Exploring population Pharmacokinetics of Vancomycin While Using Different Anticoagulant Modalities during Continuous Venovenous Haemodiafiltration (CVVHDF)

Session Information

- **Pharmacokinetics, Pharmacodynamics, Pharmacogenomics**
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Background

Uncertainty remains concerning pharmacokinetics (PK) of antimicrobials in critically ill patients due to the scarcity of data and the heterogeneity of the patient cohort. Our aim was to describe the population PK estimates and the influence of patient covariates and anticoagulant modality on PK of vancomycin, following intermittent infusion in intensive care patients receiving CVVHDF.

Methods

Vancomycin dose and concentration data (peak, trough) were collected retrospectively from the electronic health records of 31 critically ill patients (n = 280 levels). A one-compartment model was used to describe the vancomycin concentration-time profiles using Pmetrics software. For brevity, only $R^2$ values are presented here, from observed vs. population predicted concentration plots. Dosing intervals were classified according to the dialysis modality for the majority of the
dosing interval i.e. 1) dialysis with citrate anticoagulation (60 levels) 2) dialysis with non-citrate anticoagulation (120 levels) or 3) not on dialysis (44 levels). Continuous covariates were: cumulative fluid balance, effluent flow rate, blood flow rate, body weight, albumin concentration and age.

Results

An acceptable base model was produced using the Elimination Rate Constant (Ke) and Volume of Distribution (V) (R^2 0.51). The mean ± SD of vancomycin PK estimates were: V 80.65 ± 22.65 L; Ke 0.03 ± 0.01 h^-1. The best population predicted models included cumulative fluid balance and albumin concentration as covariates (R^2 = 0.59 for both). The concentrations in the citrate group correlated best with the population predicted models as compared to the non-citrate dialysis and not on dialysis cohorts, with R^2 of 0.86, 0.58 and 0.28, respectively.

Conclusion

Cumulative fluid balance and albumin concentration data along with citrate anticoagulation status are suggested as covariates for further analysis with richer data, to optimise covariate PK modelling of vancomycin in ICU patients on CVVHDF, and support dose optimisation. Interestingly, the less variable PK estimates in the citrate group model suggest that the anticoagulant modality used might be associated with observed PK variability.