that trough-only dosing underestimated AUC, potentially increasing the risk of toxicity and unnecessarily high doses.[5] Aljefri et al found that an AUC < 650 mg h/L was associated with less nephrotoxicity, and that use of an AUC monitoring strategy was less likely to lead to nephrotoxicity versus trough monitoring strategies.[6] Chavada et al identified a higher likelihood of nephrotoxicity in patients with a 24-hour AUC of > 563 mg h/L.[4] After the implementation of AUC-based dosing at Detroit Medical Center, AUC-based dosing was found to be associated with a lower likelihood of nephrotoxicity, lower total daily doses and AUC levels, and lower trough levels.[7]

Considering this evidence, recently

updated guidelines now suggest the use of AUC-guided dosing.[8] An AUC/MIC ≥ 400 will remain the recommended efficacy target (for bactericidal activity). The guidelines note an increased risk of nephrotoxicity as both trough concentrations and AUC increase, specifically above trough levels of 15-20 mg/L and above an AUC of 650-1300 mg h/L. The suggested goal AUC to maximize efficacy and reduce toxicity is therefore 400-600 mg h/L. Notably, this guidance will no longer recommend trough-only monitoring, with a 15-20 mg/L goal, for patients with serious methicillin-resistant Staphylococcus aureus (MRSA) infections.

AUC-based dosing can be accomplished with Bayesian estimations or pharmacokinetic (PK) equations. The Bayesian approach uses probability estimations to dose based on both population data and patient-specific information.[9] Due to the financial implications of purchasing Bayesian dosing software, the use of PK equations might be an appealing alternative. The PK approach consists of collecting two vancomycin levels between the time of drug distribution and the time of the next dose, and then calculating the patient-specific AUC from these values. Like current PK trough-monitoring approaches, this equation-based approach will not provide accurate estimations in situations such as rapid decline in renal function. As compared to Bayesian software, Turner et al found that the equation-based method can produce similar or better accuracy and bias in calculation of the AUC.[10] In response to the growing evidence in favor of AUC-based dosing, several institutions have begun to adopt AUC-based vancomycin dosing and monitoring. A 2019 survey of institutions reported that 23.1% of academic medical centers have implemented AUC-based monitoring.[11] Of the sites that had not implemented AUC-based monitoring, 88.3% did not plan to implement, or were unsure about implementing, AUC-based dosing. The most common barrier to implementation was unfamiliarity with this dosing strategy.

Consistent with many inpatient pharmacy departments, the pharmacists at Ascension St. Clare's Hospital autonomously dose vancomycin under a consult service. Approximately one-third of Staphylococcus aureus isolates at this site are methicillin resistant; therefore, it is important to have this medication available.[12] Following local guidelines, vancomycin is currently dosed with a goal trough concentration of 10-20 mg/L, or, for complicated infections, 15-20 mg/L.[13] Empiric dosing to achieve these goals often includes initial doses of 15-20 mg/kg actual body weight administered every 8 to 24 hours, depending on renal function or other patient-specific factors. There is a maximum of 2.5 grams per dose. Loading

TABLE 1. Baseline Survey Results

Question	Response Options	Result, No. (%)
Do you feel confident in your ability to dose vancomycin therapy based on trough concentrations?	Yes	25 (89.3)
	Somewhat	3 (10.7)
	No	0 (0)
What is the preferred kinetic measure for vancomycin efficacy?	Peak	1 (3.6)
	AUC/MIC	15 (53.6)
	Trough	11 (39.3)
	Peak/MIC	1 (3.6)
Vancomycin trough levels are equated/associated with efficacy.[a]	True	21 (75)
	False	6 (21.4)
What is the preferred trough level for the effective treatment of meningitis?	10-15 mcg/ml	0 (0)
	15-20 mcg/ml	26 (92.9)
	10-20 mcg/ml	0 (0)
	>20mcg/ml	2 (7.1)
Vancomycin peak levels are equated/associated with toxicity.	True	14 (50)
	False	14 (50)
What is the preferred AUC/MIC[b] ratio for the effective treatment of most indications?[a]	>200	2 (7.1)
	>400	20 (71.4)
	>600	3 (10.7)
	<800	0 (0)
Vancomycin trough levels are equated/associated with toxicity.	True	17 (60.7)
	False	11 (39.3)
Do you feel confident in your ability to dose vancomycin therapy based on AUC calculations?	Yes	0 (0)
	Somewhat	1 (3.6)
	No	27 (96.4)
How many years have you been practicing as a pharmacist?[a,c]	Free Response, <10 years	9 (32.1)
	Free Response, ≥10 years	18 (64.3)

aSome respondents did not select an answer
bAUC = area under the curve, MIC = minimum inhibitory concentration
cFree response reported as <10 or ≥10 years for the purposes of this publication

