



Case report

Use of Argatroban for anticoagulation during cardiopulmonary bypass in a patient with heparin allergy

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Abstract

The use of Argatroban for treatment of heparin-induced thrombocytopenia (HIT) and for percutaneous coronary intervention in patients with HIT is well described and FDA approved. The use of Argatroban for cardiopulmonary bypass remains off label and the subject of a few case reports. We report the case of a patient with a heparin allergy requiring cardiopulmonary bypass (CPB) for mitral valve replacement. Argatroban was successfully used as anticoagulation for CPB.

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1. Case report

A 70-year-old Russian male presented for mitral valve replacement for severe mitral regurgitation, confirmed by transesophageal echocardiogram, which also showed a dilated left atrium and moderate pulmonary hypertension. His past medical history included a cerebrovascular accident with no residual deficit, chronic atrial fibrillation for which he was taking coumadin, a duodenal ulcer, type II diabetes, benign prostatic hypertrophy, and bilateral cataract and glaucoma surgery. He had a myocardial infarction and PTCA in 1998. During that admission the patient developed a marked rash and itching after administration of intravenous heparin, which was documented by the medical staff. He had a known allergy to penicillins. Preoperative consultation by the allergologist was obtained and the patient underwent allergy testing for porcine heparin, which was negative. Preoperative evaluation by a hematologist did not reveal any hematological disorders. Coronary angiogram showed significant stenosis in the right coronary artery and an EF of 45%. He was admitted for surgery, having stopped coumadin five days prior. Due to his history of heparin allergy the decision was made to use Argatroban for anticoagulation during CPB.

The procedure was performed with a radial arterial line; non-heparin coated right internal jugular central venous and Swan–Ganz catheter, and transesophageal echocardiogram. The CPB circuit utilized non-heparin bonded non-coated

tubing, and a cell saver reservoir was spliced into the CPB circuit as a cardiomy reservoir. Citrate phosphate dextrose in 0.9% saline was used as anticoagulation for the cell saver circuit. The CPB circuit was primed with 4200 µg of Argatroban. The patient was given 29,400 µg (350 µg/kg) of Argatroban prior to ascending aortic and bicaval cannulation, and an infusion of Argatroban at 25 µg/kg/min was started. The celite activated clotting time (ACT) was only 230 s after 12 min, so a second bolus of 15,200 µg was given and the infusion rate increased to 40 µg/kg/min. CBP was commenced 69 min after the first dose of Argatroban with an ACT of 320 s, international normalized ratio (INR) of 9.9, PTT > 100 s, PT > 120 s. The peak ACT was 476 s on CPB. After institution of CPB, cardiac arrest was achieved by warm antegrade cardioplegia given via the aortic root, and then cold cardioplegia given via the coronary sinus. The patient's temperature was allowed to drift, reaching a minimum of 34.1 °C. The distal anastomosis of the reversed saphenous vein to the posterior descending artery was performed first. The mitral valve was replaced with a 27 mm St. Jude's mechanical prosthesis. Rewarming was commenced and the proximal anastomosis was performed. The patient was successfully weaned off cardiopulmonary bypass, with the Argatroban being stopped once cardiac activity had recommenced and the aortic cross-clamp had been removed. The total CPB time was 90 min, with the aortic cross-clamp time being 65 min. The patient was decannulated and all surgical sources of bleeding stopped. Following completion of closure, the ACT was still 305 s, and there was still a moderate amount of bleeding. Six units of fresh frozen plasma and two pooled donor units of platelets were administered with a cessation of

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bleeding. The patient also received two units of packed red blood cells post CPB in the operating room. The patient left the operating room approximately two hours after the Argatroban was stopped with an ACT of 276 s with minimal drainage from the chest tubes.

Postoperatively the patient did well. There was no neurological injury, and he was extubated on the operative night. He required rate control with digoxin and metoprolol for his atrial fibrillation, and was anticoagulated only with coumadin starting on postoperative day two. He was discharged on postoperative day nine when his INR became therapeutic.

2. Comment

The FDA approved Argatroban in June 2000 for treatment of thrombosis in patients with heparin-induced thrombocytopenia (HIT), and for use in percutaneous coronary intervention (PCI) in patients with HIT. Its use as an anticoagulant for cardiopulmonary bypass remains off-label. There are a few reported cases in the literature of its use as an anticoagulant in patients with HIT undergoing cardiopulmonary bypass for cardiac surgery [1–3].

This patient had a documented history of an allergic reaction to heparin, and we chose to use Argatroban for CPB to avoid a potential allergic reaction, although the allergy testing for porcine heparin was negative. This patient required the highest dose of Argatroban recommended for PCI (40 µg/kg/min) to achieve an adequate ACT for CPB (Argatroban prescribing information (AR:L8); available at: <http://us.gsk.com/products/assets/us>). Bleeding post CPB was corrected with administration of appropriate blood products.

We did note early signs of coagulation in the venous reservoir twenty minutes post CPB, and we, therefore, discarded 1200 ml of blood from the reservoir. In the future we will consider continuing the Argatroban infusion until all the blood in the reservoir is retransfused, rather than stopping it immediately following removal of the cross-clamp as we did in this case. However, this may delay the achievement of adequate hemostasis prior to closing. Consideration is also being given to utilizing Argatroban in the CPB circuit in case we need to return to cardiopulmonary bypass.

We decided preoperatively not to address this patient's atrial fibrillation to limit the operative time. A mechanical prosthesis was used as the patient was going to need anticoagulation for his atrial fibrillation, it would avoid a future reoperation for re-replacement of his mitral valve, and the patient's preference to have a mechanical valve.

The successful outcome of this case supports the use of Argatroban as an alternative to heparin for anticoagulation in CPB in patients with a contraindication to heparin administration.

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