

Case Reports

A Case of Successful Thromboelastographic Guided Resuscitation after Postpartum Hemorrhage and Cardiac Arrest

M. Hurwich, MD;* D. Zimmer, DVM;† E. Guerra, CCP;* E. Evans, CCP;* T. Shire, CCP;*
M. Abernathy, MD;‡ J.T. Shreve, MS;† G.R. Kolettis, MS;† M.T. McCurdy, MD;¶
E.J. Castellino, PhD;†§ M. Walsh, MD†§

*Department of Anesthesiology, Memorial Hospital, South Bend, Indiana; †Indiana University School of Medicine, South Bend at the Notre Dame Campus, South Bend, Indiana; ‡Department of Maternal-Fetal Medicine, St. Vincent Hospital, Indianapolis, Indiana; §W.M. Keck Center for Transgene Research, University of Notre Dame, Notre Dame, Indiana; and the ¶Departments of Critical Care and Emergency Medicine, University of Maryland School of Medicine Baltimore, Maryland

Presented as a Poster No. 105 at the Thrombosis and Hemostasis Summit of North America, Chicago, Illinois, April 10–12, 2014.

Abstract: Amniotic fluid embolism (AFE) is an unusual cause of life threatening peri partum hemorrhage (PPH). AFE resuscitation is often associated with renal and respiratory insufficiency, and a coagulopathy similar to disseminated intravascular coagulation (DIC). Resuscitation requires immediate recognition and limited use of crystalloid. We present a case of PPH caused by AFE with resultant cardiac arrest, renal and respiratory failure, and DIC-like coagulopathy, whose successful resuscitation was guided by perfusionist-directed serial thromboelastography (TEG). Viscoelastic tests (VET)s, including the TEG and rotational thromboelastometry (ROTEM), may provide more individualized blood component therapy (BCT) in the treatment of severe PPH associated with AFE as has been previously noted with trauma resuscitation in the literature. However, VET's efficacy is often limited

by a lack of standardization, quality assurance norms, and consistent operator proficiency. We suggest that there may be a role for perfusionists adept at utilizing TEG in the optimization of BCT and adjunctive hemostatic agents in severely hemorrhagic patients. This patient's successful resuscitation demonstrates the importance of resuscitation guided by the perfusionist or other medical professionals with expertise in TEG guided resuscitation and how the administration of specific blood products and hemostatic agents guided by the TEG can help optimize patient outcomes in comparison to traditional 1:1:1 packed red blood cells (PRBC) /fresh frozen plasma (FFP) /platelets ratios given to severely hemorrhaging patients. **Keywords:** blood component transfusion, embolism, amniotic fluid, postpartum hemorrhage, thromboelastography, tranexamic acid. *J Extra Corpor Technol. 2016;48:194-7*

Postpartum hemorrhage (PPH) is a leading cause of maternal mortality worldwide, with amniotic fluid embolism (AFE) an unusual cause (1,2). AFE resuscitation can be complicated by renal and respiratory sequelae, and a coagulopathy comparable to disseminated intravascular coagulation (DIC) (2,3). Successful resuscitation requires immediate recognition and limited use of crystalloid.

Literature evaluating trauma and obstetric patients complicated by hemorrhage suggests that viscoelastic tests (VETs), including thromboelastography (TEG) and rotational thromboelastometry (ROTEM), may provide more individualized blood component therapy (BCT) (2–7). However, VET's efficacy is often limited as there is a lack of standardization, quality assurance norms, and operator proficiency (5–7). We suggest that there may be a role for perfusionists adept at using TEG in the optimization of BCT and adjunctive hemostatic agents (AHA) in hemorrhagic patients and in particular for patients bleeding from AFE.