TABLE 2. Baseline Characteristics

Subject Parameter	Result
Mean (+/-SD[a]) age, years	60.56 (12.09)
Median (IQR[b]) age, years	61 (15.25)
No. (%) male sex	27 (62.8)
Mean (+/-SD) wt, kg	85.58 (23.02)
Median (IQR) wt, kg	86 (27.25)
Mean (+/-SD) ht, cm	170.96 (12.71)
Median (IQR) ht, cm	172.35 (19.68)
Mean (+/-SD) baseline serum creatinine, mg/dl	0.90(0.37)
Median (IQR) baseline serum creatinine, mg/dl	0.9 (0.48)
Mean (+/-SD) no. of concomitant nephrotoxins	1.41 (0.93)
Median (IQR) no. of concomitant nephrotoxins	1 (1)
No. (%) pt with existing nephrotoxicity within 72 hours before vancomycin initiation	4 (9.3)
No. (%) pt with baseline serum creatinine >2 mg/dL	0 (0)
No. (%) pt receiving:	
ACEi/ARB[c]	8 (18.6)
Acyclovir	2 (4.7)
Allopurinol	1 (2.3)
Aminoglycoside	0 (0)
Amphotericin B	0 (0)
Piperacillin/tazobactam	8 (18.6)
Cyclosporine	0 (0)
Tacrolimus	0 (0)

TABLE 2. Baseline Characteristics Cont.

Subject Parameter	Result
Cidofovir	0 (0)
Cisplatin	0 (0)
Contrast dye	21 (48.8)
Diuretics (loop or thiazide)	14 (32.6)
Fluoroquinolone	4 (9.3)
Foscarnet	0 (0)
Lithium	1 (2.3)
Mannitol	0 (0)
Methotrexate	0 (0)
Mitomycin-C	0 (0)
NSAIDs[d]	5 (11.6)
Pamidronate	0 (0)
Zoledronate	0 (0)
Pentamidine	0 (0)
Phenytoin	0 (0)
Rifampin	0 (0)
Sulfonamides	1 (2.3)
No. (%) pt with antibiotics, other concomitant	40 (93)
No. (%) pt with critical care admission	16 (37.2)
No. (%) pt with initial culture results positive	16(37.2)

[a]SD = standard deviation
[b]IQR = interquartile range
[c]ACEi = angiotensin converting enzyme inhibitor, ARB = angiotensin receptor blocker
[d]NSAIDs = non-steroidal anti-inflammatory drugs

doses of 25-30 mg/kg may be utilized for complicated infections. Pharmacist-guided vancomycin dosing and monitoring might differ between organizations, based on aggressiveness per indication, or due to varying practices such as dose capping. While various sites have shown positive clinical results of AUC-based dosing, the baseline AUC achieved with trough-based dosing is rarely reported for comparison.

To better understand the efficacy and safety of current trough-based dosing and monitoring strategies employed at this site, this study proposes calculation of the AUC achieved as well as incidence of nephrotoxicity in relation to the AUC.

Methods

This study was formally evaluated by the Ascension Wisconsin Institutional Review Board (IRB) and determined to be exempt from IRB review.

Outcomes

Primary: To evaluate how well current institutional practice (traditional trough-based dosing) achieved target AUC levels, the percent of AUC levels within the desired therapeutic range (400-600 mg h/L) was measured. The percent of AUC levels above and below the range (> 600 mg h/L or and < 400 mg h/L) was also measured. To assess the incidence of nephrotoxicity under current institutional practice, an increase in serum creatinine of > 0.5 mg/dL or a ≥ 50% increase from baseline from day of vancomycin initiation to day 21 or termination of inpatient stay was measured.[1,14-15]

Secondary: To assess the outcome of clinical failure, the escalation of therapy to MRSA active antimicrobials (daptomycin, linezolid, or ceftaroline) was measured.

