A Retrospective Analysis of Possible Renal Toxicity Associated with Vancomycin in Patients with Health Care–Associated Methicillin-Resistant *Staphylococcus aureus* Pneumonia

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ABSTRACT

Objective: The goal of this investigation was to determine whether more aggressive vancomycin dosing is associated with greater risk for renal toxicity in patients with health care–associated pneumonia (HCAP) attributed to methicilllin-resistant *Staphylococcus aureus* (MRSA).

Methods: This was a retrospective, single-center, observational cohort study. The following information was obtained for all study patients from automated hospital, microbiology, and pharmacy databases: age, sex, weight, serial serum creatinine (SCr), age- and sex-adjusted creatinine clearance (CrCl) during receipt of vancomycin, vancomycin serum trough concentrations, duration of vancomycin therapy, and Acute Physiology and Chronic Health Evaluation II scores. Renal toxicity was defined as either a 0.5-mg/dL increase from baseline in SCr or a ≥50% increase in SCr based on serial SCr measurements. Data for patients who met the definition of renal toxicity were compared with data for those who did not.

Results: Ninety-four patients (mean [SD] age, 59.0 [15.6] years; 59 [62.8%] men; 73 (77.7%) white; mean baseline CrCl, 70.3 [23.0] mL/min) were identified as having MRSA HCAP. Forty (42.6%) patients developed renal toxicity. Patients who developed renal toxicity were significantly more likely than patients who did not develop renal toxicity to have greater mean vancomycin serum trough concentrations (20.8 [9.9] μg/mL vs 14.3 [6.7] μg/mL, respectively; $P < 0.001$), vancomycin serum trough concentrations ≥15 μg/mL (67.5% vs 40.7%; $P = 0.01$), and a prolonged duration (≥14 days) of vancomycin treatment (45.0% vs 20.4%; $P = 0.011$). Logistic regression analysis identified a maximum vancomycin serum trough concentration of ≥15 μg/mL as being independently associated with renal toxicity (adjusted odds ratio = 2.82; 95% CI, 1.02–7.74; $P = 0.045$). The overall mean change in CrCl for the study population was –13.5 (–16.0) mL/min (range, 0.0 to –62.6 mL/min). Patients with maximum measured vancomycin serum trough concentrations ≥15 μg/mL (n = 49) had significantly greater absolute changes in CrCl compared with patients with maximum measured vancomycin serum trough concentrations <15 μg/mL (n = 45) (–18.9 [–17.0] vs –7.6 [–12.5] mL/min, respectively; $P < 0.001$).

Conclusions: The results suggest that aggressive vancomycin dosing and prolonged vancomycin administration may be associated with greater risk for renal toxicity in patients with MRSA HCAP. However, this retrospective study cannot establish causation, and a prospective, randomized, double-blind trial is needed. (*Clin Ther*. 2007;29:1107–1115) Copyright © 2007 Excerpta Medica, Inc.

Key words: renal toxicity, *Staphylococcus aureus*, methicillin resistance, pneumonia.

INTRODUCTION

The American Thoracic Society and Infectious Diseases Society of America guidelines for the treatment of hospital-acquired, ventilator-associated, and health care–associated pneumonia (HCAP) recommend a

Accepted for publication April 13, 2007.
doi:10.1016/j.clinthera.2007.06.014
0149-2918/$32.00

target vancomycin serum trough concentration of 15 to 20 μg/mL for the empiric or definitive treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) infections.[1] This recommendation is based on the poor pulmonary distribution characteristics observed for vancomycin, with serum concentrations of 15 to 20 μg/mL potentially resulting in enhanced intrapulmonary drug delivery.[2,3] However, the efficacy of targeting increased vancomycin serum trough concentrations for the treatment of MRSA HCAP has not been established.[4] Two recent analyses failed to find improved outcomes in patients with MRSA infections, including HCAP, with target vancomycin trough concentrations of 15 to 20 μg/mL.[5,6]

Vancomycin-associated renal toxicity has been a point of controversy since 1958, when Geraci et al[7] published the first case series linking the two. Since then, several studies have reported an association between vancomycin serum trough concentrations and renal toxicity.[8–13] However, the definition of renal toxicity, as well as the patient population and disease severity, has varied among these studies. Therefore, we performed a retrospective observational clinical study with 2 main goals: to determine the rate of renal toxicity in patients treated with vancomycin for MRSA HCAP confirmed by bronchoalveolar lavage (BAL) cultures, and to determine whether more aggressive dosing of vancomycin, resulting in serum trough concentrations ≥15 μg/mL, was associated with renal toxicity.

