Critical Evaluation of Rotational Thromboelastometry Clotting Times

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Background

Thromboelastometry (ROTEM®) has been shown to be effective in guiding hemostatic therapies during cardiac surgery (1). Decreased plasma coagulation factor levels are usually diagnosed by prolonged clotting time (CT) on EXTEM®, which is often used interchangeably with FIBTEM® CT (Fig. 1). EXTEM® reagent contains cytochalasin D (CD), which has been shown to release platelet microparticles (MPs) that may contain procoagulants (2).

Hypothesis:

FIBTEM-CT is shorter than EXTEM-CT because cytochalasin D speeds up thrombin generation.

Aims: To

1. Check the difference between EXTEM and FIBTEM CT values at the clinical level (Experiment 1).
2. Examine the effect of cytochalasin D in thrombin generation (Experiment 2).

Experiment 1:

Methods:

â€¢ Retrospective chart review of adult patients undergoing cardiac surgery with cardiopulmonary bypass (CPB).

â€¢ Measurements points: baseline, CPB, and post-protamine.

â€¢ Parameters collected:

â€¢ Demographics, surgical data, fluid intake, transfusions, anticoagulants and mini-coagulation values.

â€¢ EXTEM-CT, FIBTEM-CT.

â€¢ EXTEM-CT and FIBTEM-CT values were compared using Mann-Whitney test and a p-value of < 0.05 was considered statistically significant.

Results: Figure 2
FIBTEM-CT was significantly shorter than EXTEM-CT at both baseline (71.4±30.5 vs. 76.1±31.1, N=118) and post protamine (74.9±18.4 vs. 82.5±18.3, N=111), (p <0.0001) measurements. FIBTEM-CT vs. EXTEM-CT comparison did not reach statistical significance (p=0.906) during CPB.

Experiment 2:

Methods:

Thrombin generation (TG) assays were performed using platelet rich plasma that was diluted in 1:3 ratios with normal plasma (NP). Subsequently, samples were tested for TG using a Calibrated Automated Thrombinscope (CAT®) before and after addition of CD at a volume of 5.33 Î¼M. TG lag times were compared using Mann-Whitney test and a p-value of <0.05 defined statistical significance.

Results: Figure 3

The Lag time of the TG assay done on NP (N=10) was significantly shorter (139.8 [71.8-178.6]) than the lag time of the TG done on NP samples that were mixed with CD (N=10), (220.2 [210.7, 236.8]), p =0.023.

Discussion:

In vivo analysis (Experiment 1) indicates FIBTEM-CT is shorter than EXTEM-CT for cardiac surgical patients at baseline and post protamine. No difference was found during CPB, which may be secondary to extreme inhibition of TG by systemic heparinization. This finding was reproduced in the ex vivo experiment, which showed a shorter lag time of TG in samples mixed with CD compared to NP only. This CD â€œenhancingâ€™ effect on TG and hence shorter FIBTEM-CT may be due to the release of pro-coagulant MPs from the surface of activated platelets (2).

Conclusions/Implications:

EXTEM-CT and FIBTEM-CT do not appear to be interchangeable because of the effect of cytochalasin D on FIBTEM-CT. Patients with significantly shorter FIBTEM-CT compared to EXTEM-CT may have highly functioning platelets and may not need any hemostatic interventions. Combined EXTEM/FIBTEM assays are recommended.

References:
