Aminoglycoside pharmacokinetics in critically-ill patients undergoing renal replacement therapy
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Introduction:
Changes to aminoglycoside (AG) pharmacokinetics during critical illness may affect attainment of pharmacokinetic targets. Use of continuous renal replacement therapies (CRRT) complicates attainment due to variable and poorly understood extracorporeal drug clearance.

Methods:
Adult patients who received a first dose of amikacin or tobramycin during CRRT between 2/1/2012 and 2/28/2017 were retrospectively evaluated. Patients were allocated to different study arms per their receipt of SLED, CVVHD, or CVVH. Two post-distributional serum levels were required for pharmacokinetic calculations. Patients were excluded if fewer than 2 serum AG levels were collected, if previous AG dose given within 7 days, if already enrolled or if pregnant. The aim of this study was to characterize first-dose AG clearance and Vd during CRRT.

Results:
A total of 80 patients were allocated to the SLED (49 subjects), CVVHD (19 subjects) and CVVH arms (12 subjects). Fifty-one patients received a median amikacin dose of 14.2 mg/kg per actual body weight (ABW) and achieved a median peak level of 27.3 mg/L. Twenty-nine patients received a median tobramycin dose of 6.4 mg/kg ABW and achieved a median peak level of 10.5 mg/L. The median clearance was 76.6 mL/min and was similar between study arms (P=0.94). The median volume of distribution was 0.55 L/kg and was similar between study arms (P=0.38). Attainment of target peak:MIC ratio of at least 10 occurred in 33% in the total study population and 41% in the subset of 37 positive cultures. No significant correlation was found between AG clearance and CRRT blood flow or pre-filter fluid rate for the 3 arms. A significant correlation between AG clearance and dialysate rate was observed in the CVVHD arm (P<0.001) but not in the SLED (P=0.85) or CVVH (P=0.19) arms.

Conclusion:
Critically ill patients undergoing CRRT have a reduced clearance, expanded volume of distribution and prolonged half-life that was not significantly different between CRRT modalities. Current dosing regimens led to low peak concentrations and poor attainment of pharmacokinetic targets.