PATIENTS AND METHODS

Study Location and Patients

This study was conducted at a university-affiliated, urban teaching hospital, Barnes-Jewish Hospital (1200 beds). During a 6.5-year period (January 1999–June 2005) all hospitalized patients with MRSA HCAP, microbiologically confirmed by BAL semiquantitative cultures, who were treated with vancomycin were eligible for this investigation. Patients with polymicrobial infection demonstrated by BAL cultures, those treated with vancomycin for <72 hours, and those with acute renal failure or requiring dialysis were excluded from evaluation. This study was approved by the Washington University School of Medicine Human Studies Committee, and informed consent was waived.

Study Design and Data Collection

A retrospective cohort design was employed to assess the effect of vancomycin serum trough concentrations on the occurrence of renal toxicity. The Barnes-Jewish Hospital protocol for intravenous administration of vancomycin requires measurement of steady-state trough concentrations, with a target of 15 to 20 μg/mL. Per protocol, all patients were initially treated with weight-based vancomycin, receiving 30 mg/kg in 2 divided doses during a 24-hour period. To identify potential study patients, a computerized list of all patients with MRSA HCAP who had received vancomycin and had available trough concentrations was generated by the Department of Medical Informatics through retrospective query of the microbiology, laboratory, and pharmacy databases at Barnes-Jewish Hospital (performed by J.A.D.). Patients could not be entered into the study more than once.

For all study patients, the following information was recorded by one of the investigators (M.N.J.): age, sex, weight, serial serum creatinine (SCr) measurements, age- and sex-adjusted creatinine clearance (CrCl) calculated during receipt of vancomycin, measured vancomycin serum trough concentrations, duration of vancomycin therapy, and Acute Physiology and Chronic Health Evaluation (APACHE) II scores. Additionally, concomitant risk factors for renal toxicity were collected, including a diagnosis of diabetes mellitus, the ratio of blood urea nitrogen (BUN) to SCr, and administration of ≥1 of the following: IV contrast dye, loop diuretics, amphotericin B deoxycholate or lipid-formulation equivalent, aminoglycosides, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, cyclosporine or tacrolimus, and/or vasopressors (norepinephrine, phenylephrine, or vasopressin). Patients must have received the potentially renally toxic medication(s) while on vancomycin and before the maximum documented SCr (SCr_{max}) during treatment. Vasopressor use was considered when it was initiated or maintained within 48 hours before SCr_{max}.

Definitions

A clinical diagnosis of MRSA HCAP required the occurrence of new and persistent radiographic infiltrates in conjunction with 2 of the following: fever, leukocytosis, and purulent tracheal aspirate or sputum. For the purposes of this study, MRSA HCAP included patients hospitalized >2 days before a MRSA-positive BAL culture was obtained, and patients with a first MRSA-positive BAL culture within 2 days of hospital admission and any of the following: admis-

sion from another health care facility (including a nursing home), receipt of chronic dialysis, and previous hospitalization within 30 days.[1]

A MEDLINE search was performed using the key words *vancomycin*, *renal failure*, *creatinine*, and *creatinine clearance*. Based on this literature review, renal toxicity was defined as either a 0.5-mg/dL increase from baseline in SCr or a ≥50% increase from baseline in SCr based on serial SCr measurements.[8–14] Baseline SCr and age- and sex-adjusted CrCl calculations were made before administration of vancomycin in all patients, using the following formula[15]:

Estimated creatinine clearance = (140 – age) (weight in kg)/(72 × serum creatinine) × 0.085 (women only)

If the patient's weight was >20% of ideal body weight (IBW), adjusted body weight (ABW) was calculated using the formula ABW = IBW + 0.4(actual body weight – IBW), with IBW (men) = 50 + 2.3 (inches above 60) and IBW (women) = 45 + 2.3 (inches above 60).