FIGURE 1. Vancomycin Therapy

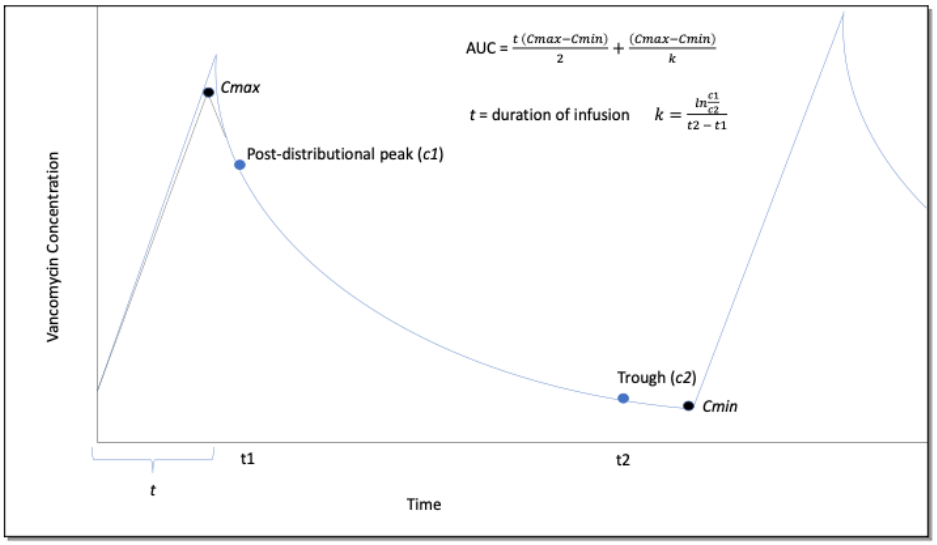

Figure 1. c1 represents the post-distributional peak drawn for the purposes of this study. c2 represents the vancomycin trough concentration drawn in standard practice. Cmax and Cmin were extrapolated to estimate the true peak and true trough, respectively. The area under the curve (AUC) per dose interval can be calculated with the equation shown, however must be multiplied by the frequency of doses per day to obtain the AUC over 24 hours.

Data collection

Baseline pharmacist knowledge and confidence information was collected by survey administration. Survey questions were developed and approved by the project team (Table 1). Surveys were distributed by residents or pharmacists across three Ascension Wisconsin hospitals: Ascension St. Mary's Hospital, Ascension St. Clare's Hospital, and Ascension All Saints Hospital.

AUC assessment was completed at Ascension St. Clare's Hospital. Adult patients with consults for pharmacy to dose vancomycin were included in this study. Pregnant patients or patients receiving renal replacement therapy were excluded from this study. Under the current institutional vancomycin dosing and monitoring guidelines, pharmacists continued to perform trough-based dosing. An additional post-distributional vancomycin concentration was drawn to allow calculation of the AUC. Levels were ordered on the same dosing interval and prior to the standard trough level as concentrations approached steady state, often between the third and fourth doses of vancomycin therapy (Figure 1). Post-distributional levels were ordered at least one hour after the end of the previous vancomycin infusion to account for distribution. Post-distributional concentrations were suppressed from the electronic health record and directly reported to the primary investigator for analysis. Median and mean AUC were also collected for comparison to the literature.

Nephrotoxicity data was obtained via prospective chart review by the primary investigator. Concomitant nephrotoxic agents from vancomycin initiation to day 21 or termination of inpatient stay were also recorded. This and all other data gathered from the patient chart was predefined and done so prospectively, except for the following: patients who required a nephrology consult after experiencing nephrotoxicity.

Statistical methods and calculations

Due to a limited anticipated patient volume, we were unable to compare nephrotoxicity incidence between patients in and outside of goal AUC range. Our prespecified analysis instead targeted nephrotoxicity in our study population as a whole, with a published comparator trial to establish desired patient enrollment. Neely et al demonstrated an incidence of 8% nephrotoxicity in trough-monitored patients and 1.13% in AUC-monitored groups.[5] Using this as a historical comparator for AUC-based monitoring, we determined a required patient enrollment of 37 patients (alpha level of 0.05 and power of 80%). Fischer's exact test was used for this categorical data analysis. The Sawchuk-Zaske method was used to calculate the area under the curve.[9,16] Using the post-distributional vancomycin concentration drawn in addition to the trough concentration drawn, the estimated AUC over a dosing interval was calculated. This was then multiplied by the doses given in each 24-hour time period to obtain the total AUC. True trough and peak values over single dosing intervals were back-extrapolated using the same exponential curve equations. Additional post hoc analysis included reporting the percent of time AUC was either supratherapeutic, subtherapeutic, or therapeutic if the true trough was supra-, sub-, or therapeutic.

