

Anticoagulation during Cardiopulmonary bypass in Patients with Heparin-Induced Thrombocytopenia using Heparin and the Platelet Glycoprotein IIb-IIIa Antagonist

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Received date: 31 Mar 2016; Accepted date: 18 Apr 2016; Published date: 22 Apr 2016.

Citation: Nandate K (2016) Anticoagulation during Cardiopulmonary bypass in Patients with Heparin-Induced Thrombocytopenia using Heparin and the Platelet Glycoprotein IIb-IIIa Antagonist. *J Clin Anesth Manag* 1(3): doi <http://dx.doi.org/10.16966/2470-9956.109>

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Introduction

Heparin induced thrombocytopenia (HIT) is a potentially devastating prothrombotic disease associated with heparin therapy usually occurring after five days or more of therapy [1]. When heparin binds to platelet factor 4 (PF4), a heparin-binding protein stored on platelets, an epitope is exposed by a conformational change in PF4. Susceptible patients develop an Immunoglobulin G (IgG) along with IgA and IgM antibody to the heparin-PF4 epitope and upon binding to the heparin-PF4 epitope the antibody forms an immune complex on the surface of platelets. The fragment c (Fc) portion of the IgG then activates the platelet, which cause microparticle release that promotes thrombin formation. Furthermore, thrombin enhances further platelet activation, release of PF4, and perpetuation of a prothrombotic state. After a patient has formed HIT antibodies, they are susceptible to HIT until they become antibody negative. Fortunately, this time is relatively short, as the average half-life of these antibodies is three months. However, urgent surgery with cardiopulmonary bypass (CPB) for patients with acute HIT is very challenging.

We described the successful anesthesia management of emergency pulmonary thromboendarterectomy for a patient with acute HIT with use of tirofiban, a platelet glycoprotein IIb- IIIa antagonist and heparin.

Case

A patient was a 60-year-old male who initially presented to an outside hospital with right knee pain and underwent incision and drainage for a diagnosis of a septic joint. Two days after this treatment, femoral vein thrombosis was observed and an inferior vena cava filter was placed and a heparin infusion was initiated. The next day, the patient started complaining of chest pain and dyspnea. Spiral computed tomography (CT) of the chest revealed multiple pulmonary emboli, and transthoracic echocardiography showed an atrial mass which was bugling through the tricuspid valve. He was diagnosed with acute pulmonary embolism.

He was transferred to our institution. On arrival, heparin-induced thrombocytopenia (HIT) was suspected due to a greater than 50% decrease in platelet count (from 213,000 to 84,000/ μ L) after being on heparin. Argatroban was given as an alternative and continued at 8-10 mcg/kg/min until one hour before the surgery was initiated. Laboratory studies for HIT were not obtained pre-operatively because results would not be available in time to impact care. His vital signs were relatively stable, but the removal of the apparent atrial thrombus was urgently needed with use of cardiopulmonary bypass (CPB).

General anesthesia was induced based on our department standard with intravenous technique consisting of etomidate (0.5 mg/kg) and fentanyl (2.5 μ g/kg). Tracheal intubation was facilitated with use of rocuronium (0.6 mg/kg). Monitoring included left radial arterial line and double lumen central line through the right internal jugular vein. General anesthesia was maintained with use of midazolam (total 10 mg), fentanyl (total 30 μ g/kg) and isofurane as needed. CPB was performed according to the hospital standard with use of non-heparin-coated lines, roller pump, and a Cobe Apex Oxygenator (Cobe Cardiovascular). At the beginning of surgery, tirofiban was given at 0.4 μ g/kg/min for thirty minutes, and the infusion rate was changed to 0.1 μ g/kg/min. Immediately before the surgeons prepared for the cannulation for ascending aorta and right atrium, a bolus of 300 IU/kg of unfractionated heparin (UFP) was administered to achieve an activated clotting time of ACT > 480 seconds. An additional 5,000 IU of UFP was given to the priming solution of CPB circuit to keep the ACT more than 480 seconds.

