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Recombinant Factor VIII Measurement in a Hemophilia A Patient Undergoing Cardiopulmonary Bypass–Supported Cardiac Surgery

Jennifer Bezaire, CCP, MSc(s);* Dorothy Thomson, MD, FRCSC;† Erick McNair, CCP, PhD‡

**Department of Health Sciences Graduate Program, College of Medicine, University of Saskatchewan, Saskatoon, Canada; †Department of Surgery, Division of Cardiac Surgery, College of Medicine, University of Saskatchewan, Saskatoon, Canada; and ‡Department of Pathology and Laboratory Medicine, Department of Surgery, Division of Cardiac Surgery College of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada*

Abstract: Patients with hemophilia A (Hem A) requiring cardiopulmonary bypass–supported cardiac surgery pose unique challenges for perioperative hemostatic management. This report describes a staged perioperative approach to clinical hematologic management as applied to an 80-year-old male of O-positive blood type with mild Hem A, who underwent successful, uncomplicated coronary artery bypass graft surgery. Hematologic management primarily consisted of normalization of plasma factor VIII levels followed by standard care. Conventional laboratory methods and point-of-care-testing methods such as thromboelastography and heparin management assays were combined to guide patient care. Minimal blood loss and minimal hemodilution techniques were also used to achieve favorable outcomes. The thorough preparation and execution of care by our multidisciplinary team from perfusion, pathology and laboratory medicine, cardiovascular surgery, transfusion services, nursing, and anesthesia, facilitated a safe, smooth, clinical course and an optimal outcome. **Keywords:** hemophilia A, factor VIII, recombinant factor VIII, thromboelastography, point-of-care testing. *J Extra Corpor Technol. 2018;50:170–7*

OVERVIEW

Coagulation factor VIII (FVIII), essential for the formation of a stable clot, is a glycoprotein produced by the liver, kidneys, endothelium, and lymphatics (1,2). It circulates in the blood as a full-length inactive co-factor in association with von Willebrand factor (vWF) and undergoes proteolytic cleavage at sites of endothelial injury by furin protease, producing a trimer consisting of three amino acid domains (A1, A2, and A3) (1,2). FVIII is then activated by thrombin, which subsequently promotes factor X activation in the presence of factor IXa, phospholipids, and calcium ions (1,2).

Hemophilia A (Hem A) is primarily an X-linked recessive genetic bleeding disorder of variable penetration that results in absent, deficient, or defective FVIII (3,4). An estimated one-third of cases are due to spontaneous mutation of the FVIII gene (5). Affected patients demonstrate spontaneous bleeding in joints, soft tissues, and vital organs as well as exaggerated bleeding from trauma, hypertension, and surgery (3,4). The spectrum of clinical severity is proportional to the level of factor activity. A factor level of less than 1% produces severe disease (60% of all cases); factor levels of 1–5% characterize moderate disease (15% of all cases); and factor levels of 6–30% represent mild disease, with bleeding only occurring following trauma or surgery (25% of all cases) (3). The normal range of plasma concentrations of FVIII is .5–1.5 IU/mL (6).

Successful recombinant factor VIII (rFVIII)–replacement therapy has increased the life expectancy of the Hem A population. Consequently, age-related comorbidities such as ischemic heart disease requiring cardiac surgery are also increasing in the Hem A population. This complex pathophysiology requires expert clinical management by a multidisciplinary team.

Patients with Hem A undergoing cardiopulmonary bypass (CPB)–supported cardiac surgery, such as coronary artery bypass grafting (CABG), have an increased risk of

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Address correspondence to: Erick McNair, CCP, PhD, Department of Pathology and Laboratory, University of Saskatchewan, Health Science Building, Room 2D30.11, 107 Wiggins Road, Saskatoon, Saskatchewan S7N 5E5, Canada. E-mail: erick.mcnair@usask.ca
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complications with hemostasis due to sternotomy, cardiac arrest, hemodilution, hypothermia, anticoagulation, and blood interface with the artificial surfaces of the pump circuit, producing inflammation, platelet dysfunction, and consumption (7–11). High dose unfractionated heparin is commonly used to achieve anticoagulation during CPB because of its prompt onset, ease of monitoring, and rapid neutralization (12). The conventional activated partial thromboplastin time (aPTT)–based one-stage coagulation method for monitoring plasma FVIII levels is adequate for patients not receiving heparin therapy (10). However, the high doses of heparin required in CPB-supported cardiac surgery cause chemical interference with conventional laboratory FVIII testing, thereby, compromising the accuracy of the results (13).

