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Abstract (publication only)

Selection of optimal empirical antimicrobial therapy against *Pseudomonas aeruginosa* in the greater New York City area

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Objectives: Selection of an appropriate antimicrobial dosing regimen based on pharmacokinetic and pharmacodynamic principles can lead to improved clinical outcomes. In light of the increasing antimicrobial resistance in North America, pharmacodynamic analysis were undertaken to establish optimal empiric coverage for *Pseudomonas aeruginosa* isolates collected in hospitals from geographically distinct locations in the greater New York City area. **Methods:** We used population pharmacokinetic models of anti – pseudomonal agents to establish Probabilities of Target Attainment in this analysis. 5000 subject Monte Carlo simulations were performed for the mean + SD creatinine clearance values of 60 + 30 ml/min and the MIC range of 0.25 to 128 µg/ml at double dilution intervals. Minimum Inhibitory Concentrations (MIC) for non-duplicate *Pseudomonas aeruginosa* isolates (n = 1104) collected from four hospitals in the greater New York City area were determined by Vitek 2 automated system. Bactericidal cumulative fraction of response (CFR) for standard doses of cefepime, imipenem, meropenem, piperacillin and tazobactam, ciprofloxacin, tobramycin, gentamicin and amikacin were calculated. Alternative approach - or extended infusion and high-dose - regimens were also modeled to improve CFRs of select agents. **Results:** The total of 29 antibiotic dosing strategies were evaluated, and only 2 achieved a CFR > 90%. CFRs for commonly used doses were: cefepime 2 g q12h, 80%; imipenem 0.5g q6h, 68%; meropenem 1 g q8h, 79%; piperacillin and tazobactam 4.5 g q6h, 62%; ciprofloxacin 0.4 g q12h, 45%; tobramycin 5 mg/kg, 74%; gentamicin 5 mg/kg, 44%; and amikacin 15 mg/kg, 71%. Prolonging the infusion time resulted in improved CFRs for all beta – lactam dosing regimens. Overall, the CFR > 90% were achieved by the 4 h infusion of meropenem 2 g q8h, and by the 3 h infusion of cefepime 2 g q8h regimens. **Conclusion:** Based on our analysis the use of conventional dosing regimens of all anti-pseudomonal agents studied appears to provide sub-optimal coverage for the treatment of *Pseudomonas aeruginosa* infections in many parts of the Greater New York City area. Selection of high dose meropenem or cefepime regimens using prolonged infusion strategies may be necessary to achieve desired clinical outcomes.