ICU
MANAGEMENT & PRACTICE

Antimicrobial Dosing in Critically Ill Patients on ECMO

Extracorporeal membrane oxygenation (ECMO) is used to support critically ill patients, but its impact on antimicrobial pharmacokinetics (PK) and pharmacodynamics (PD) presents significant challenges. ECMO circuits can affect drug delivery, leading to the sequestration of drugs, changes in the volume of distribution (Vd), decreased clearance, and longer elimination half-life. The components of the circuit, particularly in veno-arterial (VA-ECMO) and veno-venous (VV-ECMO) configurations, can adsorb drugs, especially lipophilic ones, complicating dosing. Additionally, patient factors like kidney and liver dysfunction, fluid shifts, low protein states, and immune activation affect drug metabolism and efficacy.

Given the dynamic nature of the ECMO circuit and patient physiology, therapeutic drug monitoring (TDM) may help guide dosing. However, due to limited clinical evidence and the absence of specific guidelines, dosing strategies remain individualised, relying on case series and observational data.

Optimising antimicrobial dosing for patients on ECMO remains challenging due to the complex interplay between the ECMO circuit and critical illness. ECMO circuits can sequester drugs, especially lipophilic and highly protein-bound molecules, altering PK such as volume of distribution and drug clearance. Studies have shown mixed findings on drug exposure in ECMO patients, with some suggesting reduced exposure compared to non-ECMO patients. The presence of renal dysfunction and renal replacement therapies, like continuous renal replacement therapy (CRRT), further complicates dosing. While in vitro and ex vivo studies provide some insight into ECMO's impact on drug distribution, clinical data, particularly randomised trials, is limited.

Individualised dosing, guided by TDM when available, is crucial. However, limitations in TDM availability and a lack of consensus on optimal pharmacodynamic targets for different drugs hinder effective dosing strategies. Beta-lactams, for instance, have varying recommendations for time above MIC, with extended infusions recommended for optimal pharmacodynamics. The use of oral formulations, like azoles, also requires caution due to potential erratic absorption in critically ill patients.

Future research should focus on clinical studies comparing drug levels in ECMO versus non-ECMO patients to determine whether PK changes are due to ECMO or critical illness. Additionally, investigating the impact of ECMO and CRRT on antimicrobial dosing and expanding access to drug assays could improve patient outcomes. Ultimately, a better understanding of these dynamics and more refined dosing strategies are essential for optimising antimicrobial therapy in ECMO patients.

Effective antimicrobial use in ECMO patients requires careful consideration of the complex interactions between the patient, the ECMO circuit, and antimicrobial properties. While recent clinical data has improved understanding and provided dosing recommendations, there is still a need for robust prospective studies focused on patient outcomes beyond pharmacokinetic and pharmacodynamic parameters. TDM should be used to optimise outcomes in these critically ill patients.

Source: Critical Care
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