The coagulation management stages of CPB-supported cardiac surgery are well defined (preoperative stage, pre-CPB stage, CPB stage, post-CPB stage, and postoperative stage). This report outlines a systematic approach in which FVIII levels are normalized using the most reliable methods for determining their levels during each stage. This design both guides and optimizes the management of patients with Hem A undergoing CPB-supported cardiac surgery. Our single center experience describes a novel approach where the normalization of FVIII levels and the staged, combined use of conventional, and point-of-care testing (POCT) methods for evaluating coagulation were an effective management strategy for a high-risk patient.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editor in chief of this journal on request.

DESCRIPTION

An 80-year-old, 94-kg, O-positive male, with mild Hem A, underwent cardiac investigations for exertional dyspnea while awaiting total knee replacement. Cardiac risk factors included hypertension, type II insulin–dependent diabetes, a remote 64 pack-year smoking history, and dyslipidemia. Other comorbidities included rheumatoid arthritis, myelophthisic anemia, and a cerebrovascular accident in 2010. Past history included Hodgkin's lymphoma treated in 2010 with chemotherapy, a total left hip replacement in 2016 and a total left knee replacement in 2014. He received FVIII replacement therapy for both previous orthopedic surgeries with no bleeding complications and remained negative for alloantibodies (inhibitors). Preoperative echocardiography showed depressed left ventricular systolic function (ejection fraction of 35%), apical dyskinesia, and aortic sclerosis. Coronary angiography revealed triple-vessel disease, including an occluded right coronary (RCA) and severe flow-limiting lesions in the left anterior descending (LAD) and circumflex arteries.

An interdisciplinary team comprised members from clinical perfusion, nursing, laboratory medicine, pharmacy, transfusion services, hematology, and cardiac surgery met to develop a plan of care as outlined in Table 1. Xyntha® antihemophilic factor (moroctocog alpha; Pfizer Canada, Saint-Laurent, Quebec, Canada) was provided by Saskatchewan Blood Services. It is a recombinant form of coagulation protein that increases the concentration of FVIII in the blood, thereby augmenting clot development with the intention of normalizing surgical bleeding (14). Xyntha (rFVIII) dosing was calculated based on the patient's weight to ensure a normalized range of FVIII levels perioperatively and prevent the potential complication of hyper- or hypocoagulation.

Preoperative Stage

On the morning of surgery, preoperative FVIII levels (ACL Top 750; Instrumentation Laboratory, Bedford, MA), a coagulation panel, and baseline kaolin-activated thromboelastograph (TEG) (Haemonetics Corporation, Braintree, MA) were measured. Results are shown in Table 2. The TEG demonstrated a high-normal bleeding time to clot formation (R-time) as seen in Figure 1. Based on the results, 5,000 units of rFVIII were given en route to the operating room (OR). On arrival in the OR, TEG and FVIII measurements were repeated to reassess the patient's coagulation status before surgical preparation (Table 1). This subsequent TEG (Figure 2), demonstrated a shortened R-time to clot formation, confirming normalization of enzymatic pathways of coagulation, effectiveness of the dose of rFVIII, and safety to proceed with CPB-supported surgery.

Pre-CPB Stage

The conduct of anesthesia was at the discretion of the attending anesthesiologist using narcotic and inhalation agents. Target mean arterial blood pressure and heart rate were maintained within ±20% of mean baseline values. Hemodynamic control was provided by modification of the concentration of anesthetic agents, intravenous vasoactive drugs, and volume repletion (12). Following induction, intubation, and line placement (arterial and central venous), an arterial blood sample was drawn for measurement of baseline activated clotting time (ACT; Medtronic, Minneapolis, MN), oximetry, electrolytes, and blood gas parameters (ABL Flex 90; Radiometer, London, Ontario, Canada). A heparin dose response (Hepcon®HMS; Medtronic, Minneapolis, MN) curve was generated to provide the initial heparin dose and quantities of heparin needed for the maintenance of anticoagulation throughout the CPB period.

The slope of the curve was 130 sec/unit/mL, suggestive of heparin sensitivity with a calculated heparin dose of 196 IU/kg. As per institutional protocol, the heparin dose calculation was adjusted to 350 IU/kg to ensure sufficient anticoagulation with a target ACT greater than 480 seconds

Table 1. Plan of care: Hem A patient requiring CABG surgery using CPB.

