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Impact of empiric weight-based vancomycin dosing on nephrotoxicity and mortality in geriatric patients with methicillin-resistant *Staphylococcus aureus* bacteremia

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Abstract

What is known and objective—Few studies have evaluated the effect of vancomycin dosing on the health outcomes in geriatric patients. Data are needed to determine if higher vancomycin

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dosing strategies are more effective in geriatric patients and/or lead to excessive rates of adverse events.

Methods—This study used a subset of patients ages ≥ 65 years from a multicenter, retrospective, cohort study of methicillin resistant *Staphylococcus aureus* (MRSA) bacteremia. Patients received ≥ 48 hours of empiric vancomycin between 07/01/2002 and 06/30/2008. We compared the incidence of nephrotoxicity and in-hospital mortality in patients who received guideline-recommended dosing (at least 15 mg/kg/dose) to patients who received lower dosing. Multivariable generalized mixed effects models were constructed to determine independent risk factors for nephrotoxicity and in-hospital mortality.

Results and discussion—Half of the cohort (46% of 92 patients) received guideline-recommended dosing. Empiric use of weight-based dosing did increase the percentage of patients achieving a vancomycin trough ≥ 15 mg/L (57% vs. 42%). Nephrotoxicity occurred in 32% of patients and 26% died during their hospitalization. Guideline-recommended dosing was not associated with significant changes in nephrotoxicity (OR 1.03; 95% CI 0.38–2.82) or in-hospital mortality (OR 1.01; 95% CI 0.40–2.54) in the multivariable analysis.

What is new and conclusion—In this study of geriatric patients, guideline-recommended dosing was not associated with significant changes in nephrotoxicity or mortality. Since 40% of the patients who received guideline-recommended dosing failed to achieve a target vancomycin trough of ≥ 15 mg/L, future studies should focus on dosing strategies to increase target attainment rate.

What is known and objective

Methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia is associated with high mortality rates, and age is an independent predictor of mortality.[1,2] Vancomycin remains a first-line treatment option that is commonly used for this infection. We have previously observed of those who receive vancomycin, patients older than 53 years of age are at a higher risk of death, and those above 52 years of age have an increased rate of nephrotoxicity regardless of the dosing regimen used.[3,4] However, few investigators have evaluated the effect of vancomycin dosing on the outcomes of geriatric patients. The Infectious Diseases Society of America (IDSA), American Society of Health-Systems Pharmacists (ASHP), and the Society of Infectious Diseases Pharmacists (SIDP) currently recommend that all adults with normal renal function receive weight-based dosing (15–20 mg/kg every 8–12 hours) of vancomycin.[5] This empiric dosing regimen is aimed to achieve the recommended target trough (15–20 mg/L) and area under the curve (AUC) to minimum inhibitory concentration (MIC) ratio (≥ 400). A better understanding of the effectiveness and nephrotoxicity profile weight-based vancomycin dosing is needed in geriatric patients to determine if this approach is safe and effective for these patients.

Therefore, we conducted a subset analysis of patients 65 years of age or older from a multicenter, retrospective, cohort study of patients receiving vancomycin for MRSA bacteremia. This analysis was intended to determine the effect of guideline recommended weight-based vancomycin dosing on mortality and nephrotoxicity rates in geriatric populations with MRSA bacteremia.

Methods

Study location and patients

These patients were a subgroup of previous retrospective cohort studies evaluating all hospitalized patients with MRSA bacteremia, regardless of age.[3,4] Three institutions were utilized for the study which included a 400 bed tertiary hospital, a 350 bed Veterans Affairs hospital, and a 600 bed university hospital. We identified those who were hospitalized between July 2002 and June 2008. Each institution's institutional review board (VA North Texas Health Care System, Texas Tech University Health Sciences Center, and the University of Texas Health Science Center, San Antonio) approved the study prior to initiation and waived the requirement for informed consent. We included all patients 1) who received vancomycin for at least 48 hours, 2) were 65 years of age or older, and 3) had MRSA bacteremia, confirmed by microbiologic records. Study exclusions were: vancomycin exposure during a prior hospital stay, previous MRSA infection (within six months), pregnancy, receipt of dialysis, or creatinine clearance (CrCl) of less than 30 ml/min. CrCl was determined using the Cockcroft-Gault equation with actual body weight being used for the purposes of this analysis.[6]

Study definitions

Exposure—Vancomycin doses of ≥ 30 mg/kg/day, ≥ 15 mg/kg/day for CrCl 30–50 ml/min, based on actual body weight were defined as guideline-recommended weight-based vancomycin dosing. The comparator group was comprised of all other study eligible patients who received lower vancomycin doses.