Results

There were 60 post-distributional peak levels drawn. The subsequent trough level was drawn 76.5% of the time. Therefore, a total of 46 AUC levels were calculated in 43 patients. The average patient age was 60, and the majority of patients were male and not admitted to the intensive care unit (Table 2). The average number of concomitant nephrotoxic agents administered to each patients was one. The most common of these were contrast dye, diuretics, and then piperacillin/tazobactam and ace inhibitors or angiotensin receptor inhibitors.

Baseline survey results

Of 28 survey respondents, almost 90% felt confident in trough-based dosing as compared to no respondents feeling confident (i.e. a "yes" to feeling confident) in AUC-based dosing (Table 1). The preferred kinetic measure for vancomycin efficacy was thought to be AUC/MIC by over half of respondents at 53.6%, and trough by 39.3% of respondents. The preferred AUC/MIC ratio associated with vancomycin efficacy was correctly identified as > 400 mg h/L by 71.4% of respondents. Vancomycin trough levels were thought to be associated with efficacy by 75% and associated with toxicity by 60.7% of respondents.

Primary Outcome

The percent of AUC levels within the desired therapeutic range was 39.1%

TABLE 3. Area Under the Curve Results

Subject Parameter	*Result, No. (%) unless otherwise specified*
AUC in therapeutic range, 400-600 mg h/L	18 (39.1)
Subtherapeutic AUC, <400 mg h/L	10 (21.7)
Supratherapeutic AUC, >600 mg h/L	18 (39.1)
Mean (+/-SD[a]) AUC, mg h/L	556.3 (195.1)
Median (IQR[b]) AUC, mg h/L	531.5 (204.5)
Therapeutic[c] trough	
True trough therapeutic, AUC therapeutic	7 (43.8)
True trough therapeutic, AUC subtherapeutic	1 (6.25)
True trough therapeutic, AUC supratherapeutic	8 (50)
Subtherapeutic[c] trough	
True trough subtherapeutic, AUC therapeutic	11 (52.4)
True trough subtherapeutic, AUC subtherapeutic	9 (42.9)
True trough subtherapeutic, AUC supratherapeutic	1 (4.9)
Supratherapeutic[c] trough	
True trough supratherapeutic, AUC therapeutic	0 (0)
True trough supratherapeutic, AUC subtherapeutic	0 (0)
True trough supratherapeutic, AUC supratherapeutic	9 (100)

[a]SD = standard deviation
[b]IQR = interquartile range
[c]Therapeutic trough range varied from 10-20 mcg/mL to 15-20 mcg/mL per indication

(N=18). The percent of AUC levels above therapeutic range was 39.1% (N=18), and the percent of AUC levels below therapeutic range was 21.7% (N=10). The percent of time AUC was either supra-, sub-, or therapeutic if the true trough was supra-, sub-, or therapeutic is reported in Table 3. Trough levels were within therapeutic range 34.8% of the time. If the true trough was therapeutic, the AUC was supratherapeutic 50% of the time. If the true trough was subtherapeutic, the AUC was therapeutic 52.4% of the time.

Incidence of nephrotoxicity among our study population was 16.3% (N=7). As compared to the historical control study selected, which demonstrated 1.13% nephrotoxicity in AUC-based dosing groups, our patient population experienced a significantly higher incidence of nephrotoxicity (p=0.0002). No patients presented with existing nephrotoxicity within the previous 72 hours or a baseline serum creatinine of greater than 2 mg/dL. In 4 of the 7 patients experiencing nephrotoxicity, the AUC was < 600 mg h/L and the trough was < 20 mg/L. All of these patients received either loop diuretics, piperacillin/tazobactam, non-steroidal anti-inflammatory drugs, contrast dye, or a combination of those agents during the relevant time period. In 3 of the 7 patients experiencing nephrotoxicity, the AUC was > 600 mg h/L and the trough was > 20 mg/L. Two of these patients received: either angiotensin-converting enzyme inhibitors or angiotensin receptor blockers; loop diuretics; piperacillin/tazobactam; acyclovir; contrast dye; or a combination of those agents during the relevant time period. Therefore, 6 of the 7 patients experiencing nephrotoxicity also received a concomitant nephrotoxic agent from day of vancomycin administration to day 21 or termination of inpatient stay. Two patients received formal evaluations by the nephrology service.

