1533. Pharmacokinetic (PK) and Pharmacodynamic (PD) Evaluation of Cefepime (CPM) in Obese and Non-Obese Patients
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Background. Appropriate application of antimicrobial PK/PD properties is crucial to optimizing patient outcomes. Although β-lactams are among the most utilized antimicrobials, optimal dosing strategies in obese populations are largely unknown. The objective of this study was to compare PK/PD of CPM in non-obese (NO, weight 80–100 kg) and obese (O, weight >100 kg) patients.

Methods. A prospective comparative PK/PD analysis was conducted in NO and O patients receiving CPM. Blood samples were obtained at 36, 60, 120, 240, 360, and 480 minutes after CPM infusion. CPM concentrations were determined by reversed-phase high-performance liquid chromatography. Non-compartmental PK analyses were performed, followed by Monte Carlo simulations (Oracle Crystal Ball®), 5,000 simulated patients) to estimate probability of target attainment (PATA) against common nosocomial pathogens. The desired PTA target for CPM was 8% above MIC of unbound drug (%F > MIC) ≥ 60%. Chi-squared and Mann-Whitney U tests were used for analysis.

Results. Seventeen patients were enrolled and most (94%) received CPM 2 g q8h. A significant difference in actual body weight and body mass index was observed (P < 0.001). There were no differences in other baseline or PK characteristics between the two groups. Utilizing CPM 2 g q8h, PTA ≥ 90% was not observed for organisms with an MIC of 8 μg/mL, the current CLSI breakpoint for P. aeruginosa and A. baumannii, but a PTA of 88% vs. 81% in NO and O groups, respectively. With a 6 g continuous infusion (CI), however, ≥ 90% PTA was achieved in both groups (PTA = 100% for organisms with an MIC of 8 μg/mL, while a regimen of 2 g q8h (infused over 3 hours [EI]) also provided PTA of ≥ 90% in both groups (PTA ≥ 98% vs. 92% in NO and O groups, respectively), Goal PTA was not obtained in either group for organisms with an MIC of 14 μg/mL with CPM 1 g q8h or 2 g q12h (i.e., CLSI recommended dosing for organisms with MICs of 4 μg/mL).

Conclusion. Optimizing PK/PD parameters through novel dosing strategies are essential in both the NO and O populations for optimal CPM exposure in susceptible pathogens with higher MICs. CPM 6 grams/day by either CI or EI provides more optimal PK/PD characteristics in obese patients for pathogens with MICs at or near the current CLSI-recommended breakpoint.

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