Case report

Undergoing cardiopulmonary bypass using enoxaparin only during a cardiac transplantation procedure

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Abstract

The use of enoxaparin as a replacement drug to standard heparin, for anticoagulation during extracorporeal circulation, in patients with heparin-induced thrombocytopenia, is still very limited. Enoxaparin significantly reduces thrombin formation and activity during cardiopulmonary bypass. The prolonged circulating rate, slow elimination rate and non-total reversion of enoxaparin by protamine can induce important postoperative bleeding. We are describing the first case of cardiac transplantation where enoxaparin was used as a replacement drug to standard heparin.

Keywords: Enoxaparin; Cardiac transplantation; Heparin-induced thrombocytopenia

1. Introduction

Enoxaparin, a low molecular weight heparin (LMWH), already demonstrated to be a safe and effective alternative to standard heparin in unstable coronary artery disease, but its use for undergoing CPB is still very limited [1–3]. Some authors do not indicate the use of enoxaparin because of significant blood loss [1] or because of possible cross-reactivity in cases with heparin-induced thrombocytopenia (HIT) [3]. The biodistribution and pharmacocinetics of standard heparin and enoxaparin are almost similar, except the anti Xa plasma half-life that is three times longer for enoxaparin [4]. Enoxaparin has a prolonged circulating time and the rate of plasma clearance is slower compared with heparin [5]. We are describing the first case of cardiac transplantation (CT) where enoxaparin was used as a replacement drug to standard heparin.

2. Case report

A 40-year-old man with an 8-year history of idiopathic dilated cardiomyopathy, 5-year history of diabetes, was admitted for acute heart failure. The right heart catheterism demonstrated a CI of 1.4 l/min per m², CO 2.6 l/min, wedge pressure of 25 mmHg, PAP (51–25 mmHg) and pulmonary resistance of 3.8 Wood units. He was accepted at CT waiting list. The transthoracic echocardiography revealed a LVEDD of 70 mm, LVEF of 18%, and presence of a thrombotic mass at the left atrium that treated with heparin. After 4 h the patient presented cutaneous allergic reactions (cutaneous eritema), hypotension, thrombocytopenia (65 × 10³ platelets/l). Clinical score according Greinacher [6] resulted to be 6, demonstrating a probable HIT II. It was initiated treatment with warfarine (for 3 months) immediately after withdrawal of heparin. Patient was found to tolerate enoxaparin without cross-sensitivity. The subcutaneous and intravenously (i.v.) tests for enoxaparin allergy resulted negative.

Six months later the patient underwent CT. A total dose of 25 000 UI of enoxaparin (Clexane; Rhone–Poulenc Rorer) was administered i.v.. The activated clotting time (ACT) was 182 s. It were adjuncted two other doses of 10 000 UI each of enoxaparin. The ACT before cannulation resulted to be 479 s. CT was performed according the bivacual technique. The clamping time was 74 min. At the end of CPB 500 mg of protamine were given and contemporary the remaining blood in the CPB circuit was retransfused. The ACT resulted 172 s at time of decannulation. During hemostasis the patient manifested important blood loss and significant hypotension. Eight units of fresh-frozen plasma (FFP) and 3 units of packed red blood cells...
We were not able to tolerate enoxaparin i.v. without cross-sensitivity. This was unexpected because enoxaparin is derived from unfractionated porcine heparin.

The prolonged circulating time, non-total reversion by protamine, which can reverse only 60% of the circulating LMWHs, and slower elimination of enoxaparin, increase the risk for postoperative bleeding. Other studies demonstrated that enoxaparin (100 UI/kg) causes a near-complete abolishment of platelet-dependent cyclic flow reductions, increment significantly the anti-Xa levels, anti-IIa levels, increase aPTT and template bleeding time significantly higher than heparin [7]. The impaired hepatic function found preoperatively (Table 1), due to end-stage failure, associated with an altered coagulative status was an adjunctive risk factor for significant bleeding. 4 h after protamine the ACT returned on its normal values even that bleeding continued during the first 24 postoperative hours. Other studies [3,6–7] demonstrated normal ACT values only 3 h after protamine, however, bleeding time was still prolonged during the first 24 h. Direct inhibition of platelet function by enoxaparin or activation of platelets by enoxaparin–protamine complexes that are slowly cleared, may interfere with platelet function and prolonged bleeding times. It seems that ACT alone, can not provide a precised monitoring of the anticoagulation effects of enoxaparin.

3. Discussion

HIT is a rare occurrence represented in two types: HIT I is characterized by a transitory reduction in platelets count; HIT II is characterized by a significant thrombocytopenia, cutaneous allergic manifestations, thrombosis. The patient's clinical manifestations indicated a probable HIT II, but we were not able to demonstrate in vitro, the heparin-dependent anti-platelets antibodies. In these cases, standard heparin has to be contraindicated because of the severe allergic reactions after CPB. Other alternatives as r-hirudin and heparinoid have been investigated, but none of them reduced the generation or activity of thrombin. In contrast, enoxaparin reduces significantly thrombin formation [7] and activity during CPB but does not suppress complement activation [8]. Other studies demonstrated that prostaglandins were most effective when they were administered as a supplement to heparin [9]. Partial neutralization of enoxaparin by protamine reduces the postoperative bleeding compared with no reversion of r-hirudin, which is associated with prolonged bleeding after CPB [10]. It is demonstrated that enoxaparin led to increased α-TNF and interleukin-β inducing vasodilatation and endothelial cells dysfunction.

4. Conclusion

The enoxaparin therapy permits to undergo CPB. Partial neutralization of enoxaparin by protamine compared with no reversion of other alternative drugs makes enoxaparin the drug of choice in patients with HIT undergoing cardiac operations that can tolerate LMWHs without cross-reactivity.

References


[2] Ganjoo AK, Harloff MG, Johnson WD. Cardiopulmonary bypass for heparin-induced thrombocytopenia: management with a heparin-