At the time of surgery, a large clot within the right atrium and around the junction of the inferior vena cava was found. There was also a significant amount of clot in the main pulmonary artery, and this thrombus extended beyond the pulmonary artery bifurcation. In addition, a separate clot involving the right lower lobe was also noticed by the surgeon at the time of surgery.

The first attempt to wean the patient from CPB was unsuccessful and CPB was reinstated again due to unstable hemodynamic state. Transesophageal echocardiography revealed additional clot in the right atrium and the inferior vena. After the surgical removal of this thrombus, which contained the caval filter, the patient was weaned from CPB with dopamine at 5 μ g/kg/min and epinephrine at 0.5 μ g/kg/min. Heparin was reversed with 330 mg of protamine. The continuous infusion of tirofiban was terminated at the time that protamine was administered. The patient remained in intensive care for four days until all cardiovascular support was weaned. Anticoagulation with argatroban was re-instituted immediately post-operatively after the confirmation of hemostasis was verified in ICU.

The patient received no blood products during the surgery, but received a dose of platelets (6 units) and 2 units of FFP in intensive care unit (ICU).

In the postoperative period, the platelet count slowly rebounded. Both the heparin-antibody and heparin challenge serotonin release tests were obtained and found to be positive. The patient subsequently recovered and was discharged from hospital.

Discussion

Anticoagulation during cardiopulmonary bypass in patients with HIT is a complicated issue. In the elective surgery, the surgery should be delayed up to 6 months after the occurrence of HIT to allow the antibodies for heparin to disappear [2]. However, in the case of the urgent surgery, we must proceed regardless the timing of the occurrence of HIT with use of alternatives to heparin anticoagulation. As alternatives, Hirudin, low molecular weight heparin, danaproid, Ancrod and Argatoroban has been reported. However, selecting of these alternatives to heparin anticoagulation is, due to complications such as bleeding, severe hypotension and renal impairment, still controversial [3].

Among the many alternatives, we chose tirofiban plus heparin due to the superiority of monitoring the anticoagulant effect, the potential of less bleeding with the reversal of heparin, and relatively shorter half life of tirofiban effects [4,5]. Anticoagulation during CPB in patients with HIT with use of tirofiban and heparin as described here is not a new finding. Koster et al. [5] have already reported the ten cases. However, a protocol has not been well established. We found a minor difference in the dose of bolus and continuous injection of tirofiban. They started continuous infusion of tirofiban at a rate of 0.15 µg/kg/min after bolus injection (10 µg/kg), while we started tirofiban at 0.4 µg/kg/min for thirty minutes. There was one major difference between their and our protocols. They discontinued the tirofiban infusion one hour before the termination of CPB, which they could estimate. However, we did not discontinue the continuous infusion of tirofiban until we started protamine to antagonize the effect of heparin. There are two reasons why we did not follow their protocols. First, it was very difficult for us to estimate the termination of CPB period in this case. In fact, the additional clot in the right atrium found immediately after the first trial of weaning from CPB forced us to start CPB again. Secondly, considering the action and effect of tirofiban on the heparin and platelet interaction, it may be more advisable not to discontinue tirofiban until the effect of heparin is completely antagonized by protamine. We suspect that the availability of TEG to investigate the

coagulation status or thrombus formation enabled Koster et al. [5] to terminate the infusion of tirofiban earlier than we did. While we recognize the potential superiority of TEG monitoring, it is not always available, especially for the urgent case. In this case, we were able to manage the coagulation therapy solely with use of ACT and clinical findings in the surgical field.

We report the successful management of emergency acute pulmonary thrombectomy in a patient with heparin induced thrombocytopenia. We used tirofiban plus heparin as an alternative to heparin anti-coagulant during CPB in a method modified from an already reported protocol. In the setting where TEG is not available or when there is difficulty for estimating the time of weaning from CPB, our approach to coagulation therapy for CPB may be helpful.

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