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Abstract

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Keywords

coronary artery disease, coronary artery bypass grafting, hemophilia A

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Coronary Artery Bypass Grafting in a Patient with Hemophilia A

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Abstract

With advances in care, the median age for the mild-moderate hemophilic patients has almost reached parity with the general population. However, they have a much higher rate of cardiovascular disease than their peers. The authors here present a successful case of a patient with mild hemophilia undergoing coronary artery bypass grafting (CABG) and summarize the recommendations surrounding the management of hemophilia in the perioperative setting.

Introduction

Hemophilia A is an x-linked inherited deficiency of factor VIII that is clinically manifested by excessive or spontaneous bleeding. As the clinical management has improved, the median life expectancy for patient with hemophilia has increased from 7.8 years in 1930s to 75 years in 1990s among mild-moderate disease states.^{1,2} At the same time, patients over age 35 with hemophilia experienced approximately twice the prevalence of coronary artery disease (CAD), stroke and myocardial infarction (MI) when compared to a non-Hispanic white male population.³ Since the guidance of perioperative management of the cardiac surgical patient with hemophilia is currently limited to case reports, it is important to continue to report these cases. Many procedures required for the treatment of cardiovascular disease require some degree of anticoagulation, which can be very challenging in this population. Management of anticoagulation in patients that require cardiac surgery and cardiopulmonary bypass (CPB) can be extremely complex. There are currently no guidelines to direct the hematologic management of patients in this scenario. We present one case that describes the perioperative management of a patient with mild hemophilia A undergoing coronary artery bypass graft (CABG) with CPB.

Case

This patient is a 41-year-old male with past medical history significant for hemophilia A with recently diagnosed CAD scheduled to undergo five-vessel-CABG with CPB. A random pre-operative factor VIII level was 45%. After consultation with hematologist, the following peri-operative management plan

was devised for the patient and summarized in Table 1. It was recommended that the patient should receive a bolus of recombinant factor VIII in preoperative phase followed by a low dose infusion intra and postoperatively to maintain a goal of factor VIII activity between 80-100%.

A random factor VIII level test on the morning of surgery was noted to be 15% (Fig. 1). The patient received a bolus of recombinant factor VIII (45 IU/kg) pre-operatively that was followed by an infusion of 4 IU/kg/hr. His factor VIII activity increased to 84% prior to incision. In addition, 450mL of autologous whole blood which was anticoagulated with an adenosine-calcium-dextrose solution was collected into a storage bag prior to incision. The pre-CPB period was uneventful and as decided preoperatively, an additional bolus of 25 IU/kg of factor VIII was administered prior to initiation of CPB. The additional bolus dose was used to maintain circulating

factor levels in the setting of hemodilution from the CPB priming volume, which was approximately 800 ml. Aminocaproic acid infusion was used throughout the case at 1 gram/hour as standard thrombolytic prophylaxis. Heparinization was completed per our institutional protocols with 400 units/kg. Multiple thromboelastograms (TEG) were also drawn intraoperatively to help guide the need for transfusions. The surgical course was uncomplicated until significant, diffuse bleeding and hypotension occurred during the initial attempt at separation from CPB. The factor VIII activity, as drawn immediately before heparinization, was 105% but could not be reassessed whilst on CPB due to heparin interfering with the laboratory assay for Factor VIII activity. Presuming that the factor activity was low, and recognizing the inability to determine activity, the patient was returned to CPB. In addition, the factor VIII infusion was increased to 5 IU/kg/hr and the patient also received one unit of autologous

Table 1. Major Considerations during Pre-operative Planning

Pre-Op	<ul style="list-style-type: none"> Recombinant factor VIII 45 IU/kg bolus pre-operatively Calculated as $(100-15) \times 0.5 = 42.5$ (rounded by pharmacy to 45 IU/kg)
Intra-Op	<ul style="list-style-type: none"> 3 IU/kg/hr infusion intra and post-operatively, can be increased by 1 IU if needed Considering the increased volume of distribution, another bolus of 25IU/kg was administered after discussing the effect that CPB priming solution and CPB circuit would have on the circulating blood volume Draw random post-operative level
Post-Op	<ul style="list-style-type: none"> Goal 80-100% factor VIII activity for first 3 days Day 4-10: 30 IU/kg q12-24h Day 11-14 (or longer based on wound healing): 20-30 IU/kg q12-24h