Outcomes—Nephrotoxicity was defined as an increase in serum creatinine (SCr) by greater than 0.5 mg/dl or a 50% increase from baseline on at least two consecutive laboratory tests from the initiation to the completion of vancomycin therapy.[5] Any patient death occurring within the index hospital stay was classified as in-hospital mortality.

Independent variables—Each study institution utilized its own vancomycin assay to determine trough concentrations, which was used for routine medical care. All vancomycin concentrations labeled as "trough" by the laboratory staff at the participating institutions as part of standard medical care were included in the analysis. Concomitant nephrotoxins included receipt of intravenous contrast, aminoglycosides, or vasopressors. The Charlson comorbidity index was used to quantify comorbid conditions.[7] Severity of illness was characterized by the Pitt bacteremia score.[8,9] Advanced age was defined as 80 years of age or older. Intensive care unit (ICU) residence was defined as the patient being located in the ICU at the time of vancomycin initiation.

Statistical Analysis

We selected candidate variables for consideration in the univariable and multivariable models *a priori*. A 45% nephrotoxicity rate and a 30% in-hospital mortality rate were expected given the results of previous studies.[3,4] We determined that four variables could be included in the multivariable model for nephrotoxicity and three variables in a multivariable model for mortality. One hundred patients would be required for the multivariable analyses

according to these assumptions to have 5–10 events per variable included to avoid over fitting the multivariable model.[10] The initial univariable analysis included receipt of guideline-recommended weight-based vancomycin dosing, patient age, nephrotoxicity, vancomycin trough greater than 15 mg/L, vancomycin duration greater than 15 days, use of concomitant nephrotoxins, baseline serum creatinine, Pitt bacteremia score of 4 or greater, ICU residence at time of vancomycin initiation, weight of 100 kilograms or greater, hospital length of stay, ICU length of stay, and gender.[3,4,11,12] A Chi-square or Fisher's Exact test was used for univariable associations as appropriate. The guideline-recommended vancomycin trough concentration range of 15–20 mg/L was used to define the cutoff of 15 mg/L.[5] Vancomycin trough concentrations above this cutoff are also associated with nephrotoxicity.[11–16] Previous literature has shown that a Pitt bacteremia score of 4 or greater has higher sensitivity and specificity for predicting severity of illness.[17] Past studies have also shown that weight of 100 kilograms or greater is associated with an increased risk of nephrotoxicity.[4,13]

The change-in-estimate method was utilized to select variables for the final multivariable model based on changes in the estimated exposure effect. Any variable demonstrating a 10% change in the exposure effect was determined to be a confounder and kept in the final model. All variables conceptually regarded as biologically reasonable causes of nephrotoxicity or mortality were also considered for inclusion in the multivariable model. A generalized linear mixed-effect model was utilized to identify independent risk factors for nephrotoxicity and mortality. To account for clustering, hospital site was treated as a random effect whereas other covariates were treated as fixed effects. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated for each variable in the multivariable model.

Statistical significance was defined as a two-tailed p-value < 0.05. All analyses were performed using STATA 12 (StataCorp. 2011. Stata Statistical Software: Release 12. College Station, TX: StataCorp LP).

Results

There were 798 patients with MRSA bacteremia of which 337 patients who met the inclusion and exclusion. Of these, 92 patients were 65 years of age or older and included in the analysis (Table 1). Guideline-recommended weight-based dosing was provided to 46% of patients. Most of the patients were Caucasian race (76%) and male gender (90%). The guideline-recommended weight-based dosing group received higher daily doses of vancomycin (31 vs. 22 mg/kg/day; $p<0.001$) and achieved vancomycin troughs of 15 mg/L or greater more frequently (57% vs. 42%; $p = 0.15$) and had a higher median area under the curve (621 vs. 430 mg.hr/L, $p<0.001$). One-third of patients had a trough > 20 mg/L which was not statistically different between weight-based and lower dosing (38 vs. 30%, $p = 0.41$). The patients receiving guideline-recommended weight-based dosing also weighed less than patients receiving lower dosing (62 vs. 86 kg; $p < 0.001$). This is likely due to 87% of patients receiving 1 gram every 12 hours dosing. The sources of bacteremia were bloodstream catheter related (26%), pulmonary (26%), skin/muscle (19%), genitourinary (10%), and other (2%). The source for the MRSA bacteremia could not be identified for 17% of patients.

