Title

Fibrin Degradation Products: Potential Therapeutic Targets in Trauma Induced Coagulopathy

Authors

Nate Dow, MD, MS; Chang Yeop Han, PhD; Nathan White, MD, MS, FACEP, DRTM

Background and Objectives

Trauma is a leading cause of death worldwide and the leading cause of death in the United States for young people and most early preventable deaths in this setting are due to uncontrolled hemorrhage. Trauma-induced coagulopathy (TIC) complicates post-injury care and is associated with an increased risk of morbidity and mortality, but the underlying mechanisms that drive TIC are poorly understood. Fibrin degradation products (FDPs) are often elevated in critical illness including massive trauma and are recognized as a risk factor for coagulopathy. This work aims to investigate the role of individual FDPs in anticoagulation, clot formation and fibrinolysis.

Methods

Purified FDPs, including fragment X, Y, D, E and D-dimer were titrated into human plasma (control, 0.16 µg/mL and 10 µg/mL concentrations) and clot formation, characteristics and lys is were characterized using Rotational Thromboelastometry (ROTEM). Parameters measured included clotting time (CT), α-angle, maximum clot firmness (MCF), lysis index at 45 min (LI-45) and maximum lysis (ML). Thrombin generation and plasmin generation with purified FDPs added to human plasma were also measured in separate assays.

Results

Samples enriched with FDP fragments D, X and D-Dimer showed an LI-45 and ROTEM tracing suggestive of enhanced fibrinolysis. Only FDP fragment X was associated with decreased MCF during clot formation. Time to peak plasmin activity was shortened and peak plasmin activity was increased when D-dimer and D fragments were present. Thrombin generation was unchanged following FDP treatment.

Conclusion

FDPs, p articularly fragments D and D-Dimer, enhance fibrinolysis by increasing plasmin activity. Fragment X affects clot formation primarily by disrupting fibrin polymerization during clot formation. Traditionally, tranexamic acid (TXA) has been a key therapeutic in TIC by inhibiting the conversion of plasminogen to plasmin. This work suggests that pro-thrombolytic FDPs may also be a therapeutic target. Further work, both in samples from trauma patients and in whole blood, is needed to further characterize the impact of individual FDPs on clotting parameters and plasmin activity after injury.