Successful Aortic Valve Replacement Surgery in a Patient with Severe Haemophilia a with Low Titre Inhibitor

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Abstract In spite of the modern day innovations, managing severe Haemophilia patients with inhibitors continues to be a challenge. The management of patients with severe haemophilia with inhibitors who are undergoing major surgeries like open heart surgery is technically demanding, fraught with peri-operative complications and needs a multidisciplinary approach. We describe a young man with severe haemophilia with low titre inhibitors who underwent a successful open heart surgery and aortic valve replacement, supported only with bolus doses of Factor VIII and tranexamic acid without any complications.

Keywords Haemophilia · Inhibitors · Cardiac surgery · Aortic valve replacement

Introduction

Cardiac surgery is unique amongst all the surgeries performed as far as the coagulation management is concerned. Major surgery, complexed with use of intraoperative heparinization, use of extracorporeal circulation system, and cardioplegia gives rise to many coagulation abnormalities.

Instances of severe coagulopathies arising intra- or post-operatively are not uncommon in patients undergoing cardiac surgery. The valve replacement surgeries form a special situation amongst the cardiac surgeries for the types of valves used and the need for tight anticoagulation postoperatively [1, 2]. This could pose an extremely challenging task in patients with severe haemophilia as the haemostasis has to be balanced with anticoagulation. There are reports of valve replacement surgeries done in moderate to severe haemophilic patients [3, 4]. Most often tissue valves are used and many a time postoperative anticoagulation is not given [5]. With a multidisciplinary team approach the morbidity and mortality of cardiac surgeries in haemophilia patients have substantially reduced. However, there are only a few instances of performing cardiac surgery in severe haemophilia patients with presence of inhibitors [6]. Here we describe a patient of severe haemophilia with low titre inhibitors, successfully undergoing aortic valve replacement under the cover of recombinant factor VIII support only without any intra- or post-operative complications. To the best of our knowledge, this seems to be the first case report of severe haemophilia A with low titre inhibitors successfully undergoing prosthetic aortic valve replacement surgery.

Case Report

History

A 23-year-old young patient, known case of severe haemophilia, was referred to our centre for the management of rheumatic heart disease with breathlessness and palpitations with NYHA class 3. On evaluation, he was found to have severe aortic regurgitation necessitating aortic valve

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replacement surgery. Patient was admitted and a multi-disciplinary team comprising of cardiac surgeons, haematologist, anaesthetists, transfusion physician, critical care specialist, physiotherapist and nursing staff was formed to manage the patient. The local Haemophilia Society came to the assistance of patient with full supply of recombinant factor VIII.

Inhibitor Profile

Patient's baseline factor VIII levels were $<1\%$ and he had baseline factor VIII inhibitor levels of 2.8 BU. An initial bolus dose of 2,000 U of factor VIII given did not elicit any anamnestic reactions.

Peri-operative Management

The patient was given a bolus dose of recombinant factor VIII, 6,000 IU 1 h before surgery. A 15 min post-dosing factor VIII assay was done to ensure increment in factor levels (83.7 %). Patient was taken up for surgery with assistance of extracorporeal circulatory support. Patient's deformed valve was replaced with bio-prosthetic valve in order to avoid post surgical long term anticoagulation. After the surgery another dose of 2,000 U of factor VIII was given. Factor VIII levels were done on daily basis and accordingly dose of factor VIII was titrated. First 3 post-operative days he was given 2,000 IU of factor VIII twice daily and thereafter it was tapered over next 10 days depending on his recovery. Figure 1 demonstrates the postoperative factor VIII support till day 14. Patient was managed with a factor VIII level above 80 % in the initial 4–5 days and then was maintained at around 40 % for next 5 days. In view of rapid recovery without any complications, factor VIII doses were tapered rapidly, only to maintain a factor VIII level of above 5 % from day 10

Fig. 1 Total dose of factor VIII used during the post operative period charted on a daily basis. The total dose was given in two equal doses 12 h apart from day 1 onwards

Fig. 2 Factor VIII levels during the post operative period charted on daily basis

onwards. Figure 2 demonstrates the factor VIII levels during peri-operative period. A total of 38158 IU of recombinant factor VIII was used for the patient. Patient was given tranexamic acid from day-1 to 14 of the surgery. Patient was given IV Heparin infusion for first 48 h and then switched to LMWH, which was given for 10 days. Patient had an excellent post operative recovery. He was extubated on day 1 of surgery with removal of ICD tubes by day 3 with total ICD drain less than 600 mL, and healing of sternotomy wound within 10 days. Patient was discharged on 15th post operative day in a stable condition. Patient was not given any kind anticoagulation on discharge. 1 year following the surgery, patient is doing well with normal aortic valve function without any complications.

