Rotational Thromboelastometry as a Tool for Decision Making, Diagnosis, and Management of High-Risk Obstetric Patients in a Tertiary Care Center: A Case Series

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CASE REPORT

Please cite this paper as: Fiol AG, Fardelmann KL, Salimi N, Abdel-Razeq S, Mancini P, Alian A, et. al. Rotational thromboelastometry as a tool for decision making, diagnosis, and management of high-risk obstetric patients in a tertiary care center: A case series. Women's Health Research [2021] 3(1): 32-37.

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ABSTRACT

The use of point of care viscoelastic testing (POCVT) to guide hemorrhage management, decision making, and diagnosis is just starting to be explored. We present a case series exemplifying the use of the Rotational thromboelastometry (ROTEM) to guide blood product management during a postpartum hemorrhage, determine the safety of neuraxial anesthesia, tease out the effects of unfractionated heparin in a patient with abnormal baseline prothrombin time, and aid early detection of a coagulopathy when concerned for an anaphylactoid syndrome of pregnancy. We argue that POCVT monitoring can help anesthesiologists with more than just blood product management on the obstetrical floors.

Key Words: Rotational thromboelastometry, hemorrhage, neuraxial anesthesia, coagulopathy, heparin, cascade.

ABBREVIATIONS

A10 = amplitude at 10 minutes from clot initiation;

APLS = antiphospholipid syndrome;

ASP = anaphylactoid syndrome of pregnancy;

Cryo = cryoprecipitate;

CT – clotting time;

DIC = disseminated intravascular coagulopathy;

EBL = estimated blood loss;

EXTEM = extrinsic cascade coagulation assessment;

FC = fibrinogen concentrate;

FFP = fresh frozen plasma;

FIBTEM = fibrinogen determination;

HELLP = hemolysis, elevated liver enzyme and low platelet syndrome;

HEPTEM = heparinase assay;

INTEM = intrinsic cascade coagulation assessment;

PLT = platelets;

POCVT = point of care viscoelastic testing;

PPH = postpartum hemorrhage;

PTT = partial thromboplastin time;

PRBC = packed red blood cell;

ROTEM = Rotational thromboelastometry;

TEE = transesophageal echocardiogram.

TACO = transfusion-associated circulatory overload

INTRODUCTION

The use of point of care viscoelastic testing (POCVT) has proved beneficial for blood product transfusion management in cases of postpartum hemorrhage (PPH) [1–3]. This technology allows for personalized instead of formulaic transfusion management for the obstetric patient in cases of PPH [1–3]. With the increasing complexity of our obstetric population, POCVT has improved our ability to aid in decision-making beyond transfusion of blood products [2, 4–7]. At times, blood work results (e.g., fibrinogen, platelet count) may take up to 45 minutes, whereas POCVT may result in 20-30 min [8].

In this case series, we present the use of Rotational thromboelastometry (ROTEM) in a tertiary care center for blood product transfusion management and as a tool to aid in diagnosis and anesthetic decision making. This device provides information related to the intrinsic (InTEM), extrinsic (ExTEM) coagulation pathways and fibrinogen contribution to clot strength (FibTEM). In certain cases, we utilize a heparinase assay (HEPTEM) to evaluate the contribution of heparin on the coagulation cascade. We present a case series that exemplifies the use of ROTEM to 1) guide blood product management in a case of postpartum hemorrhage; 2) aid with the decision-making process to determine safety of neuraxial anesthesia for a patient with hemolysis, elevated liver enzymes and low platelets (HELLP syndrome), and another with antiphospholipid syndrome (APS). Lastly, 3) we describe the use of ROTEM to aid in the diagnosis and management in a case of anaphylactoid syndrome of pregnancy. The institutional review board approved these cases, and written consent was obtained from all women herein reported.

See Table 1 for summary of blood work and ROTEM values for the cases described.