SCr_{max} was defined as the highest SCr value during receipt of vancomycin. Minimum SCr (SCr_{min}) was defined as the lowest SCr value before SCr_{max} during receipt of vancomycin or just before initiation of vancomycin. The presence of diabetes was defined as the need for insulin or an oral hypoglycemic agent before or during the patient's hospitalization.

Pharmacokinetic Data

Vancomycin trough concentrations were obtained from serum specimens collected ≤30 minutes before the administration time at steady state. Steady-state conditions were considered to be achieved after 3 doses of a particular vancomycin regimen (ie, 1 g IV q12h) based on the half-life for an individual patient, calculated as follows[15]:

$$k_e = 0.00083\ (CrCl) + 0.0044$$

Steady-state concentrations were estimated to be achieved in 65 (69%) patients within 36 hours of initiation of vancomycin, 16 (17%) patients within 48 hours of initiation, and the remaining 13 (14%) patients between 49 and 100 hours after starting vancomycin therapy. Vancomycin serum concentrations collected outside the 30-minute window were mathematically extrapolated as follows to represent a true trough concentration (n = 11)[15]:

$$\text{True trough} = \text{measured concentration} \times e\ ([-k_e \times \text{time true}] - \text{time actual}),$$

with *time actual* representing the actual time of trough assessment and *time true* representing the correct time of trough assessment.

Statistical Analysis

All comparisons were unpaired, and all tests of significance were 2-tailed. Continuous variables were compared using the Student *t* test for normally distributed variables and the Mann-Whitney *U* test for nonnormally distributed variables. The χ^2 test was used to compare categoric variables. The primary data analysis compared patients who met the study definition for renal toxicity with those who did not. Values are expressed as mean (SD) for continuous variables and as a percentage of the group from which they were derived for categoric variables. *P* was 2-tailed, and $P \leq 0.05$ was considered statistically significant.

We performed multiple logistic regression analyses using SPSS for Windows version 11.0 (SPSS Inc., Chicago, Illinois). Multivariate analysis was performed using models that were judged a priori to be clinically sound[16]; this was prospectively determined to be necessary to avoid producing spuriously significant results with multiple comparisons. All potential risk factors that were significant at the 0.2 level in univariate analyses were entered into the model. A stepwise approach was used to enter new terms into the logistic regression model, in which renal toxicity was the dependent outcome variable and 0.05 was set as the limit for the acceptance or removal of new terms.

RESULTS

Patients

The study cohort consisted of 94 patients. Their mean (SD) age was 59.0 (15.6) years (range, 22–90 years). The mean APACHE II score was 20.2 (8.3) (range, 3–37). There were 59 (62.8%) men and 35 (37.2%) women. Seventy-three (77.7%) patients were white, and 21 (22.3%) were black, Hispanic, or Asian American. The in-hospital mortality rate for the entire cohort was 27.7%, and the mean hospital length of stay was 35.6 (27.6) days.

Forty (42.6%) patients developed renal toxicity while receiving vancomycin for the treatment of MRSA HCAP. Patients developing renal toxicity did not differ significantly from those without renal toxicity in