The comparator study used similar exclusion criteria to our project; both excluded patients with any type of renal replacement therapy. The comparator study also excluded patients with an expected survival of < 72 hours. They used the same definition of nephrotoxicity; however, they only included patients in their analysis if nephrotoxicity was thought to be more attributable to vancomycin than to another cause by their primary team. To replicate this, we controlled for those patients with an AUC < 600 mg h/L and a trough < 20 mg/L, assuming these patients were less likely to have vancomycin as the primary cause of nephrotoxicity. The remaining 3 patients were not admitted to the critical care unit during the study period, perhaps reflecting that those patients would have a longer expected survival and a similar acuity to patients in the historical control study. When controlled for these factors post-hoc, our patient population did not experience significantly higher nephrotoxicity versus the AUC-based dosing group of the comparator study, (7% vs 1.13%, p=0.0524).

Secondary Outcomes

One patient required escalation of therapy to an alternate MRSA active antimicrobial, ceftaroline. In this case, the culture reported susceptibility to vancomycin with MIC=1. The calculated AUC was 615 mg h/L and true trough was 17.8 mg/L. Escalation was attributed to clinical failure of vancomycin.

The average AUC value in our population was a mean of 556.3 mg h/L (SD 195.1) or a median value of 531.5 mg h/L (IQR 204.5). Two AUC values were excluded from this calculation. The excluded values were determined to be over 600 mg h/L; however, the exact AUC was not able to be calculated due to the post-distributional peak obtained being reported as > 50 mcg/mL instead of an exact value.

Discussion

We found that the majority of AUC levels obtained during trough-based dosing were outside of the desired 400-600 mg h/L goal range. We also demonstrated that a therapeutic trough predicted a

therapeutic AUC less than 50% of the time, and that a therapeutic AUC was actually more likely to be obtained with a subtherapeutic trough result. The results of this small, single-center analysis align with many previously published reports. It is useful to compare our outcomes to several comparator trials.

While Neely et al reported 75% of patients within AUC/MIC target range with trough-based dosing, they used a target AUC range of 400-800 mg h/L.[5] This is difficult to compare to our study, which used the well-established goal range of 400-600 mg h/L. Finch et al, however, did examine the median AUC among its study groups. Our median AUC was 531.5 mg h/L (IQR 204.5) as compared to 471.5 (361.5–576.7) reported in their AUC-based dosing group.[7] Notably, our reported median AUC also excluded two outlier AUC values. In each of these cases, the AUC was supratherapeutic but could not be calculated due to post-distributional peaks above the assay range. This suggests our median AUC values are higher than those seen in AUC-based dosing.

We also found a relatively high incidence of nephrotoxicity, confounded by the administration of multiple additional nephrotoxic agents. Our study reported the same median number of concomitant nephrotoxins as Finch et al at one per patient over the duration of the study period, but produced a higher incidence of nephrotoxicity.[7] As compared to Neely et al, our trough-based dosing produced a nephrotoxicity incidence of 16.3%, higher than the 8% reported in their trough-based dosing groups, and also significantly higher than the 1.13% total reported in AUC-based dosing groups.[5]

Considering the high rate of concomitant nephrotoxins administered to our patients, it is difficult to attribute the nephrotoxicity seen in this study to vancomycin alone. Six of the 7 patients received at least one concomitant nephrotoxic agent during the study period. Of those 7 patients who met our definition of nephrotoxicity, only 3 also met the parameters for supratherapeutic trough or AUC. When our data was controlled to reflect nephrotoxicity most likely attributable to vancomycin, there was no longer a significant difference seen compared to AUC-based dosing groups reported in Neely et al.