CASE 1

A 44-year-old G7P6 with a past surgical history of 5 previous cesarean deliveries and concern for focal placenta accreta presents at 36 weeks gestation for scheduled repeat cesarean section. Upon admission and after intravenous cannulation, a sodium citrate anticoagulant tube was utilized for baseline ROTEM analysis (Table 1). Intraoperatively, a placenta percreta was noted, requiring hysterectomy, bilateral salpingectomy, and cystotomy repair. After an initial 2L estimated blood loss (EBL) and administration of 2 units of packed red blood cells (PRBC), a follow-up ROTEM revealed normal coagulation parameters, yet a drop in the Fibrinogen ThromboElastoMetry Amplitude at 10 min (FIBTEM A10) from 24 mm to 17 mm was noted. Based on this finding and the concern for ongoing blood loss, 2 units of cryoprecipitate (Cryo) and 2 units of PRBC were ordered and transfused upon arrival. One hour later, after 6L EBL, the ROTEM revealed an additional drop in FIBTEM A10 to 9 mm. At this point, 4 units of Cryo, 8 units of PRBC and 1 unit of platelets (PLT) were transfused, and fibrinogen concentrate was ordered. The subsequent FIBTEM A10 was 8mm, necessitating transfusion of 2 additional units of Cryo, administration of 5g fibrinogen concentrate (FC), and 6 units of PRBC. One hour and 50 min after the blood product transfusion, the ROTEM showed a corrected FIBTEM A10 of 27 mm. The total EBL was estimated at 8L.

CASE 2-3

A 26-year-old G1P0 at 36 and 4 days of gestational age was admitted with a diagnosis of preeclampsia with severe features based on new-onset severe range blood pressures (160/100 mmHg) and proteinuria. Upon admission, her blood work revealed a platelet count (PLT) of 152 x 1000 μL. Twelve hours after admission, the patient requested an epidural for labor pain management, but we did not have a recent PLT count. Hence, a ROTEM was ordered before epidural placement. The ROTEM results were notable for prolonged clotting time in the Intrinsic pathway ThromboElastoMetry (INTEM) test.

A stat CBC and CMP were ordered and resulted 30 min after the ROTEM reading. The PLT count was 72 x 1000 μL, and liver enzymes were elevated. Although hemolysis (H)

was not confirmed at the time, the patient was diagnosed with HELLP syndrome. Since the patient had not made cervical change for 3 hours and was remote from vaginal delivery, cesarean delivery was deemed necessary. General anesthesia was induced utilizing propofol and succinylcholine, given her sudden drop in PLT and a prolonged INTEM Clotting Time (CT). An intraoperative CBC, coagulation panel and ROTEM were sent for analysis. Results revealed worsening thrombocytopenia, hypofibrinogenemia, and elevated partial thromboplastin time (PTT). ROTEM results confirmed a prolonged INTEM CT, as well as a reduced A10 for INTEM, EXTEM, and FIBTEM. The patient's coagulopathy was managed utilizing 2 units of FFP, 1 unit of cryoprecipitate, and 2 units of platelets with subsequent normalization of her INTEM and EXTEM A10.

CASE 3

A 41-year-old G8P0 with PMH of antiphospholipid syndrome (APLS) and history of deep venous thrombosis on therapeutic heparin (18,000 units twice a day) was admitted at 26 weeks gestation for inpatient management in the setting of fetal growth restriction, abnormal Doppler studies and preeclampsia. Given persistent absent end-diastolic flow with intermittent reversal, oligohydramnios, and non-reassuring fetal testing, it was decided that the patient needed to be delivered via cesarean delivery at 28 weeks. The plan was to stop anticoagulation 24 hours before the procedure. Given her baseline elevated PTT (40s), the use of this test to confirm the lack of heparin effect was less than ideal. The INTEM/Heparin ThromboElastoMetry (HEPTEM) ratio helped determine the absence of residual heparin effect. Twenty hours after discontinuing heparin, the INTEM/HEPTEM ratio was noted to be 1.5. At the 25 hours after heparin discontinuation, the INTEM/HEPTEM ratio was 1.08. This suggested that there was no heparin effect, and the patient had a cesarean delivery under neuraxial anesthesia

CASE 4

A 32-year-old G1P0 presented for a scheduled primary CD for known complete placenta previa. Spinal anesthesia was performed, and shortly after uterine incision, the patient became hypotensive and apneic. She was quickly intubated as her infant daughter was delivered without complication. Volume resuscitation, as well as pressor support, was initiated. Intra-operative transesophageal echocardiogram (TEE) revealed dilated right ventricle and right atrium, moderate tricuspid regurgitation, and pulmonary artery dilation. A ROTEM was sent, and the results confirmed disseminated intravascular coagulation (DIC). The clinical picture was that of anaphylactoid syndrome of pregnancy. The coagulopathy was corrected as demonstrated with the aid of ROTEM results. On postoperative day one, the patient made a full neurologic recovery and was transferred to the postpartum unit.

