Abstract (oral session)

**Pulmonary target attainment rates of short- and extended-infusion meropenem regimens based on simulated epithelial lining fluid levels**

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Objectives: Meropenem (MER) is a broad spectrum carbapenem antibiotic frequently used in the treatment of gram negative pneumonias. The objective of this study was to describe the effects of prolonging the infusion time or lowering the dose and shortening the dosing interval on the Probability of Target Attainment (PTA) of MER at doubling MIC dilutions based on total epithelial lining fluid (ELF) levels. Methods: Population pharmacokinetic (n=39) model for MER in patients with ventilator associated pneumonia was used in this analysis. The standard doses of 0.5g, 1g and 2g MER every 6 and 8 hours were 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 32 mg/L, and for the target of 40% \( fT > MIC \). Results: Based on ELF levels, all MER regimens evaluated showed PTAs of less than 90% at the MIC of greater than 1mg/L. When MER is infused over 4 hours at the 8 hour interval, an increase of up to 20% in target attainment rates can be expected at each MIC dilution, as compared to the short infusion times. The PTAs of short infusion 1g every 6 hours and 2 g every 8 hours regimens are 92/89%, 89/86%, 85/82%, 78/76%, and 69/70%, at the MICs of 0.0625, 0.125, 0.25, 0.5, and 1 mg/L, respectively. At the same MICs, the short infusion 0.5g every 6 hours and 1g every 8 hours regimens are expected to achieve PTAs of 89/86%, 85/82%, 78/76%, 69/70% and 58/60%, respectively. Conclusion: We conclude that at the target of 40% \( fT > MIC \), prolonging the infusion of MER from 0.5 hour to 4 hours would have modest effects on the PTAs based on simulated ELF levels. In addition, our analysis confirms similar target attainment rates at the site of infection for dosing strategies that employ a 50% reduction in the dose to be administered as a short infusion time at more frequent (every 6 hours instead of every 8 hours) interval as compared to the commonly used traditional dosing regimens.