terms of age, SCr_{min} and the corresponding calculated CrCl, or the presence of diabetes, but they did have significantly greater APACHE II scores (P = 0.006) (**Figure 1, Table I**). Patients developing renal toxicity were significantly more likely to have a measured vancomycin steady-state serum trough concentration ≥15 µg/mL (P = 0.010) and to receive ≥14 days of vancomycin therapy (P = 0.011) (**Table II**). Stratification of patients according to their measured vancomycin steady-state serum trough concentrations indicated a statistically significant relationship with the occurrence of renal toxicity (P = 0.002) (**Figure 2**). A BUN:SCr ratio >20 (P = 0.027) and administration of vasopressors (P = 0.003) were also significantly greater among patients developing renal toxicity compared with those who did not develop renal toxicity (**Table III**). Among patients developing renal toxicity, the SCr_{max} was temporally observed to follow the maximum vancomycin steady-state serum trough concentration by at least 24 hours in 34 (85.0%) patients. None of the patients developing renal toxicity went on to require dialysis during their hospitalization. Twenty-nine (72.5%) patients with renal toxicity had subsequent reductions in SCr toward baseline values before hospital discharge. Patients developing renal toxicity had significantly higher in-hospital mortality rates compared with those who did not develop renal toxicity (18 [45%] vs 8 [15%], respectively; P = 0.001) and greater mean (SD) hospital lengths of stay (44.8 [28.9] vs 28.7 [24.7] days; P = 0.006).

The overall increase in SCr in the study population was a mean (SD) of 0.38 (0.61) mg/dL (range, 0.0–3.10 mg/dL), with a corresponding decrease in calculated CrCl of 13.5 (16.0) mL/min. The change in SCr was 47.0% (54.4%) (range, 0%–266.7%). Compared with patients with maximum measured vancomycin steady-state serum trough concentrations <15 µg/mL (n = 45), patients with maximum trough concentrations ≥15 µg/mL (n = 49) had significantly greater SCr_{max} concentrations (1.1 [0.55] vs 1.7 [0.88] mg/dL, respectively; P < 0.001), absolute changes in SCr (0.24 [0.28] vs 0.61 [0.73] mg/dL; P = 0.002), and percent changes in SCr (32.4% [35.9] vs 60.3% [64.6]; P = 0.012). Correspondingly, patients with maximum measured vancomycin steady-state serum trough concentrations ≥15 µg/mL had a significantly greater minimum calculated CrCl compared with patients with maximum measured vancomycin steady-state serum trough concentrations <15 µg/mL (65.4 [27.2] vs 49.0 [19.6] mL/min, respectively; P = 0.001), absolute reduction in calculated CrCl (18.9 [17.0] vs 7.6 [12.5] mL/min; P < 0.001), and percent change in calculated CrCl (–26.3% [21.5] vs –10.7% [15.8]; P < 0.001).

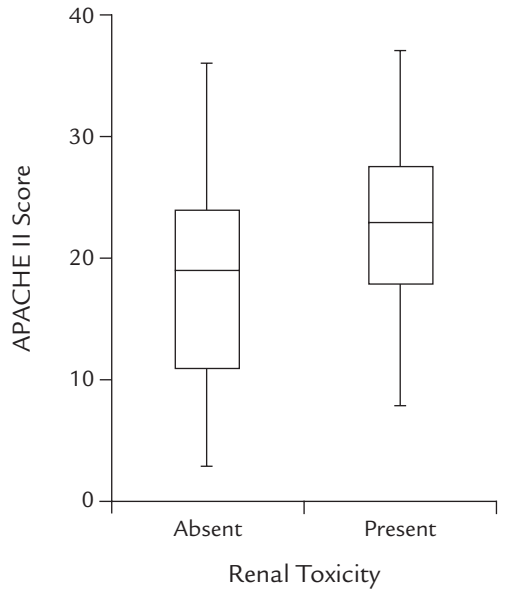

Figure 1. Box plots of Acute Physiology and Chronic Health Evaluation (APACHE) II scores. The boxes represent the 25th to 75th percentiles, with the 50th percentile represented by the solid line within the boxes. The 10th and 90th percentiles are indicated as capped bars.

A secondary analysis was performed in patients without exposure to vasopressors. Eighty (85.1%) patients did not receive vasopressor agents during the study period, 29 (36.3%) of whom developed renal toxicity (**Table II**). Patients developing renal toxicity were significantly more likely to receive ≥14 days of therapy with vancomycin (P = 0.007) and to achieve greater vancomycin steady-state serum trough concentrations (P = 0.003) (**Table II**).

Multivariate Analysis

Multiple logistic regression analysis identified achievement of a vancomycin steady-state serum trough concentration ≥15 µg/mL as an independent predictor of renal toxicity (**Table IV**). A second multivariate analysis was performed excluding patients receiving vasopressors to validate the findings of the first analysis in this subgroup. Receiving ≥14 days of

Table I. Baseline patient characteristics.

