Case Report

Coagulopathy After Cardiopulmonary Bypass in Jehovah's Witness Patients: Management of Two Cases Using Fractionated Components and Factor VIIa

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BACKGROUND: Changes in the Jehovah's Witness (JW) blood refusal policy now give members the personal choice to accept certain processed fractions of blood, such as factor concentrates and cryoprecipitate.
METHODS: Two JW patients undergoing complex aortic surgery who developed severe microvascular bleeding after prolonged use of cardiopulmonary bypass were treated with recombinant activated factor VII, cryoprecipitate, and antithrombin concentrate.
RESULTS: Cardiopulmonary bypass-induced coagulopathy was successfully treated, allowing chest closure without evidence of thrombotic complications.
CONCLUSIONS: Processed blood fractions can be a valuable adjuvant to drugs when treating bleeding in JW patients.
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Cardiopulmonary bypass (CPB) intervals >2.5 h are associated with life-threatening microvascular bleeding (1). This presents a clinical challenge when caring for Jehovah's Witness (JW) patients who refuse transfusion of red cells, platelets, and fresh frozen plasma. Antifibrinolytics, desmopressin, and recombinant activated factor VII (rFVIIa) have all been administered to successfully treat CPB-induced coagulopathy in these patients (2–4). However, clinicians might overlook administering blood fractions acceptable to JW patients because of the misconception that anything derived from blood is forbidden.

In June 2000, *Watchtower*, the official JW publication, defined the "primary components" of blood as red cells, white cells, plasma, and platelets (5,6). Although religious followers were instructed to continue to refuse transfusion of these specific products, individual believers could decide for themselves to accept processed fractions of the "primary components." The following cases illustrate the use of processed blood fractions, specifically cryoprecipitate and antithrombin (AT) concentrate, along with rFVIIa to treat life-threatening bleeding after complex aortic surgery.

CASE REPORTS

Case 1

A 37-year-old JW patient with Marfan's Syndrome presented for repair of an aortic root aneurysm. Given the potential for severe bleeding complications, the patient had an extensive preoperative interview with both a hematologist and the attending anesthesiologist. Although the patient refused to accept transfusion of any "primary component," he was agreeable to the use of fractionated portions of blood. Administration of albumin, cryoprecipitate, and plasma proteins, such as factor concentrates, were specifically discussed and deemed acceptable to the patient. Additional blood conservation measures included acute normovolemic hemodilution (ANH) and use of a cell-saver as previously described in JW patients (2). An aprotinin dose of 2 million kallikrein inhibitor units (KIU) was placed in the CPB pump prime, an initial loading dose of 2 million KIU was given before sternotomy, and an infusion of 500,000 KIU/h was run throughout the procedure. Heparin was administered to keep the kaolin activated clotting time (ACT)> 480 s. The aortic root was replaced with a valved conduit, and the coronary arteries reimplanted after a CPB time of 155 min. After separation from CPB, protamine administration, and reinfusion of the ANH blood, the ACT was 118 s. Unfortunately, repair of severe surgical bleeding required reheparinization and CPB reinstitution for an additional 139 min. After the total CPB time of 294 min, diffuse microvascular bleeding persisted, despite the administration of 300 mg of protamine. Laboratory values showed hematocrit 23%,

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platelet count 63×10^3 mm^{-3}, and fibrinogen 69 mg/dL. To support hemostasis, 20 U of cryoprecipitate were administered, followed by 7.2 mg of rFVIIa (90 μg/kg). Bleeding quickly slowed sufficiently for chest closure. Transesophageal echocardiography at the time did not show evidence of intracardiac or intravascular thrombus formation. In the intensive care unit, AT activity level was 13%. To prevent potential thromboembolic sequelae, 620 U of AT concentrate were administered. Chest tube drainage was one liter over the next 24 h and the hematocrit remained stable at 20%. The patient was transferred from the ICU on the 10th postoperative day without evidence of thrombotic events.

Case 2

A 57-year-old JW patient presented for ascending aortic aneurysm repair. As with the preceding case, intraoperative blood conservation included ANH, cell-saver, aprotinin administration, and preoperative consent for use of selected processed blood fractions. Replacement of the ascending aorta required 183 min of CPB. After protamine and ANH blood re-infusion, the ACT was 137 s, but persistent microvascular bleeding prevented chest closure. Laboratory results showed hematocrit 20%, platelet count 61×10^3 mm^{-3}, and fibrinogen level 122 mg/dL. Ten units of cryoprecipitate were administered before 9.6 mg of rFVIIa (110 μg/kg). Hemostasis was rapidly achieved and chest tube drainage over the next 12 h was <500 mL. AT levels before and after rFVIIa were 40% and 38%, respectively, with no evidence of thrombus seen on transesophageal echocardiography. The patient was transferred out of the intensive care unit on the first postoperative day and showed no evidence of prothrombotic events.

DISCUSSION

Our two cases describe successful hemostasis management with rFVIIa and processed blood fractions in JW patients after prolonged CPB. Although new JW doctrines still forbid believers to accept transfusion of the four "primary components," defined as red cells, white cells, platelets, and plasma, individual members are allowed to decide for themselves regarding the use of recombinant or processed fractions of blood components. Our use of cryoprecipitate, rFVIIa, and AT concentrate safely reversed life-threatening coagulopathy and likely contributed to the good outcomes of these patients.

