EV0009

ePoster Viewing

Antimicrobials: antibiotic usage

Comparative evaluation of the predictive performance of three different structural population pharmacokinetic models to predict future voriconazole concentration

A. Farkas[1,2], L. Feng Guan[3], P. Villasurda[4], M. Dolton[5], J. Roberts[6]

[1]*Optimum Dosing Strategies, Bloomingdale- NJ, USA*

[2]*Vassar Brothers Medical Center, Poughkeepsie- NY, USA*

[3]*University of Buffalo School of Pharmacy, Buffalo- NY, USA*

[4]*Touro College of Pharmacy, New York- NY, USA*

[5]*School of Biomedical Engineering- University of Southern California, Los Angeles- CA, USA*

[6]*Burns Trauma and Critical Care Research Centre- The University of Queensland, Brisbane, Australia*

Objectives: Therapeutic drug monitoring (TDM) of voriconazole in clinical practice has been strongly advocated in recent years to improve the safety and efficacy profile of this agent. Bayesian methods for voriconazole TDM have been studied before,but there are no reports comparing the accuracy and precision of predictions of published models. Furthermore, the comparative accuracy of linear, mixed linear and non-linear, or fully nonlinear models may be of interest. The goal of this study was to compare the performance of these three methods coupled with Bayesian feedback for predicting voriconazole concentrations.

Methods: Voriconazole concentrations from an independent dataset of hematopoietic stem cell recipient patients were used in this analysis. Voriconazole was administered by intermittent IV infusion. The models were coded into Individually Designed Optimum Dosing Strategies (ID-ODS™) online and used as the Bayesian prior in a sequential design. Observed levels were predicted where for each concentration the data available to that point were entered and used to estimate a prediction. The mean prediction error (ME) and mean squared prediction error (MSE) and their 95% confidence intervals (95%CI) were calculated to measure absolute bias and precision, while delta ME (Δ ME) and delta MSE (Δ MSE) and their 95% CI to measure relative bias and precision, respectively.

Results: 317 voriconazole levels were analyzed. MEs (95%CI) ranged from 0.02 (-0.08, 0.13), 0.29 (0.20, 0.38)to 0.3 (0.20 to 0.39) while the MSEs (95%CI) from 0.91 (0.60, 1.21), 0.73 (0.54, 0.93), to 0.81 (0.58 to 1.05) for the linear, mixed, and non-linear models, respectively, indicating a non-significant difference in bias for the linear method. When compared relative to the linear method, both the mixed and non-linear approaches showed higher Δ MEs of 0.26 (0.19, 0.33) to 0.27 (0.17, 0.37) and non-significantly lower Δ MSEs of -0.17 (-0.39, 0.05) and -0.09 (-0.39, 0.20), respectively.

Conclusion: Simulations with the linear model were found to be more accurate and similarly precise at predicting voriconazole concentrations versus the mixed or non-linear method evaluated here. Further analyses are needed to determine predictive performance following orally administered voriconazole and the performance of linear models in patients who display significant saturation of voriconazole elimination.