

Management of Anticoagulation and Hemostasis for Pediatric Extracorporeal Membrane Oxygenation



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KEYWORDS

- Anticoagulation • Congenital heart defect • Extracorporeal membrane oxygenation
- Heparin • Platelet function • Thromboelastography

KEY POINTS

- Extracorporeal membrane oxygenation (ECMO) circuit causes activation of multiple systems, including thrombin generation, inflammation, platelet activation and endothelial dysfunction. Prolonged hemostatic activation can lead to consumption of coagulation factors and reduced platelet aggregation. Commonly used medications may also inhibit platelets.
- A delicate balance between the use of antihemostatic agents to reduce thrombotic events in the circuit and patient and the preservation of hemostatic potential to prevent severe bleeding in the patient is required.
- Unfractionated heparin is the most common anticoagulation agent used.
- Activated clot time is the most common monitoring test, but may not be an accurate measure of anticoagulation for children on ECMO.
- A comprehensive evaluation of relational hemostasis is required to optimize antihemostatic therapy and blood product administration to improve outcomes for children requiring ECMO.

INTRODUCTION

The use of anticoagulation/antihemostatic agents in children, for either prevention or treatment of thrombotic complications, is increasing, although their use is still relatively rare when compared with adults.¹ There are many challenges to the use of anticoagulants in children, as listed in **Box 1**.² These challenges become apparent in the

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Box 1**Challenges to use of anticoagulation agents in children**

- Developmental hemostasis
- Limited pharmacokinetic and pharmacodynamics data for anticoagulation agents
- Different epidemiology of thromboembolism and risks of anticoagulation therapy
- Fewer pediatric formulations of common anticoagulation agents
- Restricted diagnostic evaluation due to need of sedation for diagnostic studies
- Irregular anticoagulation therapy monitoring due to difficult vascular access
- Inadequate validation of current diagnostic and treatment algorithms
- Lack of widespread experience and limited expertise
- Required collaborative approach with a multidisciplinary team
- Compliance concerns with high reliance on caregivers

Adapted from Monagle P, Newall F, Campbell J. Anticoagulation in neonates and children: pitfalls and dilemmas. Blood Rev 2010;24:151–62.

management of extracorporeal membrane oxygenation (ECMO), one of the most complex clinical scenarios in children. In this article, anticoagulation management, hemostatic adjuncts, and blood products transfusion in children requiring ECMO are the focal point. Antihemostatic agents to include all therapeutics that reduce thrombin formation or inhibit platelet aggregation are defined. Anticoagulants are medications that specifically reduce thrombin formation. Medications that inhibit platelets are antiplatelet agents.

Approximately 1500 to 2000 children (neonatal and pediatric) are placed on ECMO every year according to data collected at the Extracorporeal Life Support Organization (ELSO) centers.³ Despite wider use and growing expertise, the survival rate has remained static since 2006 to 2012 at 66% to 70% (neonatal respiratory ECMO), 53% to 61% (pediatric respiratory ECMO), 41% to 46% (<30 days, cardiac ECMO), 48% to 62% (30 days to <1 year of age, cardiac ECMO), and 57% to 69% (>1 year to <16 years, cardiac ECMO).³ Deaths are frequently related to severe hemorrhagic and thromboembolic complications and range between 30% and 40%.^{3,4} Hemorrhagic and thromboembolic complications occur in this population because of alterations in hemostasis. The causes of these complications are in part due to the nonendothelial surface of extracorporeal circuit that activates both coagulation and inflammation and the use of anticoagulants to prevent thrombotic events. Also important is the underlying illness that may contribute to either a hypercoagulable or a hypocoagulable state due to immune and endothelial dysfunction as well as consumption of hemostatic factors.^{5–8} Last, although uncommon, heparin-induced thrombocytopenia (HIT) or severe allergy to heparin can increase the risk of thrombotic events. Here, **ECMO-induced coagulopathy (EIC)** is defined as a pathophysiologic state of hemostasis for children on ECMO that can result in varying manifestations that range from a hypercoagulable to a hypocoagulable manifestation.

ECMO-INDUCED COAGULOPATHY***The ECMO Circuit***

A typical ECMO circuit consists of cannulas, polyvinyl tubing with or without heparin coating, a roller or centrifugal pump, and a silicone membrane oxygenator. These components of the ECMO circuit are artificial and lead to activation of multiple

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