

**P2015 Rechallenging patients with vancomycin after previously experiencing acute kidney injury and alterations in the vancomycin exposure-toxicity threshold**

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**Background:** Vancomycin exposure is known to be associated with acute kidney injury (AKI). Study objectives were to: (1) quantify the vancomycin exposure threshold associated with AKI in patients who have previous history vancomycin-related AKI and (2) determine if exposure thresholds vary between primary to secondary AKI.

**Materials/methods:** A retrospective cohort study was conducted among patients in the Upstate New York Veterans' Healthcare Administration from 2000-2015. Inclusion criteria for analysis of primary AKI: (1) age  $\geq 18$  years; (2) hospitalized; (3) receipt of two courses of vancomycin  $\geq 48$  hours separated by  $\geq 7$  days; (4) non-dialysis and (5) experienced AKI after primary vancomycin course. The occurrence of AKI was defined as 0.5mg/dL increase in serum creatinine or 50% decline in creatinine clearance (CRCL, Cockcroft Gault method & adjusted body weight). Vancomycin area under the curve at steady state (AUC<sub>ss</sub>) was estimated in each patient using BestDose version 1.126.

**Results:** Within the initial cohort, the incidence of primary AKI was 591/3845 (15.4%) and the AUC<sub>ss</sub> threshold associated with primary AKI was 685 mg\*h/L. Patients with an AUC<sub>ss</sub>  $\geq / < 685$  mg\*h/L had a significantly different risk of primary AKI (26.6% versus 12.5%,  $p < 0.001$ ). Among patients who experienced a primary AKI, 124 patients received vancomycin during a subsequent hospitalization. The incidence of secondary AKI was 32/124 (25.8%). The AUC<sub>ss</sub> associated with secondary AKI was 400 mg\*h/L. Patients with AUC<sub>ss</sub>  $\geq 400$  mg\*h/L had a significantly higher occurrence of secondary AKI than those with AUC<sub>ss</sub>  $< 400$  mg\*h/L (35.3% versus 14.3%,  $p = 0.008$ ). In multivariate analyses, AUC<sub>ss</sub> was independently associated with secondary AKI (hazard ratio: 2.47, 95% CI: 1.07-5.71,  $p = 0.04$ ) after adjustment for APACHE-II score  $\geq 19$  and weight  $\geq 115$ kg.

**Conclusions:** In patients with a history of vancomycin-related AKI, the AUC<sub>ss</sub> threshold associated with secondary AKI on subsequent exposure was 400 mg\*h/L and alternative agents may need to be considered.