Discussion

Generally, maintenance of factor level between 100–150 % is desired during cardiac surgery and in initial 10–14 days post-surgery [5]. However, to maintain that levels of factor VIII, huge doses of recombinant factor VIII are required. In an otherwise healthy young patient who is undergoing elective cardiac surgery, maintaining factor levels more than 100 % may not be needed for adequate haemostasis. Our patient had excellent haemostasis with factor levels maintained above 80 % in the initial 5 days followed by around 40 % for next 5 days. This would surely reduce the costs involved with such surgeries due to reduced factor VIII usage. Our patient needed around 30–40 % less factor VIII doses as compared to the previous reports [7]. Though there are no clear cut evidence based guidelines on mode of factor replacement, general consensus is to give a continuous infusion of Factor VIII after a bolus dose and titrated to keep factor VIII levels above 100 % [7]. This method is supposed to reduce the inhibitor development and avoids

the risk of break through bleeding episodes during trough levels of factor VIII. However this may not be entirely true, as there are instances of managing patients with severe haemophilia with intermittent bolus doses of recombinant factor VIII levels without any complications [4, 7]. The main drawback of using a continuous infusion would be the requirements of large quantities of factor VIII which can be a limitation in a country with limited resources like ours. Hence we decided to manage the patient with intermittent bolus doses with daily monitoring of trough levels of factor VIII. The trough levels were maintained above 5 %. Managing Haemophilia patients with low titre inhibitors can be tricky as the titre levels can jump during the peri-operative period. Hence it would be prudent to have back up of Activated Prothrombin complex concentrates and/or activated recombinant factor VII for emergency management of bleeding. Since our patient did not show anamnestic reaction, and since there was good increment in factor VIII levels with each dose of factor VIII, we did not repeat inhibitor levels. There was no necessity for the use of activated factor VIIa or activated prothrombin complex concentrates at any point during or after the surgery. Optimal coagulation was reflected by a smooth and rapid postoperative recovery. There is no consensus on post-operative anticoagulation in patients who got prosthetic valves. Initial case reports mention the use of warfarin in the first 3–6 months after the surgery along with factor VIII supplements and a very close monitoring of APTT and PT [7]. This approach is very complex and fraught with complications like life threatening haemorrhages if not managed properly. However instances of avoiding anticoagulation post-valve replacement can be encountered in the literature [4, 5, and 7]. Here we did not give the patient any form of anticoagulation post-operatively. At 1 year post-surgery patient is fine with adequate valve function. This is reassuring for physicians working in countries where education among patients regarding the importance of oral anticoagulation is low. Unlike the predisposition for coronary artery disease in haemophilia patients, the chances of prosthetic valve dysfunction are extremely low, especially when baseline factor levels are <1 % [5]. However it is important to note that the anticoagulation can be avoided only in cases of bio-prosthetic valve replacements, and not in metallic valve replacements. Prosthetic valve produces a severe challenge on thrombohemorrhagic balance. Generally anticoagulation in haemophilia patients in western countries has been given along with factor replacement therapy under various circumstances. Although this is

rational for a developing country like ours it may not be always feasible for financial reasons to give these patients regular factor replacement [8, 9].

Conclusions

Cardiac surgery in severe haemophilia patients with low titre inhibitors can be accomplished safely with bolus doses of recombinant factor VIII. Adequate haemostasis can be achieved with factor levels maintained above 80 % in the initial post-operative period followed by a rapid taper depending on patient recovery over next 2 weeks to reduce the cost involved. Prosthetic valve is preferred for valve replacement surgeries and post-operative anticoagulation is not necessary.

Disclosures The authors report no declarations of interest and no competing interests.

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