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Probability of Pharmacodynamic Target Attainment with Standard and Prolonged-Infusion Antibiotic Regimens for Empiric Therapy in Adults with Hospital-Acquired Pneumonia.

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BACKGROUND: The pharmacodynamic characteristics of antibiotics should be considered when choosing empiric dosage regimens for the treatment of pneumonia. OBJECTIVE: This study compared the probabilities of achieving requisite pharmacodynamic exposure (ie, f T > MIC, AUC/MIC) for antibiotics given for the empiric treatment of hospital-acquired pneumonia (HAP) as recommended by the 2005 guidelines of the American Thoracic Society and the Infectious Diseases Society of America.

METHODS: In a 5000-patient Monte Carlo simulation, pharmacodynamic analyses were performed for standard doses of cefepime, ceftazidime, ceftriaxone, ciprofloxacin, ertapenem, imipenem, levofloxacin, meropenem, and piperacillin/tazobactam. Prolonged 3-hour infusion regimens were also evaluated for anti-pseudomonal beta-lactams. MIC data were incorporated from the 2007 Meropenem Yearly Susceptibility Test Information Collection, a national surveillance study. The weighted cumulative fraction of response (wCFR) against common pneumonia pathogens was determined for each regimen. A second scenario was conducted by altering the pathogen prevalence to assess wCFR for late-onset pneumonia (ie, HAP in patients with prolonged mechanical ventilation). Optimal wCFR was defined a priori as >or=90%.

RESULTS: Among the 0.5-hour infusions, cefepime, ceftazidime, and meropenem had the highest wCFRs (>or=90%) against pathogens that cause HAP (cefepime, 1 g q8h, 92.8%; 2 g q8h, 97.2%; 2 g q12h, 94.3%; ceftazidime, 2 g q8h, 93.2%; meropenem, 1 g q8h, 90.9%; 2 g q8h, 93.9%). Imipenem (500 mg q6h, 85.5%; 1 g q8h, 88.1%) and piperacillin/tazobactam (4.5 g q6h, 80.5%) as 0.5-hour infusions were nearly optimal, whereas ceftriaxone, ertapenem, and the fluoroquinolones had the lowest wCFR values. All regimens showed lower wCFRs for late-onset pneumonia than for HAP. Optimal wCFRs were found only with prolonged (3-hour) infusions of 2 g q8h for ceftazidime (94.5%) and meropenem (90.1%), whereas cefepime 2 g q8h achieved optimal wCFR with both a 0.5-hour infusion (93.1%) and a 3-hour infusion (95.3%).

CONCLUSIONS: Results of this model suggest that standard doses of most antipseudomonal beta-lactams (cefepime, ceftazidime, and meropenem) had high probabilities of achieving optimal pharmacodynamic exposure as empiric therapy for HAP, whereas the low probabilities predicted from ceftriaxone, ertapenem, and the fluoroquinolones suggest that these agents would be inappropriate as monotherapy. For late-onset HAP, prolonged infusions of cefepime, ceftazidime, and meropenem offered the highest probabilities of achieving bactericidal exposure.

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