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Activated factor VII in excessive bleeding during ECMO run

Mohamed Salim Kabbani

Address for Correspondence:

Mohamed Salim Kabbani

King Abdulaziz Medical City, Ministry of National Guard
Health Affairs, Riyadh, Kingdom of Saudi Arabia
Email: kabbanim@ngha.med.sa

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Bleeding is a common complication in patients undergoing extracorporeal membrane oxygenation (ECMO) management.¹ It requires immediate management to achieve hemostasis, replace blood, and compensate volume loss. Refractory hemorrhage can be lethal and can lead to massive transfusions with all their known complications. Refractory bleeding and massive transfusions in ECMO patients are associated with high mortality even after decannulation. Management of bleeding in ECMO patients requires thorough evaluation with multi-disciplinary approach that addresses surgical causes of bleeding, correction of coagulopathy, and the balanced use of anticoagulation factors to prevent circuit clotting, avoid excessive bleeding, and replace different blood products as needed. Adjusting anticoagulants and the use of fresh frozen plasma (FFP) with correction of thrombocytopenia can control common bleeding events. Management of refractory hemorrhage may require exploration for surgical bleeding and administration of platelets, packed red blood cells (pRBCs), cryoprecipitate, anti-fibrinolytics, and selective coagulation factors. In some cases, however, the bleeding is diffuse and cannot be controlled surgically. The use of activated factor VII (rFVIIa) at different described doses for patients on ECMO with refractory bleeding has been tried.^{2,3} There are many reports indicating successful use with live-saving outcome.³ Unfortunately, there are also some conflicting results with the use of rFVIIa regarding failure to control bleeding or the risk of intravascular thrombosis or circuit clotting. Furthermore, there are reports about catastrophic outcome or fatal thrombosis when rFVIIa was used in ECMO cases.⁴ Therefore, the medication is currently recommended as off-label prescription. It should be used with extreme caution with clear patient/family awareness about potential complications. The recommended doses are not established and range

from 24 to 174 $\mu\text{g}/\text{kg}$.² Some centers will administer lower doses of rFVIIa (25–50 $\mu\text{g}/\text{kg}$) and, if more than one dose is required, it is not administered more often than every 2–4 hours. Some centers recommended the use of prothrombin complex concentrate (PCC), which contains unactivated factors II, VII, IX, and X, and therefore, potentially have less risk of thrombosis. To correct a prolonged prothrombin time (PT) and activated partial thromboplastin time (APTT) during ECMO run in patients with active bleeding, PCC 25–50 international units/kg can be administered.⁵ In summary, bleeding during ECMO remains a serious problem, which increases mortality risk. rFVIIa has been used successfully but with awareness of the risk of thrombosis. Clinical trials comparing alternative anticoagulation regimens are needed to determine efficacy, dosing, and safety of rFVIIa in patients suffering from refractory bleeding while on ECMO.

Unfortunately, until such evidence is available, the ECMO care team is left with few evidence-based interventions to prevent and treat serious bleeding. This presentation will discuss the use of rFVIIa in ECMO patients with focus on its benefits in controlling refractory bleeding, and the risk of thrombosis and circuit clotting associated with it. The discussion will include suggestions for recommended doses, how to monitor for thrombosis, and the potential risk/benefit of using rFVIIa in the management of life-threatening bleeding in patients on ECMO.

Keywords: ECMO, activated factor rFVIIa, bleeding, thrombosis

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