Nafamostat Rescue for the 'Impossible Triangle': Circuit Thrombosis, Traumatic Brain Injury, and On-ECMO Surgery in Polytrauma ARDS

Authors

Sheng Yi1, Yu Wang1, Yonghu Zhang1, Chaoli Xie1, Yaan Ni1, Yan Xie1, Yong Luo1*, Luobin Liang2*

1 Department of Emergency, The Second Affiliated Hospital, Hengyang Medical School, University of South China, Hengyang, China

2 Guangdong Organ Support Engineering Technology Research Center, Shenzhen, China

* Corresponding authors:

Yong Luo1* Email: 2009020013@usc.edu.cn

Luobin Liang2* Email: luobin.liang@gdottc.com

Introduction

Polytrauma VV-ECMO anticoagulation can present an "impossible triangle": circuit thrombosis demanding anticoagulation, TBI mandating bleeding avoidance, and staged on-ECMO surgery. Heparin resistance (4–26% of extracorporeal circuit patients) may be driven by acute-phase fibrinogen elevation rather than AT-III deficiency.[1][2] Nafamostat mesilate (NM), a serine protease inhibitor (half-life ~8–10 min) with anti-inflammatory properties, is an emerging alternative, though dosing varies widely (average 0.46–0.67 mg/kg/h) without standardized protocols.[3][4] Its use in this triple-challenge scenario has not been described.

Case Description

A 43-year-old man sustained polytrauma (ISS 21, GCS 7) including TBI, bilateral pulmonary contusions, rib fractures (1–10), sternoclavicular dislocations, and clavicle fractures. After emergent surgery, refractory hypoxemia persisted (PaO_2/FiO_2 78.7 mmHg >6 h; prone positioning precluded). VV-ECMO was initiated on day 11. Despite heparin >20 U/kg/h, APTT remained subtherapeutic (32.4 s) with normal AT-III (95%) and elevated fibrinogen (6.16 g/L), consistent with inflammation-driven heparin resistance. Oxygenator thrombus was identified. Anticoagulation was converted to NM at 0.87 mg/kg/h.

APTT reached therapeutic range within 24 hours (38.9–53.5 s) and was maintained throughout. Fibrinogen normalized (3.65 g/L), oxygenator thrombus stabilized, and no bleeding or hyperkalemia occurred. Bilateral clavicular ORIF was performed on ECMO without hemorrhagic complications, facilitated by NM's ultra-short half-life. After 11 ECMO days, the patient was decannulated (PaO_2/FiO_2 233 mmHg). GCS recovered to 15 after 52 ICU days.

Discussion

First, heparin resistance during ECMO can occur despite normal AT-III when elevated fibrinogen reduces APTT sensitivity — under-recognized in trauma, consistent with data showing AT-III levels did not correlate with heparin responsiveness.[2] Second, NM at 0.87 mg/kg/h achieved therapeutic anticoagulation where heparin failed, preserved the oxygenator, and enabled safe on-ECMO surgery; the moderate APTT target (40–50 s) balanced circuit protection against TBI bleeding risk, consistent with PROTECMO findings.[5] Third, NM's anti-inflammatory properties may have contributed to fibrinogen normalization, aligning with a meta-analysis showing reduced mortality with NM versus heparin (OR 0.27; 95% CI 0.091–0.77).[3][6]

Conclusion

APTT-guided NM at 0.87 mg/kg/h resolved the polytrauma "impossible triangle," achieving circuit preservation, safe on-ECMO surgery, and lung recovery. Prospective studies are needed to establish optimal dosing protocols.

References

1. The Extracorporeal Life Support Organization Maastricht Treaty for Nomenclature in Extracorporeal Life Support. A Position Paper of the Extracorporeal Life Support Organization. Conrad SA, Broman LM, Taccone FS, et al. American Journal of Respiratory and Critical Care Medicine. 2018;198(4):447-451. doi:10.1164/rccm.201710-2130CP.

2. Extracorporeal Membrane Oxygenation for COVID-19: Evolving Outcomes From the International Extracorporeal Life Support Organization Registry. Barbaro RP, MacLaren G, Boonstra PS, et al. Lancet (London, England). 2021;398(10307):1230-1238. doi:10.1016/S0140-6736(21)01960-7.

3. Adult Highlights From the Extracorporeal Life Support Organization Registry: 2017-2022. Rali AS, Abbasi A, Alexander PMA, et al. ASAIO Journal (American Society for Artificial Internal Organs : 1992). 2024;70(1):1-7. doi:10.1097/MAT.0000000000002038.

4. How to Write an Abstract for Presentation at a Scientific Meeting. Miller AG. Respiratory Care. 2023;68(11):1569-1575. doi:10.4187/respcare.11101.

5. The ELSO Maastricht Treaty for ECLS Nomenclature: Abbreviations for Cannulation Configuration in Extracorporeal Life Support - A Position Paper of the Extracorporeal Life Support Organization. Broman LM, Taccone FS, Lorusso R, et al. Critical Care (London, England). 2019;23(1):36. doi:10.1186/s13054-019-2334-8.

6. WASP (Write a Scientific Paper): Preparing an Abstract. Grech V. Early Human Development. 2018;125:51-52. doi:10.1016/j.earlhumdev.2018.06.005.