Nephrotoxicity occurred in 32% of patients, with no difference between guideline-recommended and lower dosing (31% vs. 32%; p = 0.91). Guideline-recommended weight-based dosing was not a significant predictor of nephrotoxicity in either the univariable (OR 0.97; 95% CI 0.53–1.78) or multivariable analysis (OR 1.03; 95% CI 0.38–2.82). Factors that were significantly associated with nephrotoxicity in the univariable analysis included Pitt bacteremia score ≥ 4, ICU residence, and concomitant nephrotixin use. Of these variables, only the ICU residence remained significantly associated with nephrotoxicity in the multivariable analysis.

The in-hospital mortality rate was 26%, with no difference between guideline-recommended (26%) or lower dosing (26%) (Table 3). Factors that were significant in the univariable analysis were Pitt bacteremia score ≥ 4 and ICU residence. ICU residence was the only factor significantly associated with mortality in the multivariable model.

Discussion

We found that in patients ≥ 65 year of age with MRSA bacteremia, the provision of guideline-recommended weight-based vancomycin dosing helped more patients reach a vancomycin trough of ≥ 15 mg/L. However, this increased target attainment rate was not associated with a statistically significant impact on nephrotoxicity or in-hospital mortality. Approximately one in three patients in this geriatric subgroup experienced nephrotoxicity with a quarter of the study population dying during their hospital stay. Nephrotoxicity and in-hospital mortality rates were virtually identical when comparing weight-based vancomycin dosing to lower dosing.

The nephrotoxicity rate of 32% in this study falls within the 11–42% range observed by other investigators.[11, 14–16, 18] The only factor found to be significantly associated with nephrotoxicity was a ICU residence. Other studies have shown that severity of illness is significantly associated with nephrotoxicity whether measured by Pitt bacteremia score or ICU residence.[12, 13, 15] We were unable to detect a significant association between concomitant nephrotoxin use and nephrotoxicity in our multivariable analysis, although this risk factor has been identified by others.[11,12] This may be due to the fact that patients with a higher severity of illness may be more likely to receive concomitant nephrotoxic agents. Another possible reason is that we did not document the dose and duration of the concomitant nephrotoxin used. A larger cohort of geriatric patients with MRSA bacteremia would have also increased the likelihood of finding a significant association.

The 26% mortality rate observed in our cohort is similar to that observed by other investigators.[18] ICU residence was the only factor significantly associated with in-hospital mortality in our cohort. It is interesting that over 40% of patients failed to reach the guideline-recommended trough concentration regardless of the dosing strategy used. This finding is in agreement with Neely and colleagues that expect 60% of patients to fail to achieve a vancomycin trough concentration of 15 mg/L.[19] These results may indicate that alternative dosing strategies are needed in geriatric patients to achieve the target vancomycin trough concentrations and/or area under the curve values recommended by the vancomycin guideline. The guideline recommends individual pharmacokinetic adjustments and

verification of serum target achievement, but this approach may not provide timely target attainment for a substantial amount of patients.[5]

Our study is limited by several factors. While the retrospective nature of our study may produce a more "real world" evaluation of safety and effectiveness of guideline-recommended vancomycin dosing, this approach is also susceptible to the introduction of selection bias from measured and/or unmeasured variables. Vancomycin dosing according to the guidelines may have been by default instead of attempting to provide more aggressive dosing due to the study period being prior to the publication of the guideline. This is also likely why the guideline-recommended group weighed less than the lower-dosing group. MIC data were also not routinely reported during the study period at the study institutions. However, this study was focused on the impact of empiric dosing and the MIC is not typically available to the clinician at the time of providing an empiric dosing regimen. The small sample size limited the number of variables that could be included in the multivariable analysis without over fitting the model and provided less precise estimates. A study specifically designed to evaluate vancomycin dosing in geriatric patients could provide more insights than the current subanalysis. However, we were unable to find other studies focused on the effect of vancomycin dosing on mortality or nephrotoxicity of a geriatric population. Therefore, this limited sample provides more evidence for geriatric patients than was previously available. None of the study institutions utilized loading doses for vancomycin during the study period, so we are unable to comment on the effect of vancomycin loading doses on safety or effectiveness.

