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Larger Vancomycin Doses (>= 4 grams/day) are Associated with an Increased Incidence of Nephrotoxicity.

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Recent guidelines recommend vancomycin trough concentrations between 15-20 mg/L. In response, some clinicians increased vancomycin dosing to >/=4 gm/day. Scant data are available regarding toxicities associated with higher vancomycin doses. The purpose of this study was to examine vancomycin-associated nephrotoxicity at >/= 4 gm/day. To accomplish the study objective, a cohort study among a random selection of patients receiving vancomycin or linezolid between 2005- 2006. Patients were included if they were (1) >/= 18yrs, (2) non-neutropenic, (3) therapy for > 48 hours, (4) baseline serum creatinine < 2.0mg/dL, (5) non-cystic fibrosis, and (6) no intravenous contrast dye within seven days. For drug exposure, three treatment strata were created: standard vancomycin dose (< 4 gm/day), high vancomycin dose (>/= 4 gm/day), and linezolid. Nephrotoxicity was defined as a serum creatinine increase of 0.5mg/dl or 50%, whichever was greater, after therapy initiation. Stratified Kaplan-Meier analysis and Cox modeling were used to compare time-to-nephrotoxicity across groups. During the study, 246 vancomycin patients (26 >/=4g/day; 220 <4g/day) and 45 linezolid patients met the criteria. A significant difference in nephrotoxicity was noted between patients receiving vancomycin >/= 4 gm/day, vancomycin < 4 gm/day, and linezolid (34.6% vs. 10.9% vs. 6.7%, p-value=0.001) and Kaplan-Meier analysis identified significant differences in time-to-nephrotoxicity for the high vancomycin dose cohort compared to the standard dose and linezolid. In the Cox model, vancomycin >/= 4 g/day, total body weight >/= 101.4 kg, estimated creatinine clearance </= 86.6 ml/min, and ICU residence were independently associated with time-to-nephrotoxicity. The data suggest that higher dose vancomycin regimens are associated with a higher likelihood of vancomycin-related nephrotoxicity.

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