Session XIVB: Papers 54-63
Paper 56: 2:40 PM - 3:00 PM

P-SELECTIN ANTIBODY TREATMENT AFTER BLUNT THORACIC TRAUMA PREVENTS PULMONARY ARTERIAL THROMBOSIS WITHOUT SYSTEMIC COAGULATION CONSEQUENCES

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Invited Discussant: Amy Makley, MD

Introduction: Thromboembolic events within the pulmonary vasculature remain a major cause of potentially preventable morbidity and mortality after traumatic injury. Currently, the management of this complication is suboptimal as both its prevention and treatment require pharmacologic anticoagulation. Assessment of the risks and benefits of systemic anticoagulation in trauma patients is frequently complicated by the risk of recurrent bleeding from coexisting injuries such as solid organ lacerations or traumatic brain injuries. Previously, in a murine model of blunt thoracic trauma we provided evidence of de novo pulmonary thrombosis associated with an increase in the expression of the cell adhesion molecule, P-selectin. Additionally, we exhibited that systemic administration of a P-Selectin blocking antibody prevented early pulmonary thrombus formation. In this study we perform viscoelastic testing to investigate if P-selectin inhibition has a detrimental impact on normal hemostasis. We hypothesize that P-Selectin blocking antibody will not adversely affect systemic anticoagulation.

Methods: A murine model of medium velocity lateral thoracic trauma was used. Wild type mice were divided into sham control and experimental injury groups. Thirty minutes after trauma, mice were treated with one of the following: P-Selectin blocking antibody, isotype control antibody, low dose heparin, high dose heparin or normal saline. At 90 minutes, whole blood was collected via the inferior vena cava for characterization of coagulation by Viscoelastic Coagulation Monitor (VCM VetTM; Entegrion, Durham, NC), a variation of standard thromboelastography. Mean clotting time, clot formation time, clot kinetics (alpha-angle) and maximum clot firmness were compared between each treatment group.

Results: In both sham and trauma groups, compared to vehicle (normal saline) alone, no statistical difference was noted in any coagulation parameters after injection with P-selectin antibody, isotype control, or low dose heparin. In contrast, mice that received high dose heparin had significantly longer clotting times ($p<0.001$), clot formation times ($p<0.001$), lower alpha angles ($P<0.001$) and lower clot firmness ($P<0.001$). Notably, in mice subject to trauma we found that P-selectin antibody treated group had a significantly higher alpha-angle ($P<0.05$) compared to either the low dose or high dose heparin treatment groups ($p<0.05$; T-test).

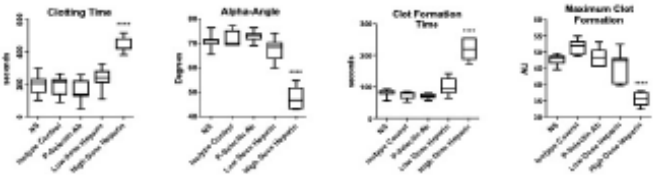

Figure 1 : Viscoelastic testing results 90 minutes after trauma (n=7-8 in each group).

Conclusion: Administration of P-Selectin blocking antibody did not adversely affect systemic anticoagulation as measured by viscoelastic testing. Additionally, when compared to both prophylactic and treatment doses of heparin, P-selectin inhibition had less anticoagulant effect on clotting kinetics as demonstrated by a higher alpha-angle. This data further endorses P-selectin inhibition as a potentially effective and targeted therapy that may circumvent the complications associated with pharmacologic anticoagulation.