We present a patient with peri-partum AFE, severe hemorrhage, cardiac arrest, renal and respiratory failure, and DIC-like coagulopathy, whose resuscitation was

Received for publication June 20, 2016; accepted October 13, 2016.
Address correspondence to: M. Walsh, MD, Emergency Department, Memorial Hospital, 615 N Michigan Street, South Bend, IN 46601.
E-mail: markwalshmd@gmail.com

J.T. Shreve is a share holder for Geneopedia Corp., a personal exome sequencing company. M. Walsh has received research grants from Haemonetics and the Speaker's Bureau at Boehinger Ingleheim.

successfully guided by perfusionist-directed serial TEGs. This patient's resuscitation without further thromboembolic complications demonstrates the importance of BCT and AHA administration guided by a perfusionist, or another medical professional with expertise in TEG-guided resuscitation. Furthermore, this case emphasizes how the administration of specific blood products and hemostatic agents guided by the TEG can optimize patient outcomes compared to traditional 1:1:1 ratios of packed red blood cells (PRBCs)/fresh frozen plasma (FFP)/platelets in severely hemorrhaging patients.

DESCRIPTION

A 35-year-old Caucasian female suddenly developed severe respiratory distress during induction of labor at term for her second child. Subsequently, she progressed to respiratory failure and ultimately cardiac arrest. Cardiopulmonary resuscitation with massive transfusion of BCT and AHA was initiated immediately. An emergency cesarean section was undertaken resulting in the delivery of a viable and healthy male. The patient developed PPH with >2,000 mL estimated blood loss. Following the cesarean section, the patient exhibited uncontrolled bleeding. AFE and associated severe DIC like state were diagnosed based on clinical condition and a hematocrit (HCT) of 18% (normal HCT 34.9–44.5%), prothrombin time (PT) >106 seconds (normal PT 11.9–14.6 seconds), international normalized ratio (INR) >10 (normal INR = 1), activated partial thromboplastin time (aPTT) >300 seconds (normal aPTT 24.8–35.7 seconds), D-dimer >20 $\mu\text{g/mL}$ (normal D-dimer .23–20 $\mu\text{g/mL}$), fibrin degradation products >20 $\mu\text{g/mL}$ (normal .5–10.0 $\mu\text{g/mL}$), and von Clauss method fibrinogen <60 mg/dL (normal von Clauss method fibrinogen 150–400 $\mu\text{g/dL}$).

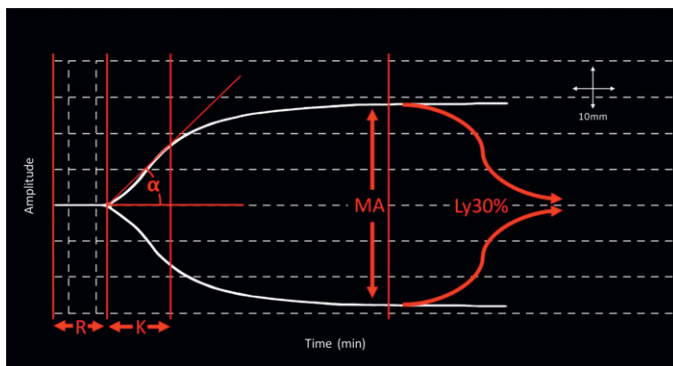


Figure 1. Normal thromboelastography demonstrates clot development and fibrinolysis as a function of time. Factor dependent development of the initial fibrin clot is measured by R. The kinetics of clot formation are reflected by K and α . The maximal clot strength is measured by maximum amplitude (MA). Percent clot lysis at 30 minutes after MA (Ly30%) reflects the rate of fibrinolysis.

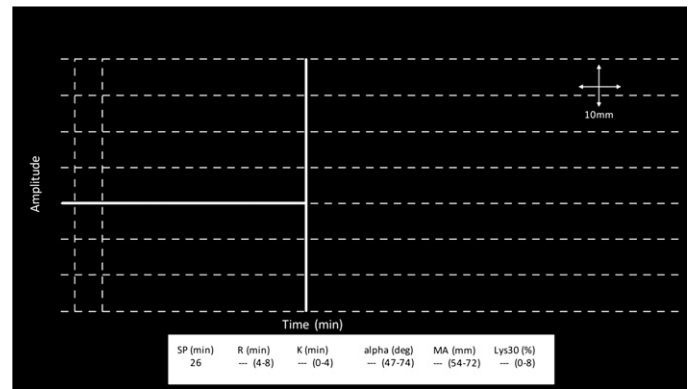


Figure 2. The initial thromboelastography demonstrates no clot development with a flat baseline appearance. This result was repeated with the same finding and reflects a profound coagulopathy. Time 23:30.

