Sepsis: basic mechanisms
A721 - Differential modulation of plasminogen activator mediated thrombolysis by recombinant thrombomodulin and activated protein c

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Introduction:
Urokinase (UK) and tissue plasminogen activator (tPA) mediate thrombolytic actions by activating endogenous plasminogen. Thrombomodulin (TM) complexes with thrombin to activate Protein C and thrombin activatable fibrinolysis inhibitor (TAFI). Activated Protein C (APC) modulates coagulation by digesting factors V and VIII and activates fibrinolysis by decreasing PAI-1 functionality.

Methods:
The purpose of this study is to compare the effects of rTM and APC on urokinase and tPA mediated thrombolysis utilizing thromboelastography.

Results:
Native whole blood was activated using a diluted intrinsic activator (APTT reagent, Triniclot). The modulation of thrombolysis by tPA and UK (Abbott, Chicago, USA) was studied by supplementing these agents to whole blood and monitoring TEG profiles. APC (Haematologic Technologies, VT, USA) and rTM (Asahi Kasai Pharma, Tokyo, Japan) were supplemented to the activated blood at 0.02 – 3.0 ug/ml. The modulation of tPA and UK induced thrombolysis by APC and rTM was studied in terms of thromboelastograph patterns. The effect of both APC and rTM on plasma based systems supplemented with tPA was also investigated.

Conclusion:
In comparison to rTM, APC produced a stronger anticoagulant effect in terms of r time, k time, angle and MA. 3.0ug/ml rTM and APC did not produce any direct fibrinolytic effects. APC also produced strong augmentation of the lytic of effects of tPA and urokinase. rTM at lower concentrations produced stabilization of clot resisting fibrinolysis.