What is new and conclusions

In this study, approximately one in three geriatric patients developed nephrotoxicity and over one in four patients died. We did not observe a significant association between guideline-recommended dosing and nephrotoxicity or mortality. Since 40% of the patients receiving guideline-recommended dosing failed to achieve a target vancomycin trough of ≥ 15 mg/L, future studies should focus on dosing strategies to increase target attainment rate.

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References

1. Wyllie DH, Crook DW, Peto TE. Mortality after Staphylococcus aureus bacteraemia in two hospitals in Oxfordshire, 1997–2003: cohort study. BMJ. 2006; 333:281. [PubMed: 16798756]
2. Kaasch AJ, Barlow G, Edgeworth JD, et al. Staphylococcus aureus bloodstream infection: A pooled analysis of five prospective, observational studies. J Infect. 2014; 68:242–251. [PubMed: 24247070]

3. Hall RG 2nd, Giuliano CA, Haase KK, et al. Empiric guideline-recommended weight-based vancomycin dosing and mortality in methicillin-resistant Staphylococcus aureus bacteremia: a retrospective cohort study. BMC Infect Dis. 2012; 12:104. [PubMed: 22540223]

4. Hall RG 2nd, Hazlewood KA, Brouse SD, et al. Empiric guideline-recommended weight-based vancomycin dosing and nephrotoxicity rates in patients with methicillin-resistant Staphylococcus aureus bacteremia: a retrospective cohort study. BMC Pharmacol Toxicol. 2013; 14:12. [PubMed: 23402420]

5. 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; 66:82–98. [PubMed: 19106348]

6. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron. 1976; 16:31–41. [PubMed: 1244564]

7. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987; 40:373–383. [PubMed: 3558716]

8. Chow JW, Fine MJ, Shlaes DM, et al. Enterobacter bacteremia: clinical features and emergence of antibiotic resistance during therapy. Ann Intern Med. 1991; 115:585–590. [PubMed: 1892329]

9. Chow JW, Yu VL. Combination antibiotic therapy versus monotherapy for gram-negative bacteraemia: a commentary. Int J Antimicrob Agents. 1999; 11:7–12. [PubMed: 10075272]

10. Concato J, Feinstein AR, Holford TR. The risk of determining risk with multivariable models. Ann Intern Med. 1993; 118:201–210. [PubMed: 8417638]

11. Hidayat LK, Hsu DI, Quist R, Shriner KA, Wong-Beringer A. High-dose vancomycin therapy for methicillin-resistant Staphylococcus aureus infections: efficacy and toxicity. Arch Intern Med. 2006; 166:2138–2144. [PubMed: 17060545]

12. van Hal SJ, Paterson DL, Lodise TP. Systematic review and meta-analysis of vancomycin-induced nephrotoxicity associated with dosing schedules that maintain troughs between 15 and 20 milligrams per liter. Antimicrob Agents Chemother. 2013; 57:734–744. [PubMed: 23165462]

13. Lodise TP, Lomaestro B, Graves J, Drusano GL. Larger vancomycin doses (at least four grams per day) are associated with an increased incidence of nephrotoxicity. Antimicrob Agents Chemother. 2008; 52:1330–1336. [PubMed: 18227177]

14. Pritchard L, Baker C, Leggett J, Sehdev P, Brown A, Bayley KB. Increasing vancomycin serum trough concentrations and incidence of nephrotoxicity. Am J Med. 2010; 123:1143–1149. [PubMed: 21183005]

15. Lodise TP, Patel N, Lomaestro BM, Rodvold KA, Drusano GL. Relationship between initial vancomycin concentration-time profile and nephrotoxicity among hospitalized patients. Clin Infect Dis. 2009; 49:507–514. [PubMed: 19586413]

16. Jeffres MN, Isakow W, Doherty JA, Micek ST, Kollef MH. A retrospective analysis of possible renal toxicity associated with vancomycin in patients with health care-associated methicillin-resistant Staphylococcus aureus pneumonia. Clin Ther. 2007; 29:1107–1115. [PubMed: 17692725]

17. Rhee JY, Kwon KT, Ki HK, et al. Scoring systems for prediction of mortality in patients with intensive care unit-acquired sepsis: a comparison of the Pitt bacteremia score and the Acute Physiology and Chronic Health Evaluation II scoring systems. Shock. 2009; 31:146–150. [PubMed: 18636041]

18. Kullar R, Davis SL, Levine DP, Rybak MJ. Impact of vancomycin exposure on outcomes in patients with methicillin-resistant Staphylococcus aureus bacteremia: support for consensus guidelines suggested targets. Clin Infect Dis. 2011; 52:975–981. [PubMed: 21460309]

