Development of a Population Pharmacokinetic Model for Vancomycin on an Extracorporeal Membrane Oxygenation (ECMO) Therapy Patient Population

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Objectives: Vancomycin is a frequently used antibiotic in the treatment of critically ill individuals. However, information detailing pharmacokinetics for patients undergoing extracorporeal membrane oxygenation (ECMO) therapy is relatively sparse. This study looks to develop a population pharmacokinetic model for vancomycin in ECMO patients to identify the presence of meaningful covariates.

Methods: A structural model was developed using non-linear mixed effects modeling (NONMEM VII) on the concentration-time profiles of 14 ECMO patients who received an infusion of 1–2 g of vancomycin over 1-2 hours. Vancomycin concentrations were measured 0.5, 1, 2, 4, and 6 hours upon completion of the infusion. The model discrimination was based on the objective function value (OFV), the goodness of fit plots, and parameter estimates. A covariate model was developed using the stepwise forward inclusion backwards elimination method (p<0.05).

Results: A two-compartment model with log-normally distributed inter-subject variability and proportional residual error model, was found to better describe vancomycin disposition than a one-compartmental model (∆OFV = -33.0). The median central volume of distribution (Vc) was 21.3 L in ECMO patients, while the peripheral volume of distribution (Vp) was 24.4 L. The median clearance was 3.96 L/h, while the intercompartmental clearance (Q) was 11.5 L/h. Covariates of weight and creatinine clearance were found to have a significant effect on the central volume of distribution and the clearance, respectively, using a centered linear model (p<0.05).

Conclusions: This study demonstrates the appropriateness of using a two-compartment model to describe the disposition of vancomycin given to ECMO patients.

References: