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Abstract (poster session)

Pharmacodynamic profiling of prolonged infusion of ertapenem in critically-ill patients with early-onset ventilator-associated pneumonia through the use of a population pharmacokinetic model and Monte Carlo simulation

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Objectives: Ertapenem (ERT) is a broad spectrum carbapenem antibiotic with nonlinear protein binding characteristics best described by a two class binding site model. The objective of this study was to describe the effects of prolonging the infusion or changing frequency of administration on the Probability of Target Attainment (PTA) of ERT at doubling MIC dilutions in critically ill patients with early onset VAP. Methods: Pharmacokinetic (n=17) data for ERT in critically ill patients with early onset VAP was used in this analysis. Free ERT concentrations were calculated with the two class binding site model using measured albumin concentrations for the specific and remaining protein concentrations for the non-specific binding site. Standard dose of 1 g ERT was evaluated for PTA with Monte Carlo simulation (MCS, n=5000) using 0.5, 1, 2, 3, and 4 hour infusion times at the MIC ranges of 0.0625 to 4 mg/L at bacteriostatic (20%) and bactericidal (40%) $fT>MIC$ targets. Additionally, 0.5 g at 12 h interval infused over 0.5 h was modeled to evaluate for the impact of more frequent administration on attaining the desired pharmacodynamic target. Results: Standard dose of 1g ERT PTAs to achieve bacteriostatic effects were more than 90% up to an MIC of 0.5 mg/L for all regimens, while the PTA decreased below 80% at the MICs of 1 mg/L or more. All infusion strategies showed over 85% PTA up to the MIC of 0.25 mg/L for bactericidal targets, with an increase of nearly 3 % by each hour added to the infusion time. At the MICs of 0.5 ug/ml or higher, the PTA was less than 80% for standard and prolonged infusions, with an increase of nearly 4 % by each hour added to the infusion time. Interestingly, when the total daily dose of 1 g was divided into equal 0.5 g doses and given at 12 h intervals over 0.5 h, greatly improved (14% or more) PTAs were showed over the range of MICs for the bactericidal target. Conclusion: We conclude that prolonging the infusion of ERT would have minimal effects on the PTA. Instead, more frequent administration or giving the total daily dose in divided doses at more frequent intervals should be considered to optimize the pharmacodynamics of the highly protein bound ERT.