Pre-operative stage
1. Pre-admission clinic, draw two full blue top sodium citrate tubes for the following baseline bloodwork:
a) STAT plasma FVIII level
b) TEG
2. Based on baseline bloodwork results, give calculated dose of rFVIII 30 minutes to 1 hour before OR
3. Repeat STAT FVIII level after rFVIII is given
Intraoperative stage
1. Repeat TEG on arrival to OR
2. Administer heparin and TXA per normal protocol
CBP-stage
1. Monitor ACT and Hepcon HMS per standard protocol
2. Conduct CPB as per standard protocol; before weaning use Hepcon HMS to determine protamine dose
Post-CPB stage
1. Give protamine as per standard protocol based on Hepcon calculation
2. After protamine is given, repeat TEG, Hepcon and ACT to confirm no circulating heparin and restoration of baseline coagulation function
3. Administer rFVIII the based on FVIII level results:
a) FVIII >1.20 – consult hematology
b) FVIII .8–1.20 – no additional rFVIII required; repeat STAT FVIII level in 2 hours
c) FVIII .60–.80 – give rFVIII (calculated dose) and repeat STAT rFVIII level
d) FVIII .40–.50 – give rFVIII (calculated dose) and repeat STAT rFVIII level
e) FVIII <.40 – consult hematology
Postoperative stage
1. Please give the following based on final intra-operative FVIII results:
a) FVIII >1.20 – consult hematology
b) FVIII .80–1.20 – no additional rFVIII is required
c) FVIII .60–.80 – give rFVIII (calculated dose)
d) FVIII .40–.50 – give rFVIII (calculated dose)
e) FVIII <.40 – consult hematology
2. 8 hours postoperatively
a) Begin IV TXA 1,500 mg q 8 hours
3. 12 hours after the last rFVIII dose:
a) Draw routine FVIII level
b) Based on results, give rFVIII (calculated dose)
c) Repeat routine FVIII level 10–15 minutes after rFVIII dose
d) Repeat the aforementioned postoperative care steps (2a) through c) q 12 hours
4. The morning following surgery, consult hematology for ongoing monitoring and dose adjustments. Goals of care include:
a) Days 1–4:
Trough level >.50
Peak FVIII level <2.00
b) Days 5–9:
Trough FVIII level >.40
Peak FVIII level <2.00

Note: While receiving rFVIII, the patient's risk of thrombosis is the same as a nonhemophilia patient. Please follow your standard thromboprophylaxis protocols. Our standard protocol for postoperative thromboprophylaxis for patients with hemophilia following CABG is low dose aspirin (81 mg/day) for life.

and a heparin concentration ≥300 IU/kg before initiating CPB.

A midline sternotomy was performed and the left internal thoracic artery (LITA) and saphenous veins harvested. At the direction of the cardiovascular surgeon, unfractionated heparin was administered by the anesthesiologist. Tranexamic acid (TXA) (Pfeiffer Pharmaceuticals Inc., Atlanta, GA) was also given prior to CPB. An ACT greater than 480 seconds in conjunction with an adequate heparin concentration result was obtained before safely proceeding with CPB (Table 2).

CPB Stage

The extracorporeal circuit comprised a Sorin phosphorylcholine–coated (Sorin/Dideco, Mirandola, Modena, Italy) venous/arterial loop, a Trillium®-coated oxygenator with an integrated 25-μm arterial filter, and an open hard-shell venous reservoir (Fusion®, Trillium®, Medtronic, Minneapolis, MN). The circuit was primed according to institutional protocol with 2 L of Plasmalyte A (Baxter, Mississauga, Ontario, Canada), 10,000 IU of heparin (Sandoz Heparin®; Boucherville, Quebec, Canada), 100 mL of 25% albumin (Grifols Biologicals, Inc., Los Angeles, CA), 50 milliequivalents (50 mL) of sodium bicarbonate (Hospira, Montreal, Quebec, Canada), and 2.5 mL/kg (233 mL) of 20% mannitol (Hospira) for a total volume of 2,395 mL.

