

**Heparin/tranexamic-acid****S****Various toxicities: 4 case reports**

In a case report, 4 men aged 39-59 years were described, who developed pulmonary haemorrhage, oropharyngeal bleeding, bleeding, recurrent bleeding or haemoptysis during treatment with heparin. Additionally, two men developed lack of efficacy during treatment with tranexamic acid for pulmonary bleeding or oropharyngeal bleeding [*not all routes stated; dosages and duration of treatments to reaction onsets not stated*].

The 39-year-old man, who had Coronavirus disease 2019 (COVID-19)-induced acute respiratory distress syndrome was hospitalised for veno-venous extracorporeal membrane oxygenation therapy. He started receiving systemic anticoagulation therapy with heparin infusion. On day 14 of hospitalisation, he developed pulmonary haemorrhage associated with heparin. He started receiving tranexamic acid, platelet transfusions and plasma [fresh frozen plasma]. On day 16 of hospitalisation, severe pulmonary haemorrhage was noted. He underwent flexible bronchoscopy with tranexamic acid, epinephrine and sodium chloride [cold saline]; however, haemorrhage continued despite treatment. Further, he received multiple cryoprobe bronchoscopy sessions and were tolerated well. Heparin was temporarily held for 4 hours following the first two bronchoscopies and then restarted. However, he developed third major bleeding episode and required bronchoscopy. The heparin was then discontinued permanently and he received transfusions for prevention of haemorrhage. He remained haemodynamically stable through each bleeding episode. However, on day 20 of hospitalisation, he died due to superimposed bacterial infection and multi-organ failure.

The 59-year-old man who, had COVID-19-induced acute respiratory distress syndrome and staphylococcus pneumonia was hospitalised. He was initiated on veno-venous extracorporeal membrane oxygenation therapy. He started receiving systemic anticoagulation therapy with heparin infusion and developed pulmonary haemorrhage associated with heparin on hospitalisation day 12. He underwent flexible bronchoscopy with sodium chloride [saline ]; however worsening of bleeding was noted. He started receiving treatment with nebulised tranexamic acid for pulmonary haemorrhage; however the treatment failed. An emergency bronchoscopy was performed and demonstrated complete thrombosis of respiratory tree. A cryoprobe bronchoscopy was performed and bronchial blocker was placed in the left lower lobe due to bleeding. Heparin cessation was performed but a large mobile clot was noted on the ECMO drainage cannula through ultrasonography and heparin drip was restarted. Further, he developed massive haemoptysis associated with heparin leading to oxygenation inability and received ECMO blood flow and support. An emergency cryoprobe bronchoscopy revealed a large fibrinous clot that was removed. His heparin treatment was discontinued for remainder of ECMO course. He was ventilated, ECMO was continued and showed good compliance. On day 36 of hospitalisation, he was decannulated and discharged to rehab. Further, he was discharged home and showed full functionality.

A 53-year-old man had COVID-19-induced acute respiratory distress syndrome and refractory hypoxaemia. He was hospitalised in the ICU for veno-venous extracorporeal membrane oxygenation therapy. He started receiving anticoagulation therapy with systemic heparin infusion. On day 13 of hospitalisation, he developed oropharyngeal bleeding associated with heparin. He started receiving treatment with topical and systemic tranexamic acid for oropharyngeal bleeding; however, no response was noted. On day 22 of hospitalisation, he developed pulmonary haemorrhage associated with heparin. He received continuous renal replacement therapy, desmopressin, cryoprecipitate transfusion to maintain fibrinogen levels. On day 33 of hospitalisation, he developed two episodes of bleeding associated with heparin and were controlled with cryoprobe bronchoscopy session. His heparin therapy was discontinued and two additional session of cryoprobe bronchoscopy were performed to remove the coagulated blood. Assisted pressure release ventilation (APRV) was used and time controlled adaptive ventilation protocol (TCAV) was implemented. Further, he was successfully treated and decannulated. Eventually, discharged to rehab.

The 59-year-old man had hairy cell leukaemia and severe acute respiratory distress syndrome due to legionella pneumonia. He was hospitalised for veno-venous extracorporeal membrane oxygenation therapy for refractory hypoxaemia, worsening acidosis and inability of ventilate. He started receiving anticoagulation therapy with systemic heparin infusion and developed massive haemoptysis associated with heparin on day 6 of hospitalisation. His treatment with heparin was discontinued and received platelet transfusion and continuous renal replacement therapy. A cryotherapy was successful in stopping the bleeding. He developed recurrent bleeding associated with heparin, ongoing thrombocytopenia, underlying leukaemia and required multiple cryoprobe bronchoscopy sessions. He developed septic shock and acute kidney injury during hospitalisation and received renal replacement therapy. Multiple ventilator strategies were implement and ultimately he was decannulated and discharged from the hospital. He showed remission of malignancy and full renal recovery.