Vancomycin AUC optimisation using minimal plasma concentration monitoring

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Introduction. The area under the plasma concentration-time curve (AUC) is recommended for guiding vancomycin dosing. It is unclear which limited sampling strategy accurately predicts the 24 h AUC at steady-state (AUC_{ss24}).

Aims. To investigate the accuracy of eight limited sampling strategies with 1-2 samples taken across a single dosing interval (e.g. C_{min}, C_{max}) on doses 1-5 of treatment for predicting vancomycin AUC_{ss24} using Bayesian forecasting, including stratification by obesity, in adults.

Methods. We performed an *in-silico* simulation study using a vancomycin PK model developed by Thomson et al (2009), implemented in the Bayesian software TCI works. We simulated virtual patients using the demographic and vancomycin dosing information from 138 patients who had been through the local therapeutic drug monitoring service. For each simulate, the estimated AUC_{ss24} for each sampling strategy was compared with the simulated reference using metrics of bias and imprecision, as well as the bioequivalence criterion for low therapeutic index medicines (0.90-1.11).

Results. The simulated patients had median (range) age 65 years (19-93), actual weight 84 kg (42-180), BMI 28.2 kg/m^2 (18.1-68.6), creatinine clearance 85 mL/min (30-302), with 98% dosed every 12 hours and median (range) simulated reference AUC_{ss24} of 618 mg/L.h (172-1726). For the whole cohort, all strategies underestimated the reference AUC_{ss24} with mean prediction error (MPE) and root mean square error (RMSE) values ranging from -71 mg/L.h (95% CI -97, -44) to -59 mg/L.h (95% CI -77, -41) and 122 to 174 mg/L.h, respectively. Only the strategy using C_{min} of doses 2 and 3 met the bioequivalence criterion. For the obese cohort (56 patients), MPE and RMSE values ranged from -103 mg/L.h (95% CI -136, -71) to -141 mg/L.h (95% CI -182, -100) and 149 to 208 mg/L.h, with no strategy meeting bioequivalence. In contrast, amongst the non-obese, all strategies met bioequivalence.

Discussion. Any of the strategies implemented could estimate AUCss 0-24h in non-obese individuals with sufficient accuracy. Further research into strategies for obese individuals is required.

Thomson AH (2009) J Antimicrob Chemother 63: 1050-1057.