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

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Abstract

Background: Drug dispositions are altered in critically ill patients, including ventilator-associated pneumonia (VAP) when compared with healthy subjects leading to fluctuations of plasma concentrations.

Objective: To compare the probability of target attainment (PTA) and cumulative fraction of response (CFR) for imipenem between administration by 0.5-hour and 2-hour infusions.

Material and Method: The present study was a randomized three-way crossover in nine patients with VAP. Each patient received imipenem in three regimens consecutively: (i) a 0.5-hour infusion of 0.5 g every six hours for 24 hours; (ii) a 2-hour infusion of 0.5 g every six hours for 24 hours; and (iii) a 2-hour infusion of 1 g every six hours for 24 hours. Monte Carlo simulation was performed to determine the PTA at various regimens and the study used susceptibility patterns obtained from EUCAST and MYSTIC for assessment of CFR.

Results: For an MIC of 2 µg/ml, the PTAs achieving 40% T>MIC following a 0.5-hour infusion of 0.5 g, a 2-hour infusion of 0.5 g, and a 2-hour infusion of 1 g were 90.93%, 98.97%, and 100%, respectively. Only a 2-hour infusion of 1 g achieved 98.75% of the PTA of 40% T>MIC for an MIC of 4 µg/ml. All regimens were predicted to achieve CFR >99% against E. coli and Klebsiella spp.

Conclusion: A 2-hour infusion of 1 g regimen was predicted to have the highest PTA rates. All regimens achieved a high CFR against E. coli and Klebsiella spp.

Keywords: Pharmacokinetics/pharmacodynamics, Pharmacodynamics, Population pharmacokinetics, Imipenem, Carbapenems, Ventilator-associated pneumonia

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