Characteristic	Renal Toxicity Absent (n = 54)	Renal Toxicity Present (n = 40)	*P*
Age, mean (SD), y	57.8 (18.3)	60.6 (10.9)	0.362
Male, no. (%)	31 (57.4)	28 (70.0)	0.212
White, no. (%)	39 (72.2)	34 (85.0)	0.141
APACHE II score, mean (SD)	18.2 (8.5)	22.9 (7.4)	0.006
Diabetes mellitus, no. (%)	16 (29.6)	12 (30.0)	0.969
SCr_{min}, mean (SD), mg/dL	0.94 (0.41)	0.96 (0.43)	0.883
SCr_{min} ≥1.4 mg/dL, no. (%)	10 (18.5)	6 (15.0)	0.654
CrCl, mean (SD), mL/min	68.4 (25.8)	72.9 (18.6)	0.444

APACHE II = Acute Physiology and Chronic Health Evaluation II; SCr_{min} = minimum serum creatinine concentration; CrCl = creatinine clearance.

Table II. Vancomycin therapy and changes in renal function.

Variable	Renal Toxicity Absent (n = 54)	Renal Toxicity Present (n = 40)	*P*
Entire cohort (N = 94)			
Vancomycin trough, mean (SD), μg/mL	14.3 (6.7)	20.8 (9.9)	<0.001
Vancomycin trough ≥15 μg/mL, no. (%)	22 (40.7)	27 (67.5)	0.010
Duration of vancomycin ≥14 d, no. (%)	11 (20.4)	18 (45.0)	0.011
SCr_{max}, mean (SD), mg/dL	1.07 (0.44)	1.80 (0.96)	<0.001
SCr change, mean (SD), mg/dL	0.13 (0.12)	0.85 (0.71)	<0.001
Percent change in SCr, mean (SD)	15.9 (14.1)	88.9 (60.4)	<0.001
CrCl minimum, mean (SD), mL/min	63.9 (26.1)	47.4 (19.6)	0.001
CrCl change, mean (SD), mL/min	–4.5 (6.6)	–25.5 (17.0)	<0.001
Percent change in CrCl, mean (SD)	–6.9 (9.1)	–34.8 (21.7)	<0.001
Subgroup without vasopressor exposure (n = 80)*			
Vancomycin trough, mean (SD), μg/mL	14.4 (6.8)	20.4 (10.7)	0.003
Vancomycin trough ≥15 μg/mL, no. (%)	21 (41.2)	18 (62.1)	0.072
Duration of vancomycin ≥14 d, no. (%)	10 (19.6)	14 (48.3)	0.007
SCr_{min}, mean (SD), mg/dL	0.93 (0.40)	0.94 (0.49)	0.921
SCr_{max}, mean (SD), mg/dL	1.05 (0.41)	1.59 (0.83)	<0.001
SCr change, mean (SD), mg/dL	0.12 (0.11)	0.65 (0.50)	<0.001
Percent change in SCr, mean (SD)	15.6 (14.4)	71.7 (44.6)	<0.001
CrCl minimum, mean (SD), mL/min	64.9 (26.5)	51.8 (20.2)	0.016
CrCl change, mean (SD), mL/min	–4.4 (6.7)	–20.0 (14.9)	<0.001
Percent change in CrCl, mean (SD)	–6.6 (9.0)	–28.0 (18.7)	<0.001

SCr_{max} = maximum serum creatinine concentration; CrCl = creatinine clearance; SCr_{min} = minimum SCr.
*51 Without renal toxicity, 29 with renal toxicity.

