Abstract (revised)

Background: Supratherapeutic vancomycin (VAN) concentrations are a known risk factor for nephrotoxicity; however, factors leading to increased VAN trough concentrations are not well characterized. The purpose of this study was to identify risk factors for supratherapeutic VAN levels.

Methods: Clinical data were obtained from the University of Kentucky Center for Clinical and Translational Science Enterprise Data Trust. Basic clinical information, VAN dosing, VAN serum concentrations, serum creatinine levels, severity of illness (Charlson Comorbidity Index [CCI]), and nephrotoxic exposure were collected from 9/1/10 through 8/31/14. Multivariable logistic regression was performed to determine independent risk factors for supratherapeutic VAN levels. VAN levels were classified as non-supratherapeutic (<20 µg/mL) or supratherapeutic (>20 µg/mL).

Results: 6,529 patient encounters received VAN and had at least one VAN level. 33.9% of patients had supratherapeutic VAN trough concentrations. Patients with supratherapeutic VAN levels were older (52.4 v. 50.2 years, p<0.001), female (48.1 v. 40.2%, p<0.001), sicker (median CCI 3 v. 2, p<0.001), and had lower admission creatinine clearances (median 92.1 v. 104.0 mL/min, p<0.001). In-hospital mortality or transfer to a hospice facility (12.4 v. 7.5%, p<0.001) and increased lengths of hospitalization (median 13 v. 8 days, p<0.001) were more common in the supratherapeutic VAN group. Average daily VAN doses were equivalent (2083 v. 2125 mg/day, p=0.07). After logistic regression, factors associated with increased odds of supratherapeutic VAN troughs were baseline CrCl between 60 and 89 mL/min (OR = 1.42; 95% CI 1.25-1.61) and 30-59 mL/min (OR=1.5; 95% CI 1.26-1.78), increasing CCI (OR=1.02; 95% CI 1.00-1.04), emergency department or urgent admission (OR=1.22; 95% CI 1.03-1.46 and 1.47; 95% CI 1.21-1.78, respectively), loop diuretic use (OR=1.29; 95% CI 1.14-1.45), and greater than 7 days of VAN therapy (OR = 3.03; 95% CI 2.69-3.42).

Objective: To identify and characterize risk factors for supratherapeutic VAN levels in a large retrospective cohort

Methods: Clinical data were obtained from the University of Kentucky Center for Clinical and Translational Science Enterprise Data Trust. Basic demographic information, VAN dosing, VAN serum concentrations, serum creatinine levels, severity of illness (Charlson Comorbidity Index [CCI]), and nephrotoxic exposure were collected from 9/1/10 through 8/31/14. VAN levels were classified as non-supratherapeutic (<20 µg/mL) or supratherapeutic (>20 µg/mL).

Multivariable logistic regression was performed to determine independent risk factors for supratherapeutic VAN levels.

Conclusions: Factors associated with supratherapeutic VAN concentrations include: female gender, increasing severity of illness (via CCI), mild to moderate renal insufficiency, transfer from an outside facility, emergency or urgent admission, duration of VAN therapy greater than 7 days, and exposure to loop diuretics. Daily VAN doses between 30 and 44 mg/kg and admission from the Trauma center were associated with decreased odds of supratherapeutic VAN concentrations. These findings warrant further study.

Administration of concomitant nephrotoxic agents (aside from loop diuretics) does not appear to increase the odds of supratherapeutic VAN levels.