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Abstract (publication only)

Site-specific target attainment rates of meropenem for central nervous system infections and the benefits of extending the infusion time based on cerebrospinal fluid levels

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Objectives: Meropenem (MER) is a broad spectrum carbapenem antibiotic often used in the empirical treatment of nosocomial CNS infections. The objective of this study was to describe the effects of prolonging the infusion time on the Probability of Target Attainment (PTA) of MER at doubling MIC dilutions based on total cerebrospinal fluid (CSF) levels. **Methods:** Population pharmacokinetic (n=10) model for MER in patients with external ventriculostomies was used in this analysis. The standard dose of 2g MER every 8 hours was evaluated for PTA with Monte Carlo simulation (MCS, n=5000) using 0.5 and 4 hours infusion times at the MIC ranges of 0.0625 to 2 mg/L and for the 100% T>MIC target. **Results:** Based on total CSF levels of MER in patients with non-inflamed meninges, the standard dose of 2g MER infused over 0.5 hour is expected to achieve PTAs of > 90% up to an MIC of 0.0625 mg/L. When MER is infused over 4 hours, similar rates of target attainment success can be expected up to an MIC of 0.125 mg/L. Both infusion strategies showed PTAs less than 90% at the MIC of 0.25 mg/L or higher. Extending the infusion time resulted in an increase of the PTAs of 5 %, 7 %, 7 %, 4%, and 1 % at the MICs of 0.125, 0.25, 0.5, 1, and 2 mg/L, respectively, as compared to the PTAs achieved by the 0.5 hour infusion time. **Conclusion:** We conclude that at the target of 100% T>MIC, prolonging the infusion of MER from 0.5 hour to 4 hours would have minimal effects on the PTAs based on simulated CSF levels. Instead, the use of alternative agent for the treatment of organisms with higher MICs should be considered.