Introduction: Pregnancy is associated with a state of hypercoagulability that is protective against peripartum hemorrhage, but can increase thromboembolic complications. Dalteparin is often used for either treatment or prophylaxis against venous thromboembolism. Monitoring of dalteparin by anti-Xa levels is not routinely performed and has not been shown to correlate with risk of bleeding complications1. Thromboelastography (TEG) has been shown to detect increasing concentrations of dalteparin in maternal whole blood, but is not sensitive or specific enough to delineate between low concentrations of dalteparin2. This study sought to determine which of three activating reagents used in conjunction with thromboelastometry (ROTEM) technology is most sensitive and specific at detecting the presence of dalteparin in maternal whole blood between 0 and 1.0 U/ml anti-Xa activity.

Methods: Local ethics approval was obtained prior to study. Adult ASA I or II singleton term gestation parturients presenting for elective Cesarean section were recruited. Blood samples were collected prior to delivery and divided into five samples of 2.25 ml. 250 µl of saline (control) or dalteparin were added to each sample to yield a final factor Xa activity of 0, 0.125, 0.25, 0.5 and 1.0 U/ml. Samples were selected at random for central laboratory anti-Xa testing to verify dalteparin concentrations. ROTEM was performed separately for each sample using A) standard INTEM reagent, B) INTEM reagent diluted at 1:300 and C) INTEM-HS (high sensitivity) reagent provided by manufacturer. Primary outcomes were CT, CFT, alpha angle, A10, A20 and MCF.

Results: Interim analysis was performed after 10 patients. Dalteparin concentration was confirmed with central lab anti-Xa testing. Clotting time (CT) was the best parameter for detecting anticoagulation by dalteparin in maternal whole blood. INTEM-HS and INTEM 1:300 were superior to INTEM (standard reagent) at detecting the changes in dalteparin concentration. Both reagents showed statistically significant differences in median CT between control and dalteparin concentrations ≥ 0.125 U/ml (P < 0.05). The ROTEM CT ROC curves (Fig) for INTEM, INTEM-HS, and INTEM 1:300 yielded an AUC of 0.86, 0.95 and 0.97 respectively.

Discussion: The initial results showed that ROTEM detected increasing concentrations of dalteparin in maternal whole blood between 0 and 1.0 U/ml anti-Xa activity. CT was the most sensitive and specific parameter for detection of dalteparin. From the ROC curves, INTEM-HS and INTEM 1:300 were both superior to standard reagent in the ability to differentiate between control (0 U/ml) and anti-coagulated samples (≥ 0.125 U/ml). This technology can potentially be utilized as a point-of-care test to determine real-time anti-coagulation status of parturients on low molecular weight heparin.

References:

ROTEM Clotting Time (CT) of 3 reagents
A comparison of three reagents of ROTEM clotting time (CT) using INTEM protocol.