PHARMACOKINETICS AND PHARMACODYNAMICS OF MEROPENEM IN CHILDREN WITH SEVERE INFECTION

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Background: Physiologic changes in severe infection may affect serum drug concentrations as well as their clinical outcomes. Understanding of pharmacokinetics (PK) and pharmacodynamics (PD) of meropenem in children with sepsis is important to optimize treatment outcomes.

Objectives: (1) To describe PK of meropenem in children with severe infection and (2) to assess the PK and PD profiles of various meropenem dosage regimens in these patients.

Materials and Methods: Fourteen children with severe infection received intravenous bolus doses of meropenem (20 mg/kg/dose) every 8 hours. Serum samples were obtained before and serially after the administration of the second dose. Serum meropenem concentration-time data were analyzed using noncompartmental and compartmental models. The individual PK parameters from compartmental analysis were used to simulate the PK-PD profiles of meropenem at various dosage regimens using WinNonlin®.

Results: Patients’ median age and weight were 6.0 years (range: 4.5 - 11.8) and 20.0 kg (range: 14.0 - 46.5), respectively. Non-compartmental analysis revealed median meropenem total body clearance of 5.03 liter/hour and volume of distribution of 3.57 liter. The PK-PD profiles showed that serum meropenem concentrations in 64% of patients reached target concentrations of above 1 µg/mL. Simulation analysis showed only 79% of the patients receiving 40 mg/kg/dose of meropenem infused over 3-hour period achieves the target concentration for Pseudomonas aeruginosa (MIC=4 µg/mL).

Conclusion: A meropenem dosage of 20 mg/kg administered as an intravenous bolus dose every 8 hours appeared to be inadequate, especially for organisms with MIC values of greater than or equal to 1 µg/mL.

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