DOSE VALIDATION OF ONCE-DAILY DOSING GUIDELINES FOR GENTAMICIN IN CRITICALLY ILL PAEDIATRIC PATIENTS

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Introduction: Aminoglycosides have two unique properties which allow them to be given as once daily dosing (ODD): concentration-dependent bactericidal killing and post-antibiotic effect. Benefits of ODD include reduced risk of nephrotoxicity and ototoxicity, reduced adaptive resistance, and potential cost- and time-savings. For these reasons, ODD guidelines for gentamicin were implemented in the cardiac and paediatric intensive care units (CCCU and PICU) at SickKids.

Objectives: To validate the ability of gentamicin 9 mg/kg IV once daily to achieve pharmacokinetic targets (Cmax 16-25 mg/L, AUC 70-100 mg·hr/L, and drug free interval 4-16 hr) and to determine the efficacy and safety of ODD gentamicin in critically ill paediatric patients

Methods: A retrospective chart review was performed for all patients admitted to the CCCU or PICU from June 1, 2012 – May 31, 2013 who received gentamicin and met the study inclusion criteria. Pharmacokinetic parameters were calculated from 3 and 6 hour post-dose gentamicin levels.

Results: Thirty-five patients received 41 ODD gentamicin courses (30 in PICU, 11 in CCCU). With the first dose, twenty-one (51.22%) courses achieved the target Cmax of 16 – 25 mg/L. The median Cmax was 18.49 mg/ L (IQR 14.84 – 22.29) and median AUC was 68.00 mg·hr/L (IQR 56.63 – 84.94). Monte Carlo simulations computed that the probability of achieving Cmax target of 16-25 mg/L for the dose of 9 mg/kg was 40.55%. Twenty-eight patients defervesced by the end of gentamicin therapy and thirteen patients did not. The median change from baseline for serum creatinine was 0% (IQR -11.1% - 19%), and the median change from baseline for BUN was 0% (IQR -14% - 40%). No patient required audiometry testing.