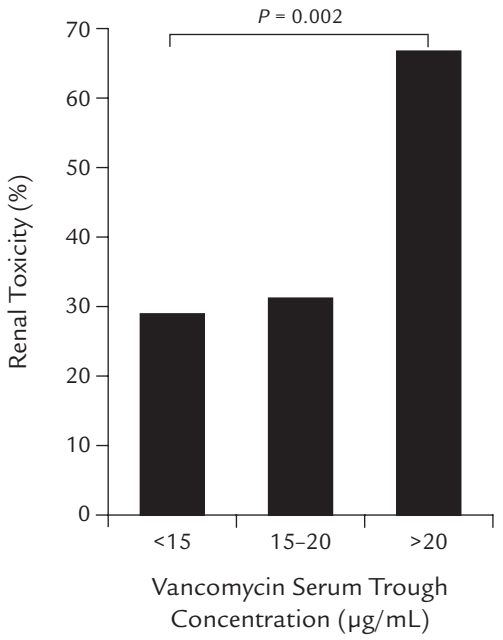

Figure 2. Occurrence of renal toxicity, stratified by vancomycin steady-state serum trough concentrations.

vancomycin therapy was found to be the only variable independently associated with the development of renal toxicity (adjusted odds ratio = 3.33; 95% CI, 1.86–5.97; $P = 0.039$).

DISCUSSION

Our results suggest that aggressive vancomycin dosing, as determined by maximum measured vancomycin serum trough concentrations ≥15 µg/mL, and prolonged vancomycin administration may be associated with renal toxicity among patients treated for MRSA HCAP.

Renal toxicity is reported to be a relatively infrequent complication of vancomycin administration, occurring in ~5% of patients, and is usually reversible.[17] Acute interstitial nephritis is a rare mechanism of action for the development of vancomycin-induced renal toxicity.[18] However, vancomycin appears to potentiate the renal toxicity of other pharmacologic agents, including aminoglycosides.[19] Cimino et al[10] evaluated 229 cancer patients treated with antibiotics. The incidence of renal toxicity was similar for patients receiving an aminoglycoside, vancomycin, or the combination of an aminoglycoside and vancomycin. However, the observed occurrence of renal toxicity was greatest among patients receiving vancomycin when serum trough concentrations were ≥10 µg/mL compared with <10 µg/mL (18.8% vs 0%, respectively; $P = 0.032$). Similarly, Rybak et al[11] found <10 µg/mL that the incidence of renal toxicity was greatest for patients treated concurrently with vancomycin and an aminoglycoside. Vancomycin serum trough concentrations >10 µg/mL and >21 days of vancomycin treatment have also been associated with the development of renal toxicity. A meta-analysis of vancomycin therapy reported similar findings.[20]

The occurrence of health care–associated infections attributed to MRSA has steadily increased over the past 15 years.[21] This has been correlated with a similar increase in the use of vancomycin.[22] However, there has also been an increase in vancomycin treatment failures in MRSA infections as a result of an upward drift in the minimum inhibitory concentrations of isolates and the presence of heteroresistant strains.[23,24] These observations, in conjunction with the poor lung tissue penetration of vancomycin,[2,3] have resulted in recommendations for increased dosing of vancomycin in MRSA HCAP to achieve serum trough concentrations of 15 to 20 µg/mL.[1] Unfortunately, this recommendation is not based on the findings of prospective clinical studies. Rello et al[25] evaluated 75 patients with microbiologically confirmed MRSA HCAP treated with glycopeptides—either teicoplanin or vancomycin (dosed to achieve serum trough concentrations of 20 µg/mL)—and 75 control patients without MRSA HCAP. Despite optimization of glycopeptide therapy, the crude mortality rate in these patients was 48%. Multivariate analysis revealed that a continuous infusion of vancomycin was associated with a reduced risk of mortality in the MRSA HCAP group ($P < 0.05$).

More recently, Jeffres et al[5] evaluated 102 patients with BAL-confirmed MRSA HCAP (mortality rate, 31.4%). Mean (SD) vancomycin trough AUC values did not differ between survivors and nonsurvivors (351 [143] and 354 [109] µg · h/mL, respectively). Stratification of vancomycin trough concentrations and AUC values yielded no relationship with hospital mortality. These authors found no evidence that greater vancomycin trough concentrations or AUC values were correlated with hospital outcome in the treatment of MRSA HCAP. Based on their results, they suggested that aggressive dosing strategies for vancomycin (eg, trough concentrations ≥15 µg/mL) may not offer any advantages in clinical efficacy over tradition-

Table III. Process-of-care variables associated with renal function. Values are no. (%).