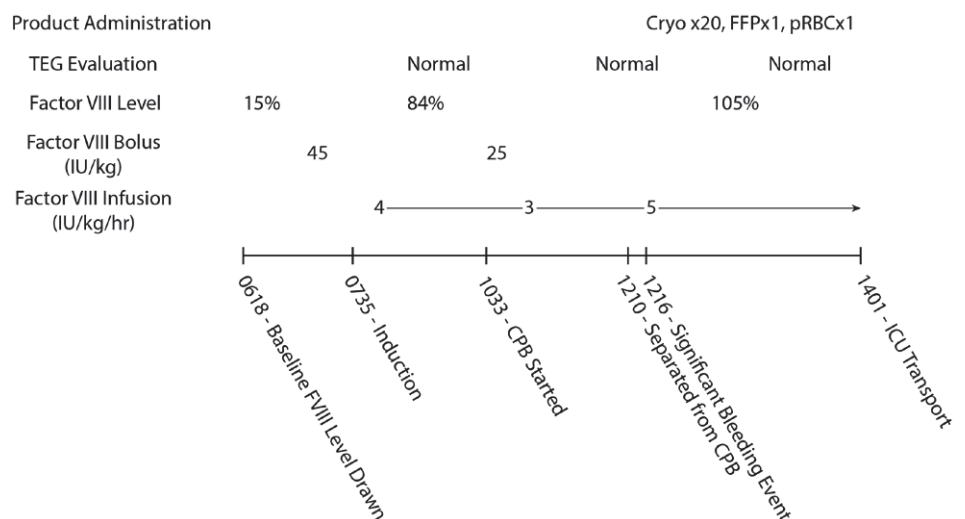


Figure 1. Illustrations of perioperative interventions and pertinent lab results.

red blood cells (RBCs), fresh frozen plasma (FFP), and two units of cryoprecipitate. After control of bleeding, the patient was then able to be separated from CPB without incident. The total blood loss for the case was 2 L, and 1L of cell saver was returned to patient (Fig.1). Factor VIII activity was 124% on post-operative (POD) day 1 and remained >100% through POD #3, at which time the infusion was stopped and bolus dosing was resumed. One unit of packed red blood cell (PRBC) was administered on POD 3, and no additional blood product was needed afterward. He remained on bolus factor VIII regimen through POD #12. Patient consent was obtained to utilize this case for educational purposes.

Discussion

Various regimens of recombinant factor VIII administration have been reported, ranging from several bolus doses to a combination of bolus doses and continuous infusions with targets of factor VIII trough levels or activity levels.⁴ Despite what should have been adequate factor activity levels, increased rates of bleeding still occur in this patient population as noted in our patient. In one study, 12% of the studied population had

to undergo re-operation due to bleeding complications as compared to 1.9% of patients undergoing CABG without a bleeding disorder.⁵ Antifibrinolytics such as tranexamic acid, or aminocaproic acid should also be considered as adjuvant for hemostasis, as it has been shown to improve the clot stability in hemophilia A patients when combined with recombinant factor VIII treatment.⁶

It is critically important to have a plan in place prior to proceeding with a high-risk operation. In this case, the anesthetic team was identified in advance and consultation with hematology was done to establish baseline activity levels and develop an approach to address bleeding. Specifically, we calculated an initial bolus dose based on the difference of measured Factor VIII activity and the desired Factor VIII activity of 100% multiplied by 0.5, which corrects for the volume of distribution. In addition, plans for blood product utilization and testing was important to help with monitoring the patient. Discussions with the laboratory personnel allowed them to have adequate reagent on hand to do the number of tests needed and the understand the limitations of the assay, such as the presence of heparin interfering with assay results. As well, it is important to consider all potential sources of

coagulopathy during surgery, especially the dilutional and consumptive processes that are inherent to the use of CPB. Discussion with the perfusion team was important to limit the CPB prime and control the amount of fluids given on CPB as they would likely impact the circulating Factor VIII levels and its activity. It is also important not to forget the possibility of development of factor VIII inhibitors. The need to continue to study this specific patient population to ensure their safety during cardiac surgery remains.

The mainstay treatment for patient with hemophilia undergoing surgery is replacement of deficient factor using specific factor concentrates.⁷ Correction of deficient factor level to 80-100% of normal is preferred prior to incision to achieve adequate hemostasis.⁸ In this case of a mild hemophilia A patient undergoing cardiothoracic surgery, once adequate hemostasis is achieved via a combination of bolus and continuous infusion of recombinant factor VIII, the peri-operative management is not significantly different from patients without hemophilia. This experience demonstrated the importance of multidisciplinary consultation and preoperative planning for the care of complex patients undergoing major surgery. ■

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