Following cannulation for CPB, retrograde autologous priming was performed to reduce the prime to 600 mL. Blood products were readily available with two units of red blood cells in the OR during the procedure. Our massive transfusion protocol was also available upon request. The patient was placed on CPB and cooled to 30°C. CPB was uneventful using laminar, nonpulsatile flow with a cardiac index ranging between 2.4–2.6 L/min. The ACTs and heparin concentrations during CPB are shown in Table 2. Additional heparin was given to maintain the ACT levels above 480 seconds and the heparin concentration above ≥ 300 μ/kg.

The aorta was cross-clamped and warm blood followed by cold blood cardioplegia (Myocardial Protection System®, Quest Medical, Allen, TX) was administered antegradely, retrogradely, and through the grafts as they were completed. CABG × 5 was performed, including saphenous vein grafts to the RCA, the diagonal, and a natural branch sequential graft to the ramus and obtuse marginal vessels. The LITA was anastomosed to the LAD. Total cross clamp time was 99 minutes. The patient was hemodynamically stable throughout the CPB period and was rewarmed to 36.8°C. He separated easily from CPB on dopamine (5 mg/kg/min) and nitroglycerin (100 μg/mL) drips. Total CPB time was 127 minutes.

Post-CPB Stage

Post-CPB, the patient was briefly paced but quickly regained a normal sinus rhythm and remained stable. The venous cannula was removed and drained into the CPB circuit. The circuit volume was reinfused and the residual volume processed by an autologous recovery system and

Table 2. Preoperative-postoperative parameters.

Parameters	Pre-op	Base-line	Pre-CPB	CPB 1	CPB 2	CPB 3	CPB 4	Post-CPB	Post-Prot	Post-op Day 1	Post-op Day 2	Post-op Day 3	Post-op Day 4	Post-op Day 5	Post-op Day 5	Post-op Day 6
Hgb (g/L)	131	127	118	93	101	94	91	91	96	113	109	99	101	104	102	103
Hct (%)	.42	38.8	36.3	28.6	30.8	29	27	27	.295	35.7	34	30.6	30.9	31.8	30.5	31.9
aPTT (sec)	59	39	–	–	–	–	–	75	46	47	44–54	46–58	47	49	47–51	44–72
INR	1	–	–	–	–	–	–	1	1.2	1.0–1.1	1–1.1	1–1.1	1	1	1	1
TXA (gm)	–	–	2	–	–	–	–	–	2	–	–	–	–	–	–	–
rFVIII (Xyntha)	5,000	–	–	–	–	–	–	2,000	–	4,000	3,500	3,000	1,500	1,000	1,000	1,000
Heparin (IU)	–	–	40,000	10,000*	10,000	–	–	–	–	–	–	–	–	–	–	–
FVIII level (U/mL)	.32	1.64	–	.86†	–	.83†	–	.81†	.83	.69–1.41	1.02–1.48	1.10–1.51	.96	1.19	.81–1.03	.74–1.12
ACT (sec)	–	150	999	999	793	999	877	–	137	–	–	–	–	–	–	–
Hepcon (μ/kg)	–	196–350	400	400	300	400	300	–	0	–	–	–	–	–	–	–
Protamine (mg)	–	–	–	–	–	–	–	412	50	–	–	–	–	–	–	–

*Prime.
†Hepzyme.
Hct, hematocrit; Hgb, hemoglobin; rFVIII, recombinant factor eight; FVIII, factor eight; pre-op, preoperative; post-op, postoperative.

returned to the patient. The protamine dose was calculated using the Hepcon HMS and administered to the patient. Table 2 shows repeat ACT, Hepcon, and FVIII levels. Figure 3 shows the patient's post-protamine TEG, demonstrating normal coagulation with a slightly prolonged, high normal R-time to clot formation. A comparison of the patient's kaolin vs. kaolin with heparinase curves (Figure 4) also confirmed that no circulating heparin was present. However, a prolonged of R-time (TEG) of 10 minutes indicated a deficiency in coagulation factor activity. Moreover, the laboratory coagulation indices were as follows: aPTT of 75 seconds, INR (international normalized ratio) of 1.0, and FVIII concentration of 0.81 units/mL. Therefore, 2,000 units of rFVIII were given to treat the reduced FVIII levels. Hemostasis was gradually achieved over a 20-minute period.

Topical warm TXA was applied to the chest cavity and the sternum was closed. Autologous cell salvage yielded 252 mL of cells, which were returned to the patient. The calculated operative blood loss was 552 mL and the patient did not require allogeneic transfusion. Chest tube losses were only 30 mL on transfer to the intensive care unit (ICU) from the OR.