19. Neely MN, Youn G, Jones B, et al. Are vancomycin troughs adequate for optimal dosing? Antimicrob Agents Chemother. 2014; 58:309–316. [PubMed: 24165176]

Table 1

Baseline characteristics of the cohort[A]

Characteristic	Guideline-recommen ded dosing (n= 42)	Lower dosing (n= 50)	p-value
Male gender (%)	88	92	0.53
Age (years)	77 (69, 84)	74 (68, 78)	0.04
Race (%)			0.54
Caucasian	71	80	
African American	17	10	
Hispanic	10	8	
Other	2	0	
Height (cm)	173 (168, 180)	178 (170, 183)	0.02
Weight (kg)	62 (57, 73)	86 (74, 99)	<0.001
Serum Creatinine (mg/dl)	1.1 (0.8, 1.4)	1.0 (0.8, 1.3)	0.49
Creatinine Clearance (ml/min)	48 (39, 67)	64 (53, 79)	0.002
Charlson comorbity index > 5	10	14	0.51
Pitt Bacteremia Score	2 (1, 3)	2 (1, 3)	0.33
Nephrotoxins (%)	45	44	0.90
Infection Source (%)			0.11
Bloodstream catheter related	26	26	
Pulmonary	24	28	
Skin/muscle	14	22	
Genitourinary	14	6	
Osteomyelitis	0	2	
Gastrointestinal	0	2	
Other	22	14	
Length of hospital stay (days)	17 (9, 42)	22 (9, 34)	0.99
Intensive Care Unit Length of stay (days)	0 (0, 11)	3 (0, 16)	0.46
Initial vancomycindose (mg/kg/day)	31 (25, 35)	22 (18, 25)	<0.001
Initial vancomycin trough (mg/l)	15 (11, 19)	12 (9, 18)	0.46

[A] = Results are presented as median (interquartile range) unless otherwise noted

Table 2

Analysis of risk factors for nephrotoxicity

Variable	Odds Ratio	95% Confidence Interval
Univariable Analysis		
Guideline-recommended vancomycin dosing	0.95	0.40–2.28
Patient age of 80 years or greater	0.37	0.12–1.17
Vancomycin trough > 15 mg/l	1.77	0.73–4.27
Vancomycin area under the curve ≥ 400 mg*hr/L	0.57	0.23–1.40
Vancomycin duration of 15 days or greater	2.16	0.88–5.30
Charlson comorbity index > 5	1.28	0.37–4.52
Pitt bacteremia score of 4 or greater	4.88	1.79–13.26
Intensive care unit residence	5.83	2.12–15.89
Concomitant nephrotoxins (aminoglycosides, intravenous contrast and vasopressors)	2.84	1.16–6.98
Weight of 100kg or greater	0.96	0.29–3.26
Multivariable Analysis		
Guideline-recommended vancomycin dosing	1.13	0.40–3.19
Patient age of 80 years or greater	0.53	0.14–2.03
Pitt bacteremia score of 4 or greater	2.71	0.88–8.32
Intensive care unit residence	3.58	1.15–11.09
Concomitant nephrotoxins (aminoglycosides, intravenous contrast and vasopressors)	1.71	0.60–4.82

Table 3

Analysis of risk factors for in-hospital mortality

Variable	Odds Ratio	95% Confidence Interval
Univariable Analysis		
Guideline-recommended vancomycin dosing	1.01	0.40–2.54
Vancomycin trough > 15 mg/l	1.06	0.42–2.65
Vancomycin duration of 15 days or greater	1.40	0.55–3.58
Vancomycin area under the curve ≥ 400 mg*hr/L	0.74	0.29–1.93
Charlson comorbity index > 5	0.60	0–2.68
Pitt Bacteremia Score of 4 or greater	3.33	1.22–9.14
Intensive care unit residence	7.14	2.28–22.08
Concomitant nephrotoxins (aminoglycosides, intravenous contrast and vasopressors)	1.69	0.67–4.25
Development of nephrotoxicity	1.84	0.71–4.79
Weight of 100kg or greater	0.47	0.00–2.08
Patient age of 80 years or greater	1.00	0.35–2.86
Multivariable Analysis		
Guideline-recommended vancomycin dosing	1.14	0.41–3.18
Pitt bacteremia score of 4 or greater	1.90	0.59–6.08
Development of nephrotoxicity	0.80	0.25–2.52
Intensive care unit residence	6.39	1.78–22.93