Poster

[P25-2] P25-2: Anti-infective drugs (2): Beta-lactams

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[P25-2-6] Population pharmacokinetic analysis of piperacillin and tazobactam by using their blood and urine level data in Japanese pediatric patients

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Background

Piperacillin/tazobactam (PIPC/TAZ), a broad-spectrum β-lactam/β-lactamase inhibitor antibiotic combination, is commonly used in the pediatric population for empiric therapy in hospitals. Since there are many limitations in evaluation of the pharmacokinetic (PK) properties in pediatric patients, only one clinical study with population PK (PPK) model was reported in Japan. Therefore, the PPK analysis, which combines the data of several pediatric clinical studies, seems to be a useful approach for constructing PK models. The aim of this study was to develop a PPK model using blood and urine concentrations of PIPC/TAZ reported in Japanese pediatric patients.

Methods

We used the concentration data of PIPC and TAZ in six separate study reports. Plasma and urine data were combined with demographic variables to produce nonlinear mixed-effects modeling program datasets that are used in PPK analyses. Fixed-effects parameters were renal clearance (CL_r), non-renal clearance (CL_{nr}), and volume of distribution.

Results

A total of 21 children, who ranged in age from 7 months to 15 years, received a 20–100 mg/kg of PIPC and 5.0-12.5 mg/kg of TAZ. A total of 76 plasma concentrations and 30 urinary excretion data were used for PPK modeling of PIPC, and 61 plasma concentrations and 26 urinary excretion data were used for TAZ. Both PIPC and TAZ concentration data best fit a one-compartment model. For PIPC, the mean values of CL_r, CL_{nr} and distribution volume were 0.232 ±0.027 L/h/kg, 0.284 ±0.035 L/h/kg and 0.230 ±0.019 L/kg, respectively. These results indicate that the clearance of PIPC in Japanese pediatric patients was due to 50% renal clearance (CL_r) and 50% non-renal clearance (CL_{nr}). For TAZ, the mean values of CL_r, CL_{nr} and distribution volume were 0.208 ±0.029 L/h/kg, 0.240 ±0.041 L/h/kg and 0.274 ±0.029 L/kg, respectively.

Conclusions

These results suggested that PPK analysis by using blood and urine levels of PIPC and TAZ was possible to evaluate the contribution of renal and non-renal clearance to PIPC and TAZ pharmacokinetic in Japanese pediatric patients.