DISCUSSION

The use of POCVT management has been shown to result in decreased PRBC administration, transfusion-associated circulatory overload (TACO), overall intensive care unit stay, and hospitalization costs [3,9,10]. Besides, ROTEM provides the means for monitoring fibrinogen trends. Although the correlation between the Clauss fibrinogen level is not linear compared to ROTEM FIBTEM ($r2 = 0.6$), the ability to predict progression to severe hemorrhage is comparable [10, 11]. The studies from Collins et al., and Snegovskikh et al., demonstrated that when utilizing a POCVT algorithm the use FFP was rarely indicated, and that Cryo was the most often needed product to aid in decreasing PRBC transfusions [3, 10]. Furthermore, a theoretical mathematical model indicates that unnecessary administration of FFP could further dilute critical factors, such as fibrinogen [9].

At our institution, we only transfuse FFP if he EXTEM CT is > 82 s or an INR > 1.5. Besides, we utilize a FIBTEM amplitude at 10 minutes (A10) of 12mm or Clauss Fibrinogen of < 200 g/L as our trigger for hypofibrinogenemia, and Fibrinogen concentrate is

considered with ongoing hemorrhage and a FIBTEM A10 < 9 mm or Clauss Fibrinogen < 150 g/L. Transfusion of PLT are considered when EXTEM A10 – FIBTEM A10 is < 30 mm or < 75 x 1000 μL with ongoing hemorrhage. As described by Collins et al., and McDonnell et al., the benefit of incorporating fibrinogen concentrate in post-partum hemorrhage (PPH) algorithms includes an effective way of replacing fibrinogen with a lower volume and viral risk associated with cryoprecipitate [12, 13].

Aside from hemorrhage, parturients often present with thrombocytopenia, which is the most common hematologic abnormality during pregnancy. Preeclampsia and HELLP syndrome account for 21 % of thrombocytopenic cases during pregnancy. In fact, the level of thrombocytopenia is a surrogate of disease severity [14]. The frequency of blood draws, and the lowest platelet count needed in the presence of preeclampsia and HELLP syndrome for the safe placement of neuraxial anesthesia remains unknown. A safe PLT count of 75 X 1000 μL for preeclampsia patients has been cited based on normal thromboelastography results in a cohort of parturients with preeclampsia and eclampsia [14]. In case 2, the ROTEM provided timely information that changed both the obstetric and anesthetic plan. Given that we had evidence of prolonged CT and poor PLT contribution to the clot formation based on an EXTEM A10 – A10 FIBTEM = 23 (normal >30), we decided to proceed with general anesthesia [15].

Besides acquired thrombocytopenia, acquired thrombophilia can complicate anesthetic decision-making. In cases of APLS, the presence of the lupus anticoagulant antibody can disrupt the antiphospholipid membranes of routine coagulation test assays. This disruption may account for discrepancies between the in-vitro and in-vivo coagulation processes. As reflected in case 3, our patient had an elevated PTT, yet she exhibited thrombotic tendencies. The INTEM/HEPTEM ratios used to confirm heparin reversal in anticoagulated patients with APLS has been previously described in cardiac and obstetric scenarios [5]. The normalization of the INTEM/HEPTEM ratio correlates with our current guidelines that recommend waiting for 24hours when the daily dose of heparin is > 20,000 units [16]. In contrast to heparin's predictable effects, unpredictable immunologic responses can lead to coagulopathy [12].

Such is the case of the Anaphylactoid syndrome of pregnancy (ASP). It is hypothesized that fetal antigens and amniotic fluid may trigger the release of vasogenic and procoagulant substances, leading to DIC [12]. Given that the diagnosis of amniotic fluid embolism is one of exclusion, the quick identification of hyperfibrinolysis by POCVT monitoring and correlation of cardiorespiratory events with the coagulopathy has proven essential for early diagnosis and management of this syndrome [12]. Our case also reflects the importance of early diagnosis and correction of the coagulopathy.

In conclusion, POCVT may prove beneficial beyond its known use for PPH management. The ability to have whole blood results within minutes offers great value to tertiary care units given their dynamic nature and acuity of care. The authors acknowledge that there is lack of evidence or validation for the use of the HEPTEM/INTEM for parturients. Besides, although the UK National institute for Health and Care Excellence (NICE) does not recommend the use of POCVT, there is growing evidence that this technology may improve clinical outcomes [8]. The use of ROTEM could help establish the presence of coagulopathies or aid in decisions regarding anticoagulation. In some instances, the presence of a coagulopathy may help to diagnose and manage cases of ASP. More research is needed to confirm the utility of POCVT devices for decision-making.

