The population pharmacokinetics and dose optimization of polymyxin B in critically ill patients with or without extracorporeal membrane oxygenation

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Abstract

Aims: The objectives of this study were to determine the population pharmacokinetics (PK) model of polymyxin B in critically ill patients with or without extracorporeal membrane oxygenation (ECMO) support that investigated the influence of ECMO on PK variability and to identify an optimal dosing strategy. Methods: Forty-four critically ill patients were enrolled, including eight patients with ECMO support. Eight serial serum samples were collected from each patient at steady state. The population PK was determined using NONMEM and Monte Carlo simulation was performed to evaluate the exposures of different dosing regimens. Results: The PK analyses included 342 steady-state concentrations and a two-compartment model was optimal for polymyxin B PK data modelling. In the final model, creatinine clearance (CLCR) was the significant covariate on CL (typical value 1.27 L/h; between-subject variability 15.1%) and ECMO did not show a significant impact on the polymyxin B PK. Additionally, we found that the PK parameter estimates of patients with and without ECMO support were mostly similar. Based on Monte Carlo simulations, the dose escalation of polymyxin B in patients with increased CLCR improved the probability of achieving required exposure. For patients with CLCR[?]120 mL/min, a dosage regimen of 100mg every 12h may represent the optimal regimen at an MIC of 1 mg/L. Conclusion: The impact of ECMO on the polymyxin B PK is likely to be minimal. Our study showed a potential relationship between CLCR and polymyxin B CL, and the dose of polymyxin B should be adjusted in patients with increased CLCR.

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