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Poster Session VI
PK/PD of antibiotics against Gram-negatives

USE OF BAYESIAN PHARMACOKINETIC MODELS TO PREDICT MEROPENEM CONCENTRATIONS IN CRITICALLY ILL PATIENTS – APPLICATION TO THERAPEUTIC DRUG MONITORING

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Objectives: Therapeutic Drug Monitoring (TDM) is an efficient tool for optimizing the therapeutics of drugs. Applying Bayesian feedback to TDM is a method that can accurately describe patient pharmacokinetics based with only minimal data. The goal of this study was to establish the agreement between observed pharmacokinetic data with a Bayesian feedback as well as a non-Bayesian model of meropenem in critically ill patients.

Methods: Total meropenem concentrations were measured in critically ill patients as part of a clinical TDM program. Meropenem was administered by either intermittent or extended infusion. A two compartment population pharmacokinetic model incorporating body weight and creatinine clearance as covariates was coded in the R language into Individually Designed Optimum Dosing Strategies – Scientific (ID-ODS - S®) and was used to calculate the meropenem concentrations, allowing for the change in model parameters from dose to dose. Difference plots of observed versus predicted concentrations (with or without feedback) were constructed to evaluate the agreement between the observed and predicted concentrations. Bias and precision of the two models as predictors of observed concentrations were determined by the mean differences,95% limits of agreement and their corresponding 95% confidence intervals (95%CI).

Results: 290 meropenem concentrations from 34 patients were available for analysis. Relative percentage difference plots were constructed to increase the normality of the data. Here observed versus model predicted concentrations with or without feedback showed non-significant bias with a mean (95%CI) % difference of 1.81 (-1.82, 5.45) % and -0.93 (-8.17, 6.30) %, respectively. Predictions with as compared to without feedback showed improved precision illustrated by a narrower range of 95% (95%CI) lower and upper limits of agreements of -59.89 (-66.17, -53.61) % to 63.52 (57.25,69.80) % and -123.65 (-136.13, -111.17) % to 121.78 (109.30,134.26) %, respectively.

Conclusion: Model based simulations with and without Bayesian feedback were found to be similarly accurate, while the method with Bayesian feedback resulted in better precision of predicted meropenem concentrations in this group of critically ill patients. These highly individualized Bayesian models further enable practitioners to correctly describe the pharmacokinetics of meropenem in their patients, which in turn ensures more accurate dose adjustments in a clinical TDM program focusing on the optimal dosing of meropenem.