Population pharmacokinetics of meropenem in pediatric patients: a concurrent analysis of the plasma and urine concentration data

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Background: This study aimed to develop a population pharmacokinetic model for meropenem in Japanese pediatric patients, specifically focusing on the drug urinary excretion process. This study also aimed to use this model to assess the pharmacodynamics of meropenem regimens against common bacterial populations.

Methods: Pharmacokinetic data (229 plasma samples and 61 urine samples) were collected from 40 infected children (age, 0.2–14.8 years; body weight, 3.8–64.0 kg) in nine separate studies. The data were concurrently fitted into a multi-compartment model using the NONMEM program. The developed model was then used for a pharmacodynamic Monte Carlo simulation to estimate the probabilities of attaining the bactericidal target (40% of the time for which the free drug concentration remains above the MIC for the bacterium).

Results: In the final population pharmacokinetic model, body weight (BW, kg) was the most significant covariate as follows: CLR (L/h) = 0.254 × BW, CLNR (L/h) = 3.45, VC (L) = 0.272 × BW, Q (L/h) = 1.65 and VP (L) = 0.228 × BW, where CLR and CLNR are the renal and non-renal clearances, VP and VC are the volumes of distribution of the central and peripheral compartments, and Q is the intercompartmental (central–peripheral) clearance. The pharmacodynamic assessment based on this model showed that regimens of 10–40 mg/kg, three times a day (0.5-h infusions), achieved a target attainment probability of >80% against clinical isolates of Escherichia coli (MIC90 = 0.03 mg/L), Streptococcus pneumoniae (MIC90 = 0.5 mg/L), methicillin-susceptible Staphylococcus aureus (MIC90 = 0.12 mg/L), Haemophilus influenzae (MIC90 = 0.25 mg/L) and Pseudomonas aeruginosa (MIC90 = 1 mg/L), in most typical patients (BW = 10, 20 and 30 kg).

Conclusion: These results provide a better understanding of the pharmacokinetics of meropenem in Japanese pediatric patients. They are also useful in the choice of a meropenem regimen based on the BW of the patient and the susceptibility of the causative bacteria.

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