Postoperative Stage

The patient was transported to ICU in stable condition and extubated early the following morning. He had an uncomplicated 2-day ICU stay before being transferred to the post-cardiac surgical observation unit. Total 24-hour chest tube losses were 554 mL. FVIII levels were monitored q-12 hours postoperatively until postoperative day 2, after which time they were monitored daily until the patient was discharged home. Additional rFVIII was given in the ICU and on the post cardiac surgical observation unit based on conventional laboratory tests until the patient was discharged. The patient received a total of 22,500 IU of rFVIII throughout his length of stay and was discharged on postoperative day 7 with an FVIII level of 0.74 units/mL. The total dose of rFVIII administered to this patient is lower in comparison with other reports that have a range between 50,000 and 95,000 units. Moreover, Behave et al. reported an average of 40,000 IU in their review of 17 hemophilia patients undergoing CPB-supported cardiac surgery over a 16-year period (10).

Comment

The World Federation of Hemophilia recommends multidisciplinary, individualized planning for Hem A patients by the health-care team in consultation with a hemophilia treatment center (15). To facilitate this patient's cardiac surgery, a comprehensive health care team met in consultation with hematology and staff from the patient's Bleeding Disorder Clinic to determine the resources required to safely provide care.

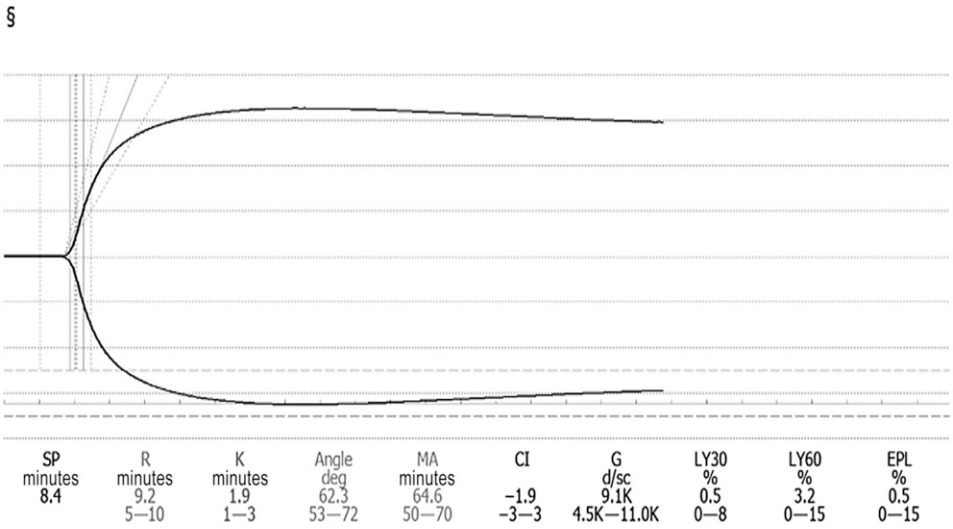

Figure 1. Baseline TEG. SP, spit point time (initial fibrin formation); R, reaction time to clot formation; K, kinetics (time taken to achieve a certain level of clot strength); Angle, measure of fibrin–platelet interaction; MA, maximum angle (clot firmness); CI, coagulation index; G, shear elastic modulus (clot strength); LY30%, amplitude at 30 minutes post-MA; LY60%, amplitude at 60 minutes post- MA; EPL%, estimated percent lysis.

Guidelines referring to the most reliable methods of monitoring FVIII therapy throughout the stages of cardiac surgery are lacking. Current data point toward TEG/thromboelastometry monitoring as an effective therapeutic strategy for optimum dosage and frequency of administration of rFVIII therapy (13,16,17). Data from the present case report suggest that, once FVIII levels have been normalized during the preoperative stage, TEG can confirm effect of treatment and the Hepcon HMS can be used during the CPB period up to heparin reversal to ensure adequate anticoagulation. The final intraoperative stage of coagulation management between reversal of heparin and the patient leaving the OR optimally uses TEG and conventional testing to guide therapy toward achieving normal coagulation with adequate hemostasis. In this case report, we present the successful use of a stage-specific combination of conventional laboratory methods and POCT for the management of a case representative of this high-risk population. The novel method of combining standard laboratory assays with TEG at precise stages of CPB-supported cardiac surgery is different from other reports that used a single method to guide coagulation therapy in this high-risk group (16). Recommendations from the International Society on Thrombosis and Hemostasis Scientific and Standardization Committee favor the measurement of the viscoelastic properties of clot formation and progression for clinical use in this patient population undergoing general surgical procedures (17). However, their report does not address the special circumstances of Hem A patients undergoing CPB-supported cardiac surgery. This case report highlights reliable methods of monitoring FVIII levels during each stage of CPB-supported cardiac surgery, thereby affording clinicians the tools for fine tuning of coagulation levels and providing the potential for enhanced care for this high-risk population.

