

SCA 45

**ARGATROBAN FOR CARDIAC SURGERY - A CASE REPORT**

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Heparin induced thrombocytopenia (HIT) and thrombosis (HITT) are immune mediated disorders induced by the administration of heparin. Anticoagulation for these patients in the cardiac surgery setting remains a clinical challenge. Argatroban, a direct thrombin inhibitor, was recently approved for the prevention and treatment of thrombosis associated with HIT. There is very limited experience, however, with its use in cardiac surgery. We present a case in which argatroban was used during coronary artery bypass grafting.

**Case Report:** A 75 year old male was transferred to our hospital on June 17, 2002 with diagnosis of a non-Q wave MI. He was noted to have an abnormally prolonged aPTT of 78.6, PT of 18.5 and a platelet count of 177. Past medical history was significant for HTN, renal insufficiency, COPD, pulmonary embolism and a previous stroke. Past surgical history included a 4 vessel CABG and an aorto-femoral bypass, both in 1977. A heparin infusion had been initiated at the outside hospital, but was discontinued sometime prior to transfer. Cardiac catheterization demonstrated three vessel disease, not amenable to angioplasty and preserved LV function. Work-up of the abnormal coagulation tests revealed the patient to be strongly positive for heparin induced platelet antibodies (HIPA), lupus anticoagulant and anticardiolipin antibodies. Lepirudin was initially attempted for anticoagulation preoperatively but was discontinued secondary to bleeding complications.

On June 26 the patient was brought to the operating suite for off-pump coronary artery bypass surgery. Given the patient's hypercoaguable state, HIPA positive status and complications with lepirudin, argatroban was chosen as the anticoagulant for the procedure. Extracorporeal circulation consisted of a roller pump, membrane oxygenator, and a hard reservoir. Argatroban was not added to the pump prime. The patient's baseline activated clotting time (ACT) and hematocrit were 216 and 28, respectively. One unit of blood was given. A bolus injection of argatroban, 2.5  $\mu$ /kg, followed by a continuous infusion at 2  $\mu$ /kg/min was started thirty minutes prior to the first anastomosis. The dose was adjusted with additional boluses and infusion titration to maintain the ACT between 300-400 seconds throughout coronary grafting. During

the final anastomosis, the patient became hemodynamically unstable requiring institution of emergent CPB. The argatroban was bolused 5  $\mu$ /kg and the infusion increased to 5  $\mu$ /kg/min to achieve an ACT greater than 400 seconds. The reservoir and bypass circuit were continuously inspected for thrombus, which was not found. Two additional units of blood were transfused while on bypass to keep the hematocrit above 20%. The argatroban infusion was discontinued at the end of cardiopulmonary bypass. Total CPB time was 60 minutes. Two units of FFP were given prophylactically, although excessive bleeding was not noted and adequate hemostasis was achieved quickly. The ACT one hour following CPB was 281. Chest tube output POD 1 was 530 cc, POD 2 230 cc, and they were removed on POD 3. The patient was discharged home on POD 9 with long-term anticoagulation.

**Discussion:** Re-exposure to heparin in patients with HIT/HITT is associated with a high risk of venous and arterial thrombosis. Standard anticoagulation for these patients requiring cardiac surgery has not been established. Current options include: delaying surgery until after the disappearance of antibodies, using heparin in conjunction with PGE1 or glycoprotein IIb/IIIa inhibitors, and direct thrombin inhibitors [1]. Argatroban is non-antigenic, concentration-dependent, affects both free and thrombus bound thrombin and is not renally excreted [2,3]. In addition, it exhibits no interaction with platelets or heparin antibodies. The main disadvantage of argatroban, like all direct thrombin inhibitors, is the lack of a known neutralizing agent (such as protamine). We chose argatroban because of this patient's HIPA+ status, history of thrombotic events (PE, CVA), renal insufficiency and failure with lepirudin titration. Our dosing regimen and titration to a therapeutic ACT was based on the reports by Kawada and Ohno [4,5].

Argatroban appears to offer several advantages for patients with HIT/HITT undergoing cardiac surgery. Its linear effect on ACT and relatively short duration of action are two important reasons why this thrombin inhibitor appears to be an acceptable choice for use in off-pump and on-pump cardiac surgery.

[1] *Curr Opin Pulm Med* 2002, 8:405-12

[2] *Drugs* 2001, 61(4):515-522

[3] *J Thorac Cardiovasc Surg* 2001, 122:1255-6

[4] *Hematol Oncol Clin North Am* 2000,14(2): 445-55

[5] *Masui* 2002, 51(1):30-33