Medication Complications in Extracorporeal Membrane Oxygenation

Ami G. Shah, PharmD[a,*], Michelle Peahota, PharmD[a], Brandi N. Thoma, PharmD[a], Walter K. Kraft, MD[b]

KEYWORDS

• Pharmacology • Pharmacokinetics • Therapeutic drug monitoring

KEY POINTS

- Extracorporeal membrane oxygenation (ECMO) is associated with physiologic and biomechanical changes that can impact drug disposition.
- There are limited data describing changes in drug pharmacokinetic parameters for patients treated with ECMO.
- Changes in pharmacokinetics are often drug specific.
- Extrapolation of ECMO data from neonatal literature is limited due to significant differences in body composition and elimination pathways.
- Therapeutic drug monitoring, when possible, should be considered to individualize therapeutics in patients receiving ECMO therapy.

INTRODUCTION

Critically ill patients have alterations in the pharmacokinetic (PK) parameters that describe drug absorption, distribution, metabolism, and excretion. These disturbances arise from the acute response of critical illness, including systemic inflammatory responses, organ dysfunction, altered tissue permeability, pH disturbances, changes in intravascular or extravascular space, fluid shifts, or decreased protein concentration. These PK alterations are relevant, as they may precipitate unexpected medication toxicities or impair efficacy. To optimize patient outcomes, PK changes should be as best possible identified when developing medication regimens for critically ill patients.[1–4]

[a] Department of Pharmacy, Thomas Jefferson University Hospital, 111 South 11th Street, Suite 2260, Philadelphia, PA 19107, USA; [b] Department of Pharmacology and Experimental Therapeutics, Thomas Jefferson University, 111 South 11th Street, Philadelphia, PA 19107, USA
* Corresponding author. 111 South 11th Street, Suite 2260, Philadelphia, PA 19107.
E-mail address: amishah1221@gmail.com

Crit Care Clin 33 (2017) 897–920
http://dx.doi.org/10.1016/j.ccc.2017.06.010
0749-0704/17/Published by Elsevier Inc.
criticalcare.theclinics.com

EXTRACORPOREAL MEMBRANE OXYGENATION AND PHARMACOKINETICS

Mechanical ventilation, renal replacement therapy (RRT), and extracorporeal membrane oxygenation (ECMO)[5–8] can impact drug disposition and complicate the management of critically ill patients. During ECMO therapy, a large volume of blood is extracted from the venous system and is circulated outside the body into an oxygenator (**Fig. 1**). A typical ECMO circuit consists of polyvinyl chloride (PVC) tubing, a hollow fiber (polymethylpentene) oxygenator, and a heat exchanger.[9] PK changes during critical illness are often more pronounced in the presence of ECMO. Several aspects, such as the sequestration of medications in the ECMO circuit, increased volume of distribution, and alterations in organ perfusion may alter PK parameters in patients receiving ECMO[5,7,9–12] (**Table 1**).

The effect of ECMO therapy on PK varies and is not fully elucidated for most drugs. Investigating the impact of the ECMO circuit and its resulting physiologic changes on PK and pharmacodynamics (PD) is difficult given the limited patient population on which to generate data. The ECMO population is numbered because ECMO is often a salvage therapy offered by limited number of centers. The available data investigating ECMO therapy is not only limited in size, but is typically also observational because it is difficult to conduct randomized trials with a control group. Although there is some literature available in neonatal populations, it is difficult to generalize these data to adult populations. ECMO technology is frequently evolving, and circuits' manufacturers and materials vary, further limiting data generalizability. Demands of clinical care and blood volume during critical illness make sparse PK sampling with population modeling methods the only feasible method to investigate drug PK parameters in these patients. Although this approach can identify some covariates associated with differential drug disposition, it is not possible to generate precise PK parameters under a variety of clinical scenarios.

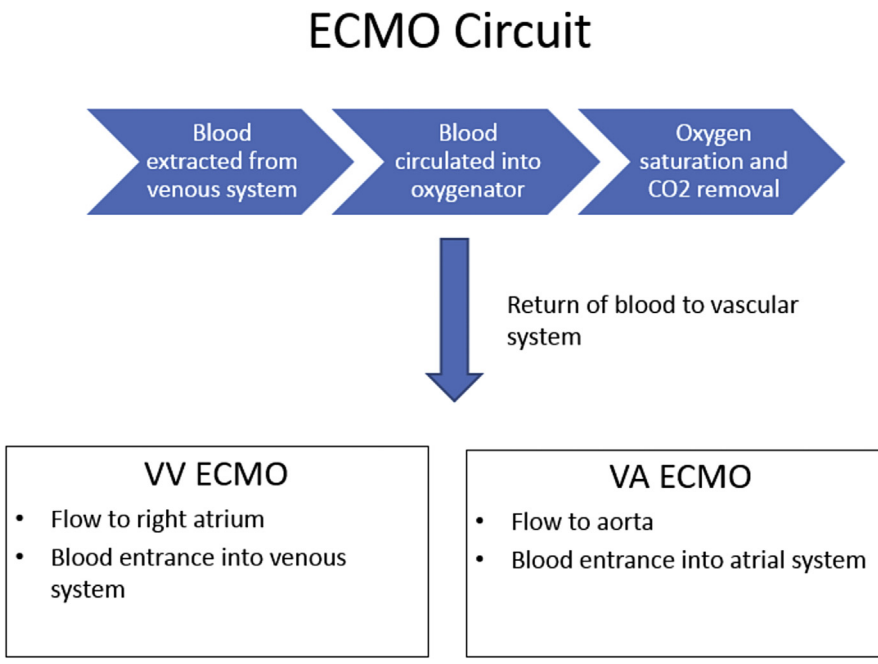

Fig. 1. ECMO configuration.