During the *preoperative stage*, we measured plasma FVIII levels using the conventional laboratory technique of aPTT-based one-stage coagulation laboratory method (10). We also measured a baseline TEG. Based on these

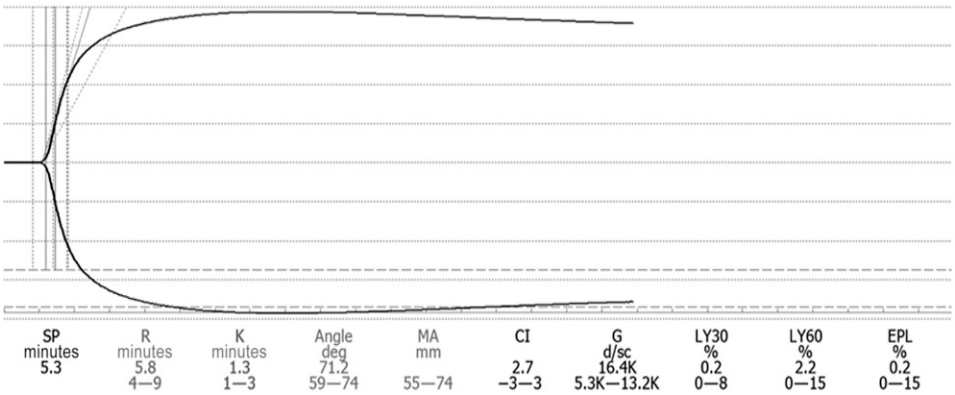

Figure 2. Post-Xyntha 5,000 U TEG. SP, spit point time (initial fibrin formation); R, reaction time to clot formation; K, kinetics (time taken to achieve a certain level of clot strength); Angle, measure of fibrin–platelet interaction; MA, maximum angle (clot firmness); CI, coagulation index; G, shear elastic modulus (clot strength); LY30%, amplitude at 30 minutes post- MA; LY60%, amplitude at 60 minutes post-MA; EPL%, estimated percent lysis.

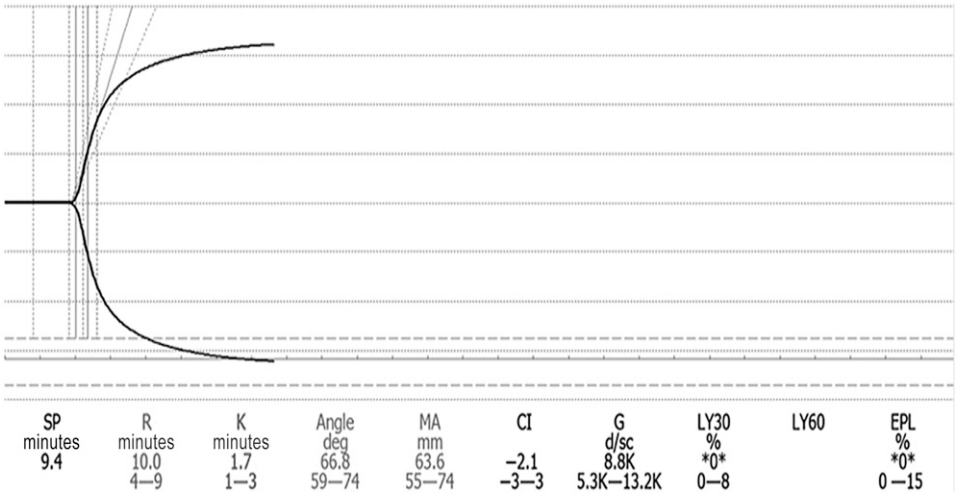

Figure 3. Post-CPB, post-protamine, post-Xyntha 2,000 U TEG. SP, spit point time (initial fibrin formation); R, reaction time to clot formation; K, kinetics (time taken to achieve a certain level of clot strength); Angle, measure of fibrin–platelet interaction; MA, maximum angle (clot firmness); CI, coagulation index; G, shear elastic modulus (clot strength); LY30%, amplitude at 30 minutes post-MA; LY60%, amplitude at 60 minutes post- MA; EPL%, estimated percent lysis.

