“Transfusion and infusion strategies in murine hemorrhagic shock”

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Extensive transfusion support often fails to prevent death from bleeding after trauma. Early intervention may improve outcomes, but which blood products, factor concentrates, or other drugs are the best treatment is unclear. Patients with acute traumatic coagulopathy (ATC), arising from trauma and hemorrhagic shock, have the worst prognosis. We adapted a mouse model of ATC to take place under full anesthetic cover. After trauma, anesthetized mice were subjected to pressure-defined hemorrhage, held in shock for one hour, and were then resuscitated with fluids equal in volume to the amount of shed blood. We used liver laceration as a test to determine if hemostatic control had been restored by different resuscitation fluids, and measured blood loss was quantified. Saline-treated mice lost 2- to 3-fold more blood than sham-treated animals and were coagulopathic by prothrombin time (PT) elevation post- versus pre-procedure. Murine fresh-frozen plasma (mFFP), anti-activated protein C aptamer HS02-52G, or prothrombin complex concentrates (PCC) eliminated both the bleeding tendency and PT-defined coagulopathy; fibrinogen, plasminogen activator inhibitor-1, or tranexamic acid ameliorated bleeding or coagulopathy, but not both. HS02-52G and mFFP also eliminated the changes in plasma aPC and tissue plasminogen activator levels observed in saline-treated mice. Procoagulant interventions, especially those inhibiting aPC, could be beneficial in human ATC.