Variable	Renal Toxicity Absent (n = 54)	Renal Toxicity Present (n = 40)	*P*
BUN:SCr >20	24 (44.4)	27 (67.5)	0.027
IV contrast dye*	10 (18.5)	14 (35.0)	0.070
Loop diuretic*	24 (44.4)	25 (62.5)	0.083
Amphotericin B*	3 (5.6)	2 (5.0)	0.906
Aminoglycoside*†	3 (5.6)	5 (12.5)	0.233
ACE-I or ARB*	11 (20.4)	8 (20.0)	0.965
Cyclosporine or tacrolimus*	4 (7.4)	5 (12.5)	0.407
Vasopressor‡	3 (5.6)	11 (27.5)	0.003

BUN:SCr >20 = ratio of blood urea nitrogen to serum creatinine >20; ACE-I = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker.

*Received before attainment of maximum serum creatinine concentration.

† All aminoglycosides were administered for <72 hours for empiric coverage of gram-negative bacteria before availability of culture results.

‡Received within 48 hours before SCr_{max}.

Table IV. Multivariate analysis of independent risk factors for renal toxicity.*

Variable	Adusted Odds Ratio	95% CI	*P*
IV contrast dye	2.15	0.74–6.27	0.162
BUN:SCr ratio >20	1.38	0.46–4.09	0.566
Loop diuretic	1.13	0.65–1.97	0.830
Aminoglycoside	1.29	0.50–3.34	0.788
Duration of vancomycin ≥14 d	2.55	0.88–7.39	0.084
APACHE II score (1-point increments)	1.05	0.98–1.12	0.183
Vasopressor administration	4.40	0.92–20.98	0.063
Vancomycin trough ≥15 μg/mL	2.82	1.02–7.74	0.045

BUN:SCr >20 = ratio of blood urea nitrogen to serum creatinine >20; APACHE II = Acute Physiology and Chronic Health Evaluation II.

*The listed variables were included in the logistic regression analysis. *P* = 0.631, Hosmer-Lemeshow goodness-of-fit test.

al targets (5–15 μg/mL) and that alternative agents should be considered.[26–29]

Our study has several important limitations. First, we studied only BAL-confirmed cases of MRSA HCAP; therefore, our results may not be applicable to patients in whom MRSA HCAP was diagnosed using other methods. Second, we cannot exclude the possibility that some undetermined confounding factor accounted for the observed increase in renal toxicity. Patients developing renal toxicity had a greater severity of illness, as measured by APACHE II scores. Additionally, patients developing renal toxicity were significantly more likely to require vasopressors, a marker of hypotension-induced acute tubular necrosis, and to have a greater incidence of administration of IV contrast dye and loop diuretics. Any of these factors could have contributed to the greater observed occurrence of renal toxicity. Larger, randomized, controlled, blinded studies are required to determine the occurrence of renal toxicity with higher targeted van-

comycin trough concentrations among patient groups stratified by severity of illness. Third, although we compared changes in measured SCr and CrCl with baseline values obtained before the start of vancomycin treatment, we cannot exclude the possibility that renal dysfunction unrelated to vancomycin toxicity was responsible for elevations in both SCr and vancomycin trough concentrations in some patients. It is possible that higher vancomycin serum concentrations were markers of, rather than causative factors for, renal toxicity. Finally, because of the complexity of studying the relationship between vancomycin use and renal toxicity, the study results should be viewed as hypothesis generating rather than causality proving.

CONCLUSION

The results of this study suggest that aggressive vancomycin dosing, as determined by vancomycin serum trough concentrations ≥15 μg/mL, and prolonged administration of vancomycin may be associated with renal toxicity among patients treated for MRSA HCAP.

ACKNOWLEDGMENT

This work, including all analyses, was funded by Washington University and Barnes-Jewish Hospital. The authors have no conflicts of interest relative to this work.

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