results, a calculated dose of rFVIII was administered to normalize the patient's FVIII level. ABO blood group classification has been known to influence plasma vWF and FVIII levels (18). Specifically, Hem A patients with O-type blood have lower plasma vWF levels and lower FVIII levels, as such, patients undergoing major surgery are at risk of under-dosing of rFVIII and consequently have a higher risk of bleeding complications (18). CPB-supported cardiac surgery relies heavily on ACT measurements. Low levels of FVIII can prolong ACT measurements, and therefore, normalization of FVIII levels in Hem A patients, especially those of O blood type, is essential for the correct calculation of heparin dosing for anticoagulation pre-CPB (5). Considering that patients with Hem A have deficient thrombin generation, it has been reported that a reduced heparin dose and a low dose rFVIII replacement therapy throughout the perioperative period produce an optimal outcome for CPB-supported cardiac surgery (8). However, to date this method is not in wide spread use among published clinicians. Because low FVIII levels can falsely prolong ACT measurements there may be an additional risk of thromboembolism with this method. Our approach was to normalize FVIII levels and then proceed using standard heparinization as heparin can easily be reversed post-CPB.

As guidelines on perioperative FVIII testing during CPB-supported cardiac surgery are yet to be established, we elected to repeat the TEG and FVIII levels post rFVIII dosing to examine the effect of the dose on both global hemostasis and FVIII level. Once a normal FVIII level and normal enzymatic pathways of coagulation were confirmed, then a baseline ACT was determined and a heparin dose calculated. Ensuring a normal FVIII level is critical for obtaining accurate ACT and Hepcon results. Our institution combines the use of ACT and Hepcon HMS Plus because the ACT provides information on the heparin effect, whereas the Hepcon HMS Plus provides data regarding the heparin concentration; this in turn guides the dose of heparin needed to maintain adequate

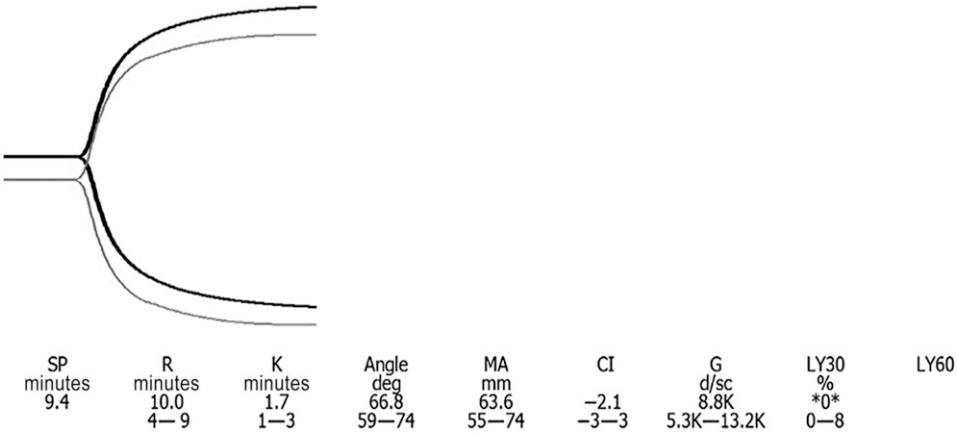

Figure 4. Comparison of TEG kaolin/TEG kaolin-heparinase curves post-CPB. SP, spit point time (initial fibrin formation); R, reaction time to clot formation; K, kinetics (time taken to achieve a certain level of clot strength); Angle, measure of fibrin–platelet interaction; MA, maximum angle (clot firmness); CI, coagulation index; G, shear elastic modulus (clot strength); LY30%, amplitude at 30 minutes post-MA; LY60%, amplitude at 60 minutes post-MA; EPL%, estimated percent lysis.

anticoagulation and the dose of protamine required for heparin neutralization (11). The combined use of the HepCon HMS Plus system and standard ACT monitoring ensures adequate anticoagulation management throughout the CPB period.

