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Pharmacokinetic Assessment of Antimicrobial Treatment of Acute Exacerbations of Chronic Obstructive Pulmonary Disease in Hospitalized Patients Colonized with Pseudomonas Aeruginosa

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Abstract : Chronic obstructive pulmonary disease (COPD), a leading cause of death globally, is characterized by chronic airflow obstruction and by acute exacerbations (AECOPDs) that are often triggered by respiratory infections. Pseudomonas aeruginosa (P. aeruginosa), a potentially serious bacterial cause of AECOPDs, is treated with targeted anti-pseudomonal antibiotics. These select few antimicrobials are often used as first-line therapy in patients who are clinically unwell and/or in those suspected of P. aeruginosa-related infection prior to confirmation, potentially contributing to antimicrobial resistance. The present study evaluates prescribing practices in patients with a confirmed sputum history of P. aeruginosa admitted for AECOPD at the McGill University Health Centre (MUHC) and treated with anti-pseudomonal antibiotics. Serum antibiotic concentrations were measured from same-day peak, trough, and mid-dose blood sampling intervals after reaching steady-state (on or after day 3), and were quantified using ultra-high-performance liquid chromatography (UHPLC). Demographic, clinical, and treatment outcomes were extracted from patient medical charts. Treatment failure was defined by respiratory-related death or mechanical ventilation after ≥3 days of antibiotics; antibiotic therapy extended beyond 2 weeks or new antibiotic regimen started; or urgent care readmission within 30 days for AECOPD. To date, 9 of 30 planned participants have completed testing: seven received ciprofloxacin, one received meropenem, and one received piperacillin-tazobactam. Due to serum sample batching requirements, at the time of writing the serum ciprofloxacin concentration results for the first 2/8 participants are presented. The first participant had serum levels of 5.45mg/L (T0), 4.74mg/L (T50), and 4.49mg/L (T100), while the second had serum levels of 5mg/L (T0), 2.6mg/L (T50), and 2.51mg/L (T100). Pharmacokinetic parameters Cmax (5.18±0.43mg/L), T1/2 (23.56±18.94hours), and AUC (181.9±155.95mg*h/l) were higher than reported monograph values and met target AUC-to-MIC ratio of >125. The patients treated with meropenem and with piperacillin-tazobactam experienced treatment failure. Preliminary results suggest that standard ciprofloxacin dosing in patients experiencing an AECOPD and colonized with P. aeruginosa appear to achieve effective serum concentrations. Final cohort results will inform the pharmacokinetic appropriateness and clinical sufficiency of current AECOPD antimicrobial strategies in P. aeruginosa-colonized patients. This study will guide clinicians in determining the appropriate dosing for AECOPD treatment to achieve therapeutic levels, optimizing outcomes and minimizing adverse effects. It could also highlight the value of routine antibiotic level monitoring in patients with treatment failure to ensure optimal serum concentrations.

Keywords : acute exacerbation, antimicrobial resistance, chronic obstructive pulmonary disease, pharmacokinetics/pharmacodynamics, Pseudomonas aeruginosa
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