As compared with a normal TEG, using a Thrombelastograph Hemostasis Analyzer System 5000 (Haemonetics Corporation, Braintree, MA) (Figure 1), the initial TEG curve indicated severe coagulopathy as represented a flat line (Figure 2). The TEG was repeated for confirmation with the same result as resuscitation of the patient ensued. Resuscitation was achieved using point of care (POC) TEG-guided, goal-directed treatment with BCT and AHA, including prothrombin complex concentrate (PCC) (Kcentra) and recombinant Factor VIIa (rFVIIa) (NovoSeven) over a 4-hour period following cardiac arrest. The administration of a total of 12 units of PRBC, 6 units of FFP, 3 units of single-donor apheresis platelets (SDAP), 2 doses of rFVIIa (13 mg in total), 4 doses of 10 units

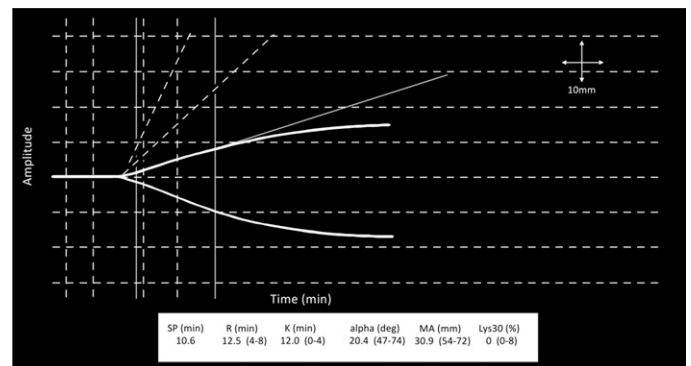


Figure 3. An early resuscitation thromboelastography (TEG). A severe coagulopathy is evident with a delayed initiation, amplification, and propagation of the clot as evidenced by prolonged R, flat alpha angle, and narrow maximum amplitude (MA). Also notable is the lack of fibrinolysis with a normal value for Ly30%. This TEG reflects the early stages of resuscitation after the patient had been given 6 units of packed red blood cell, 4 units of fresh frozen plasma, 2 units of single-donor apheresis platelet, and two 10 unit doses of cryoprecipitate and a single dose of recombinant Factor (rFVIIa) 6.5 mg (80 $\mu\text{g/kg}$). Time 00:09, 49 minutes after initial flat line TEG.

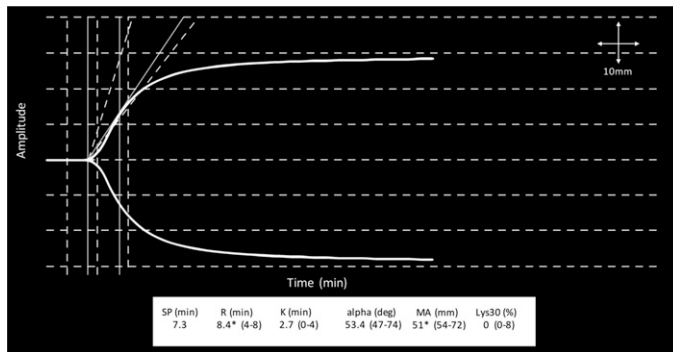


Figure 4. Approximately 2 hours after initial thromboelastography (TEG). In this tracing all measures of clot development are approaching normal limits indicating nearly complete resolution of the prior coagulopathy. The total resuscitation required 12 units of packed red blood cells, 6 units of fresh frozen plasma, 2 doses of rFVIIa (13 mg in total), four 10 unit doses of cryoprecipitate, 3 units of SDAP, and 2,000 units of four-factor prothrombin complex concentrate (PCC) (Kcentra). Because the patient was in renal and respiratory failure, the 2,000 units of four-factor PCC were given to avoid volume overload. Time 01:41, two hours 11 minutes after initial flat line TEG.