Prolonged CPB is associated with platelet dysfunction, activation of fibrinolysis, and depletion of coagulation factors (7,8). Administration of rFVIIa promotes hemostasis by binding to exposed tissue factor at vascular injury sites to initiate thrombin generation. This leads to an amplification of thrombin production, increased platelet adhesion, and cleavage of fibrinogen to form a clot (9). Fibrinogen is critically important in stabilizing the hemostatic plug via this thrombin-mediated fibrin formation, and thus repletion of fibrinogen may improve the efficacy of rFVIIa. Cryoprecipitate is a highly concentrated source of fibrinogen: 10 pooled units (50 mL) contain about 150 times more than a 250 mL bag of fresh frozen plasma. Additionally, cryoprecipitate contains high concentrations of factor VIII and Von Willebrand factor, which further enhance platelet adhesion and coagulation. The dose of rFVIIa for bleeding in cardiac surgery has not been established, but the dose in our cases is similar to the empirical dose (90–120 μg/kg) used to treat acute bleeding episodes in patients with hemophilia (10).

Although rFVIIa is presumed to act only at sites of local tissue injury, a concern with its administration in cardiac surgical patients is that tissue factor is exposed at graft anastamoses, which could lead to prothrombotic complications. A recent review of 20 case reports of rFVIIa use following CPB found a 10% incidence of thromboembolic events (11). After prolonged CPB, there is likely a delicate balance between depleted procoagulant factors and anticoagulant proteins, such as AT, protein C, and thrombomodulin. AT activity levels routinely decrease to 40%–60% after CPB without complications, however, catastrophic thrombosis has been reported with activity levels <20% (12,13). We routinely monitor AT activity in high-risk patients (CPB times >3 h, circulatory arrest cases, patients septic from endocarditis). Although there is currently no consensus as to when AT replacement is beneficial, we favor the administration of AT concentrate (500–1000 U) when activity levels become severely low in the presence of antifibrinolytic drugs. The potential drawbacks include cost and enhancing any residual heparin not neutralized with protamine.

In summary, we described two episodes of successful hemostasis management with rFVIIa and selected processed blood fractions in JW patients after prolonged CPB. Physicians should be aware of pharmacologic options and thoroughly discuss which processed blood fractions are acceptable to each individual in this patient population. Further studies are needed to evaluate the safety and efficacy of combining rFVIIa with additional fractionated blood products, including fibrinogen concentrate, and prothrombin complex concentrates.

REFERENCES

1. Despotis GJ, Filos KS, Zoys TN, et al. Factors associated with excessive postoperative blood loss and hemostatic transfusion requirements: a multivariate analysis in cardiac surgical patients. Anesth Analg 1996;82:13–21.
2. Moskowitz DM, Perelman SI, Cousineau KM, et al. Multidisciplinary management of a Jehovah's Witness patient for the removal of a renal cell carcinoma extending into the right atrium. Can J Anaesth 2002;49:402–8.
3. Beholz S, Liu R, Thoelke R, et al. Use of desmopressin and erythropoietin in an anaemic Jehovah's Witness patient with severely impaired coagulation capacity undergoing stentless aortic valve replacement. Perfusion 2001;16:485–9.
4. Tanaka KA, Waly AA, Cooper WA, Levy JH. Treatment of excessive bleeding in Jehovah's Witness patients after cardiac surgery with recombinant factor VIIa (Novoseven). Anesthesiology 2003;98:1513–15.
5. Watch Tower Bible and Tract Society. questions from readers. Watchtower 2000;June 15:29–31.
6. Muramoto O. Bioethical aspects of the recent changes in the policy of refusal of blood by Jehovah's Witnesses. BMJ 2001;322:37–9.

7. Greilich PE, Brouse CF, Beckman J, et al. Reductions in platelet contractile force correlate with duration of cardiopulmonary bypass and blood loss in patients undergoing cardiac surgery. Thromb Res 2002;105:523–9.
8. Hunt BJ, Parrat RN, Segal HC, et al. Activation of coagulation and fibrinolysis during cardiothoracic operations. Ann Thorac Surg 1998;65:712–18.
9. Lisman T, Adelmeijer J, Cauwenberghs S, et al. Recombinant factor VIIa enhances platelet adhesion and activation under flow conditions at normal and reduced platelet count. J Thromb Haemost 2005;3:742–51.
10. Hedner U. Dosing with recombinant factor VIIa based on current evidence. Semin Hematol 2004;41:35–9.
11. DiDomenico RJ, Massad MG, Kpodonu J, et al. Use of recombinant activated factor VII for bleeding following operations requiring cardiopulmonary bypass. Chest 2005;127: 1828–35.
12. Avidan MS, Levy JH, Scholz J, et al. A phase III, double-blind, placebo-controlled, multicenter study on the efficacy of recombinant human antithrombin in heparin-resistant patients scheduled to undergo cardiac surgery necessitating cardiopulmonary bypass. Anesthesiology 2005;102:276–84.
13. Heindel SW, Mill MR, Freid EB, et al. Fatal thrombosis associated with a hemi-fontan procedure, heparin-protamine reversal, and aprotinin. Anesthesiology 2001;94:369–71.