During the *CPB stage*, conventional laboratory techniques such as the aPTT-based one-stage coagulation method might not accurately measure the factor levels or coagulation parameters due to the chemical interference associated with high levels of circulating heparin (13,19). Laboratory methods that use heparinase to neutralize up to two units of heparin per mL of blood sample can lack reliability at the high heparin concentrations used for the safe conduct of CPB (5,20). Of interest is that the chromogenic FVIII assay is less likely to show interference with high levels of heparin. Our institution does not use the chromogenic assay because of costs and the longer turnaround time for results as compared with the aPTT-based one-stage coagulation method (21). Misgav et al. (13) used ACT monitoring alone for anticoagulation management during the *CPB stage*. Our method differed in that we used the combined ACT/Hepcon HMS Plus for coagulation testing during this period, thereby gaining information on both heparin effect and heparin concentration to fine-tune our anticoagulation management.

Coagulation factors can fall as much as 40% or more during CPB (5,22). Thus, measures must be taken to minimize this effect. Our prime volume was additionally reduced through retrograde autologous priming to further minimize the risk of low FVIII levels due to hemodilution. Using purposeful techniques to minimize the CPB circuit prime volume, reduce the anesthesia crystalloid volume, and ensure judicious volume replacement throughout the CPB period resulted in, our patient's post-CPB FVIII level remaining within the normal range despite falling 49% during CPB compared with the pre-CPB level.

During the *post-CPB stage* following protamine administration, the Hepcon HMS results included 0 IU/kg of circulating heparin with an ACT of 137 seconds which was below the baseline ACT of 150 seconds. The TEG R-time was longer (10 minutes), and the maximal amplitude was lower (63.6 mm) compared with baseline values. The TEG-heparinase also demonstrated a protracted TEG R-time of 10 minutes, which was consistent with the lower FVIII laboratory result. An additional 2,000 units of rFVIII were administered to ensure adequate hemostasis post-CPB. Our data are consistent with other reports in which a TEG R-time prolongation post-CPB resulted in additional administration of rFVIII (13). Gradual hemostasis was achieved with the surgeon noting that, in terms of bleeding, the chest wound appeared similar to other, nonhemophiliac patients. We submit that the normalization of FVIII levels pre-bypass and the administration of antifibrinolytics might have contributed to this observation. TXA has been reported to reduce blood loss, major bleeding, reoperation, and transfusion requirements in patients undergoing CABG with CPB (23,24); and specifically Hem A patients (25). At our institution, TXA is routinely administered following the heparin bolus and also applied topically in a solution of TXA mixed in 50 mL of warm sodium chloride gently poured into the chest wound before closure. This TXA solution is left in the wound for 10 minutes, followed by aspiration through the chest tubes (26).

A significant body of evidence supports the use of viscoelastometric POCT because of its ease of use, quick turnaround time for results, real-time–visualized monitoring, and ability to attenuate transfusions of red blood cells, fresh frozen plasma, platelets, and improve patient outcomes (16,27,28). Unfortunately, a major disadvantage of TEG is the inherent variability between repeated tests on a single sample, resulting in higher coefficient of variance (CV) values compared with standard laboratory tests that produce CV values within 5% (16). In this case report the values from viscoelastometric POCT complemented the conventional laboratory values. However, further research is needed to directly link the strategy of combined instrument guided management of FVIII levels with clinical outcomes.

The findings of this report are in agreement with Rossi et al. who suggest that favorable surgical outcomes for patients with hemophilia undergoing CPB-supported cardiac surgery can be achieved by using a team approach, a designated FVIII replacement protocol, and effective perioperative monitoring of factor levels (29).

CONCLUSION

The lack of evidenced-based guidelines complicates the management of hemophilia patients undergoing CPB-supported cardiac surgery. This case report presents an O-positive Hem A patient undergoing CPB-supported cardiac surgery in which the strategy of normalization of FVIII levels followed by usage of combined instrument guided conventional laboratory methods and POCT devices at defined stages of the surgery led to optimal perioperative management. Using the described strategy of normalizing perioperative plasma FVIII levels by replenishment with rFVIII, as well as techniques of judicious fluid administration, and antifibrinolytics, resulted in minimal differences from our other nonhemophiliac patients undergoing CPB-supported cardiac surgery. Execution of care by a multidisciplinary team facilitated a safe, smooth, clinical course and an optimal outcome for this high-risk patient.

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