each of cryoprecipitate, and 2,000 units of four-factor PCC (Kcentra) was guided by serial TEGs. Initial TEGs during the first stages of resuscitation revealed improvement but not total correction of the coagulopathy by 2 hours (Figures 1 and 3). In this case, tranexamic acid (TXA) treatment was withheld, given the absence of fibrinolysis on the post-initial resuscitation TEG.

Subsequent TEGs performed at the end of resuscitation and at the cessation of bleeding revealed a gradual return to the normal range of TEG coagulation parameters (Figure 4). The BCT and AHA administration were guided according to a previously published algorithm for TEG-guided resuscitation in coagulopathic patients (Table 1) (5). The patient's coagulopathy improved within 4 hours of cardiac arrest following TEG goal-directed BCT and AHA. She remained stable with transient respiratory insufficiency that required ventilation, and acute

Table 1. Algorithm for thromboelastographic guided blood component therapy (5).*

TEG [®] Abnormality	Blood Component Therapy
Prolonged R	Fresh frozen plasma
Prolonged K and/or reduced α angle	Cryoprecipitate/fibrinogen
Low MA	Platelets/cryoprecipitate/fibrinogen
Elevated Ly 30%	Consider antifibrinolytics

*Address other etiologies of coagulopathy: hypothermia, acidosis, continued hemorrhage, hypocalcemia, and dilution. Consider early surgery and 1:1:1 packed red blood cells, fresh frozen plasma, platelets, and packed red blood cell for damage control resuscitation and recombinant Factor VIIa for severely coagulopathic patients. Look for combined and occult causes of coagulopathy and primary fibrinolysis. MA, maximum amplitude; Ly 30%, percent clot lysis at 30 minutes.

renal failure that necessitated dialysis. She eventually made a full recovery and the child has developed normally.

COMMENT

PPH is a prevailing cause of maternal mortality and a major source of morbidity for obstetric patients worldwide (1). Resuscitation of a hemorrhaging patient is complicated by a hypercoagulable state following peri-partum resuscitation. There is real risk of fatal thromboembolism in the post-resuscitation period for patients with peri-partum hemorrhage who have received pro-coagulant agents (2). This is particularly true of a subset of patients, such as those who survive AFE who are then more prone to thrombotic complications in the recovery period. This patient was especially at risk since she was given rFVIIa, the administration of which remains a matter of continued discussion (2). There are no randomized controlled trials regarding the use of rFVIIa to treat patients with AFE who sustain a cardiac arrest. Patients who receive rFVIIa have a much higher acuity level than those who are resuscitated with standard BCT. The current literature suggests that rFVIIa should be reserved for women such as this patient with severe coagulopathy who continue to bleed heavily despite adequate component therapy (2). TXA was withheld to reduce risk of post-partum thromboembolism and because there was no evidence of fibrinolysis on serial TEG analyses. Therefore, we used factor rFVIIa in addition to other BCT to reverse the coagulopathy since there was no evidence of fibrinolysis.

Commonly used coagulation tests such as PT, INR, aPTT, platelet count, and fibrinogen analyses can take more than 1 hour to report and provide little information about fibrinolysis. TEG is a POC assay that is increasingly used in the obstetric population. It provides measurements of coagulation and fibrinolysis in 10–30 minutes (3–7). Because of varying quality assurance standards and operator proficiency (5–7), perfusionists and other medical professionals who are properly trained to perform and analyze TEG tracings quickly can play an essential role in the optimization of BCT and AHA in hemorrhagic patients (3,5–7).