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PEER REVIEW

Not commissioned. Externally peer reviewed.

TABLES

Table 1: Summary of cases perioperative blood work and Rotational thromboelastometry results

Case 1	ROTEM (unit) [normal values]	Pre-operative	EBL 2L	EBL 6L	EBL 8L		Hemostasis
Postpartum hemorrhage	EXTEM						
Placenta percreta	CT (s) [43-82]	46	38	39	60		39
	A10 (mm) [46-67]	66	61	47	38		42
	INTEM						
	CT (s) [122-208]	164	125	176	138		131
	A10 (mm) [46-67]	67	62	48	44		41
	FIBTEM						
	A10 (mm) [7-22]	24	17	9	8		27
	EXTEM A10 - FIBTEM A10	42	44	38	30		15
	Blood work (unit) [normal values]						
	Hemoglobin g/dLn [12-18]	10.1	8.7	6.6	6.3	6.8	12.4
	Platelet count (x1000/uL) [140-440]	231	180	122	101	48	56
	Fibrinogen (mg/dL) [136-464]		355	139	172	264	292
	Blood product management						
		2 U PRBC	2 U PRBC	6 U PRBC 4 U Cryo 1 U Platelets	6U PRBC 2 U Cryo 5 g FC	2 U PRBC	1 U PRBC
Case 2		Admission	Neuraxial Request		Intra-operative		Post-operative
Preeclampsia	EXTEM						
with severe feature	CT (s) [43-82]		64		60		66
HELLP syndrome	A10 (mm) [46-67]		49		35		51
	INTEM						
	CT (s) [122-208]		222		224		230
	A10 (mm) [46-67]		46		35		47
	FIBTEM						
	A10 (mm) [7-22]		14		12		17
	EXTEM A10 - FIBTEM A10		35		23		30
	EXTEM A10 - FIBTEM A10		14		12		21
	Blood work (unit) [normal values]						
	Hemoglobin g/dLn [12-18]	14.6		15	10.8		10.9
	Platelet count (x1000/uL) [140-440]	151		72	41		84
	Fibrinogen (mg/dL) [136-464]				197		375
	PT (sec) [9.6-12.6]				11.4		9.8
	INR [0.86-1.14]				1.05		0.86
	PTT (sec) [22.1-30.1]				37.2		25.6
	AST (u/L) [11-33]	46		537			
	ALT (u/L)[6-34]	31		320			
	Blood product management						
					1 U Cryo 1 U PLT 2 U FFP		
Case 3		20 hours after heparin		25 hours after heparin			
Antiphospholipid	EXTEM						
syndrome	CT (s) [43-82]	123		110			
	A10 (mm) [46-67]	70		30			
	INTEM						
	CT (s) [122-208]	308		223			
	A10 (mm) [46-67]	66		30			
	FIBTEM						
	A10 (mm) [7-22]	30		30			
	HEPTEM (unit) [normal values]						
	CT (s) [100-240]	208		205			
	INTEM/HEPTEM	1.5		1.08			
	Blood work (unit) [normal values]						
	PT (sec) [9.6-12.6]	10.4					
	INR [0.86-1.14]	0.93					
	PTT (sec) [22.1-30.1]	40					
Case 4		Intra-operative		Intra-operative		Post-operative	
Anaphylactoid	EXTEM						
syndrome of	CT (s) [43-82]	93		72		52	
pregnancy	A10 (mm) [46-67]	33		48		50	
	ML (%)	100		0		0	
	INTEM						
	CT (s) [122-208]	188		194		143	
	A10 (mm) [46-67]	33		47		48	
	ML (%)	100		0		0	
	FIBTEM						
	A10 (mm) [7-22]	4		10		11	
	Blood work (unit) [normal values]						
	Hemoglobin g/dLn [12-18]	10.7	9.8		9.8	8.4	
	Platelet count (x1000/uL) [140-440]	165	173		167	122	
	Fibrinogen (mg/dL) [136-464]		71		207		238
	PT (sec) [9.6-12.6]		12.7		12.7		11.3
	INR [0.86-1.14]		1.21		1.21		1.04
	PTT (sec) [22.1-30.1]		33.4				24.1
	Blood product management						
		2 U PRBC 3 U Cryo 2g TXA 4.356g FC			2 U PRBC	3U Cryo	