The baseline pharmacist knowledge and confidence survey demonstrated a high level of confidence in trough-based dosing ability, and a lack of confidence in AUC-based dosing ability. Not all pharmacists were able to choose the correct target AUC/MIC range or other measures related to AUC-based monitoring. Similar to the unfamiliarity reported in the recent survey by Kufel et al, this suggests a common barrier to implementation of AUC-based dosing across sites.[11] Other barriers to implementation might include the increased resources required for this method, including collection and processing of two vancomycin concentrations versus one.

There are additional similarities and differences to consider between our patient population and those in previously published reports. As compared to Neely et al, our mean patient age was older, at 60.6 years old, compared to 47.7 years old in their trough-based dosing control group, and averages of 48 and 50.3 years old in their AUC-based dosing groups each year.[5] Compared to Finch et al, however, our mean patient age was comparable to their trough-based dosing group; their mean patient age was 59.1 years, while the mean age of their AUC-based dosing group was 50 years old.[7] Our study also contained a lower proportion of males, at 63.8% versus 75-81% reported in Neely et al, but a higher proportion of males compared to the 54.2% and 56.4% reported in Finch et al.[5,7] Our average weight was higher than both comparator trials with 85.6 kg, compared to averages of 78.8-82.4 and 66-67.9 kg. Our project had a comparable average height to Neely et al at 171 cm versus their averages of 169.1-171.9 cm.[5,7] Our average baseline serum creatinine was 0.9 mg/dl compared to averages of 0.82-0.84 and medians of 0.9 reported in the same studies.[5,7]

There are several limitations to our findings. Considering the small sample size, it was not feasible to compare nephrotoxicity incidence between those patients who did or did not attain goal AUC levels. Therefore, we instead compared our nephrotoxicity incidence to a published comparator trial, which is less robust. While many of our selection criteria were similar, we were not able to exactly replicate all aspects of the comparator trial. While we did further control our data to match the methods of Neely et al, this was done post-hoc. Our limited sample size also restricted our ability to calculate the significance of our primary results, including percent of AUC levels within the desired range as well as in relation to trough level obtained. As mentioned, the majority of patients experiencing nephrotoxicity in our study also received a concomitant nephrotoxin, which limits the conclusions able to be drawn from these results. Another limitation is the conflicting results of the pharmacist knowledge and confidence survey. While only 53.6% of respondents identified the preferred kinetic measure as AUC/MIC, over 70% of pharmacists correctly identified the goal AUC/MIC target for efficacy. This suggests some baseline concerns with the survey itself.

One notable area of interest within our data includes the inability of trough levels to accurately predict the calculated AUC. This is consistent with previous reports of inconsistency between trough levels and expected AUC values.[2] Our trough levels were therapeutic 34.8% of the time, as compared to 28% reported in the trough-based dosing arm of Neely et al.[5] This might indicate that our initial achievement of trough goals is comparable to other institutions. Despite this, these trough levels do not appear to always correlate with the desired AUC values. In our population, a subtherapeutic trough level was more likely to predict a therapeutic AUC than a subtherapeutic AUC. This again correlates to previous comparator studies. When Neely et al transitioned from trough-based dosing to AUC-based dosing, their average troughs decreased without a difference in reported efficacy.[5] Additionally, this causes us to wonder whether we are placing our patients at a higher risk of nephrotoxicity with no added benefit.

Conclusion

The results of this small prospective analysis are applicable to institutions with similar dosing schemes and patient populations. This project attempted to evaluate the area under the curve as well

as nephrotoxicity seen in our trough-based vancomycin dosing and monitoring process. The results suggest that trough-based dosing might not achieve the desired AUC in all cases. A high incidence of nephrotoxicity was confounded by administration of concomitant nephrotoxic agents. Future directions include exploration of AUC-based dosing; however, the baseline pharmacist knowledge and confidence data must be taken into account as well. It will be important to ensure proper education and training to ensure pharmacists are confident in this new method if implemented.

At the time of writing, Alanna Ambrosius is a PGY-1 Pharmacy Practice Resident and Kent Cook is a Clinical Lead Pharmacist at Ascension St. Clare's Hospital in Weston, WI. Jim Davis is an Antimicrobial Stewardship Pharmacist and Justin Guthman is the Regional Director of Pharmacy for the Ascension Wisconsin, Northern Region.

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The primary author had full access to all data and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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