AFE, an unusual but often lethal complication of pregnancy, is characterized by massive systemic capillary leak, DIC, potential cardiorespiratory collapse, and renal failure (2). Prior studies have shown that excessive blood loss during delivery (>2,000 mL) can further impair hemostasis. The severe capillary leak induced respiratory and renal failure poses limits to large volume resuscitation with crystalloids and blood components. The combined use of low volumes of crystalloids and “damage control resuscitation” (DCR), which aims for a blood product resuscitation goal of a 1:1:1 ratio of

PRBC:FFP:platelets in trauma patients, has recently been applied to obstetric patients in hemorrhagic shock (4). However, POC TEG has been shown to be a reliable guide for goal-directed BCT in trauma patients receiving DCR (7). This case report demonstrates that POC TEG can successfully guide BCT and AHA in a hemorrhaging obstetric patient, reversing the coagulopathy and avoiding volume overload with PRBC, FFP, platelets, and cryoprecipitate.

AHA with PCC, rFVIIa, and TXA may simultaneously limit intravascular volume administration and reverse the coagulopathy of obstetrical patients in shock. The World Maternal Antifibrinolytic Trial recommends liberal and empiric use of TXA for obstetrical bleeding, with no dosing adjustments based on POC laboratory guidance (8). However, lower antithrombin activity associated with pregnancy increases risk for both thromboembolism and post-hemorrhagic inflammatory multi-organ failure in patients with PPH in the immediate peri-partum post resuscitation period (2). In such cases, POC TEG guidance can avoid post-resuscitative thrombotic complications of non-goal directed administration of rFVIIa, PCC, and other pro-coagulants including TXA. We suggest that when guided by serial TEG evaluations, BCT and AHA provide blood component sparing resuscitation for coagulopathic obstetric patients with severe hemorrhagic shock and allow physicians to avoid thrombotic and volume related renal and pulmonary complications of non-goal directed use of an AHA.

The utilization of skilled perfusionists and other medical professionals to perform the TEGs, interpret the tracings, and guide BCT and AHA in this life-threatening situation is a template for treatment algorithms and future standard-

ized treatments regarding PPH patients who are in hemorrhagic shock of all etiologies.

ACKNOWLEDGMENT

The research for this article was performed in South Bend, IN at Memorial Hospital.

REFERENCES

1. Lewis G. Saving mothers' lives: Reviewing maternal deaths to make motherhood safer: 2006–2008. The eighth report on confidential enquiries into maternal deaths in the United Kingdom. *Br J Obstet Gynaecol.* 2011;118:1–203.
2. Clark SL. Amniotic fluid embolism. *Obstet Gynecol.* 2014;123:337–48.
3. de Lange N, Lancé M, de Groot R, Beckers E, Henskens H, Scheepers H. Obstetric hemorrhage and coagulation: An update. Thromboelastography, thromboelastometry, and conventional coagulation tests in the diagnosis and prediction of postpartum hemorrhage. *Obstet Gynecol Surv.* 2012;67:426–35.
4. Stocks G. Monitoring transfusion requirements in major obstetric hemorrhage: Out with the old and in with the new? *Obstet Anesth Dig.* 2012;32:207–8.
5. Walsh M, Thomas SG, Howard JC, et al. Blood component therapy in trauma guided with the utilization of the perfusionist and thromboelastography. *J Extra Corpor Technol.* 2011;43:162–7.
6. Schöchel H, Voelckel W, Grassetto A, Schlimp C. Practical application of point-of-care coagulation testing to guide treatment decisions in trauma. *J Trauma Acute Care Surg.* 2013;74:1587–98.
7. Holcomb J, Minei K, Scerbo M, et al. Admission rapid thromboelastography can replace conventional coagulation tests in the emergency department: Experience with 1974 consecutive trauma patients. *Ann Surg.* 2012;256:476–86.
8. Shakur H, Elbourne D, Gülmezoglu M, et al. The WOMAN Trial (World Maternal Antifibrinolytic Trial): Tranexamic acid for the treatment of postpartum haemorrhage: An international randomised, double blind placebo controlled trial. *Trials.* 2010;11:1–14.