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Pharmacodynamics of Meropenem in Critically Ill Patients with Ventilator-Associated Pneumonia

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Abstract

Background: Pharmacokinetic changes have been found in critically ill patients, including ventilator-associated pneumonia (VAP) when compared with healthy volunteers leading to fluctuation of plasma concentrations.

Objective: To compare the probability of target attainment (PTA) and cumulative fraction of response (CFR) for meropenem between administration by a bolus injection and a 3-hour infusion.

Material and Method: The study was a randomized three-way crossover in nine patients with VAP. Each patient received meropenem in three regimens consecutively: (i) a bolus injection of 1 g every eight hours (q8h) for 24 hours; (ii) a 3-hour infusion of 1 g q8h for 24 hours; and (iii) a 3-hour infusion of 2 g q8h for 24 hours. The pharmacodynamic analysis of meropenem was performed to determine the PTA by using the Monte Carlo simulation and the study used susceptibility patterns obtained from EUCAST and MYSTIC for assessment of CFR.

Results: For an MIC of 4 µg/ml, the PTAs achieving 40% T>MIC following a bolus injection of 1 g q8h, a 3-hour infusion of 1 g q8h, and a 3-hour infusion of 2 g q8h were 87.71%, 98.80%, and 99.90%, respectively. Only the 3-hour infusion regimens were predicted to achieve a CFR ≥90% against E. coli, Klebsiella spp., P. aeruginosa, and Acinetobacter spp.

Conclusion: A 3-hour infusion of 2 g of meropenem regimen was predicted to have the highest PTA rates. Only the prolonged infusion regimens achieved a high CFR against E. coli, Klebsiella spp., P. aeruginosa, and Acinetobacter spp.

Keywords: Meropenem, Population pharmacokinetic, Pharmacokinetics/pharmacodynamics, Pharmacodynamics, Carbapenems, Ventilator-associated pneumonia

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