Poster

[P27-1] P27-1: Anti-infective drugs (6): Anti-MRSA and antifungals

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[P27-1-1] Population pharmacokinetic analysis of teicoplanin using serum cystatin C to predict renal clearance

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Background

The glomerular filtration rate (GFR) is usually estimated using serum creatinine (SCr), however, SCr is well known to be affected by various factors, thereby, showing low predictability in some patients. Recently, serum cystatin C (CysC) has been proposed as an alternative marker to SCr estimating the renal clearance. In this study, we performed a population pharmacokinetic analysis of teicoplanin (TEIC), which eliminates mainly through kidney, using CysC as a predictor for the renal clearance.

Methods

Thirty-six patients (16 males and 20 females) with MRSA infection who were administrated to the National Hospital Organization Beppu Medical Center between January 2012 and December 2013 were enrolled and gave 123 blood teicoplanin concentration data. The renal clearance was estimated either by the Hoek formula using CysC, creatinine clearance predicted by Cockcroft-Gault equation using SCr, or CysC directly. One compartment open model with inter-individual variabilities for the clearance and the volume of distribution and additive residual error model was used to estimate the population pharmacokinetic parameters for TEIC. Stability and accuracy of the model were evaluated by the bootstrap method of 200 resampled datasets. All analyses were performed by Phoenix NLME 1.4 (Certara).

Results

The model with the best predictability was the one with CysC as a predictor for the clearance, which showed better statistical significance than the models using the estimated GFR by the Hoek method or CCR. The final model was as follows:

CL (L/hr) = 0.510 * (CysC/1.4)^(-0.682)*(Body weight/60)^0.813, omega (CL) = 19.8%CV,

V (L) = 78.1, omega (V) = 42.7%CV,

Residual variability (SD) = 2.49 (mg/L).

Bootstrap model evaluation gave 100% successful runs showing the stability of the model, and the bootstrap mean and its standard deviations correlated well with the original estimates thus confirming the final model.

Conclusions

The present study shows the usefulness of CysC to better predict the pharmacokinetics of drugs eliminating mainly through the kidney such as TEIC. However, because the sample size in this study was relatively small, further investigation of the renal clearance predictability using CysC would be needed.