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Introduction:
Thromboelastographic (TEG) analysis represents a global approach to monitor the clotability of the native whole blood. rTM (recombinant Thrombomodulin) is a mild anticoagulant with pleiotropic actions which are modulated through its complexation with thrombin. Activated protein C (APC) is a stronger anticoagulant which mediates its action via digestions of factor Va and VIIIa. FEIBA (Factor VII Inhibitor Bypass Activity) contains non activated factors II, IX and X and activated factor VII. The purpose of this study is to compare the relative anticoagulant effects of rTM and APC, employing the thromboelastographic analysis and their neutralization by graded amounts of FEIBA.

Methods:
Citrated Whole Blood samples were supplemented with rTM and APC at a concentration of 3 ug/mL (n=20). TEG analysis was performed on a TEG 5000 system in which clotting was initiated by re-calcification of the whole blood and set parameters as R time, K time, MA and Angle were measured. The relative neutralization profiles of the APC and rTM by FEIBA at 1.0, 0.1, and 0.01 U/ml were investigated.

Results:
At 3ug/ml rTM produced a mild anticoagulant effect as evident by its TEG profile in terms of prolongation of R and K times and marked decrease in angle and maximum amplitude. APC at 3 ug/mL produced a relatively stronger anticoagulant effects on all of the parameters in the TEG profile. The supplementation of FEIBA at 0.1 U/mL to the whole blood mixtures containing 3 ug/mL completely neutralized rTM and resulted in the partial neutralization of APC.

Conclusion:
These results indicate APC is a stronger anticoagulant in comparison to rTM as measured by the TEG analysis. FEIBA is very effective in the neutralization of the anticoagulant effects of rTM and results in a weaker neutralization of APC. These results suggest that FEIBA can be used to neutralize rTM at much lower levels than the proposed dosing for the bleeding control of hemophilia.