Pre-emptive use of bivalirudin for emergent off-pump coronary artery bypass surgery in a suspected case of heparin-induced thrombocytopenia

Sir,

Heparin-induced thrombocytopenia (HIT) is defined as a decrease in the platelet count during or shortly following exposure to heparin. The incidence of HIT is 1–5%. HIT is a syndrome of antibody-mediated thrombocytopenia that, paradoxically, is often associated with an incidence of thrombosis. Two different types of HIT are recognized. HIT type I is a benign form not associated with an increased risk of thrombosis. HIT type II is immune mediated, and is associated with an increased risk of thrombosis. Thrombosis in HIT is associated with 20–30% mortality.[1] Recent data shows that up to 8% of all heparinised patients will develop the antibody associated with HIT, and 1–5% will progress to HIT.[1] Typically, HIT begins with the appearance of thrombocytopenia about 5 days after the start of heparin therapy. Occasionally, a more rapid fall in the platelet count occurs as in our case. Clinical suspicion is the key to diagnosis, as biochemical tests to confirm the diagnosis are not readily available and outsourcing of blood sample is frequently necessary in developing countries. The criteria for clinical diagnosis included: (a) thrombocytopenia (drop in platelet count to below one lakh or a drop of more than 50% from baseline), (b) exclusion of other causes of thrombocytopenia and (c) resolution of thrombocytopenia after cessation of heparin.[1]

A 65-year-old male patient presented with complaints of dyspnoea on exertion (NYHA class II) since the last 3 months. He had a strongly positive tread mill test and hence was put on low-molecular weight heparin (injection Enoxaparin 40 mg subcutaneously twice a day). Risk factors included long-standing diabetes mellitus and hypertension. Echocardiogram revealed grade I diastolic dysfunction with normal left ventricular systolic function and no regional wall motion abnormality. Coronary angiogram revealed significant triple vessel coronary artery disease. He was started on unfractionated injection heparin 5000 units intravenously every 6 h and posted for coronary artery bypass surgery. On investigation, he was found to have thrombocytopenia with platelet count of 1.22 lakhs/mm^3 with 2-day-earlier platelet count of 2.5 lakhs/mm^3. His repeat platelet count the next day was 1.12 lakhs/mm^3. Other biochemical and haematological parameters were normal. Pre-operatively, on the third day since admission, he developed acute chest pain with ST segment depression of 3 mm from V_1 to V_6. His vital parameters were stable. He was taken up for emergent coronary artery bypass surgery using bivalirudin (Biaflow, Sun Pharmaceuticals, Halol - 389350, Gujarat, India) as an alternative to heparin as his platelet count had fallen by more than 50% after heparin therapy. A loading dose of bivalirudin 0.75 mg/kg over 10 min followed by infusion at a rate of 1.75 mg/kg/h was commenced prior to grafting once conduits were ready. Activated clotting time (ACT) was used to monitor the adequacy of anticoagulation, values of which have been shown in Table 1. Off-pump coronary artery bypass surgery was performed successfully with grafts as follows: Left internal mammary artery to left anterior descending artery, reversed saphenous vein grafts to the posterior descending artery and two obtuse marginals. Bivalirudin infusion was stopped on completion of grafting at 90 min and ACT monitoring was continued post-operatively. The ACT returned to normal 6 h after stopping the infusion. Chest drainage in the first 6 h was 80 ml, after which tablet aspirin 150 mg and tablet clopidogrel 75 mg were given via a nasogastric tube. Total chest drainage was 310 ml, and no blood products were transfused. The post-operative course was uneventful. He was discharged on the 5th post-operative day with a platelet count of 2.16 lakhs/mm^3.

Continuation of heparin in the presence of HIT can be fatal. Other alternatives to heparin for

Table 1: Activated clotting time monitoring (Celite)

	Baseline	Intra-operative			Post-operative					
Time after bivalirudin (min)	0	5	30	90	150	210	270	330	390	450
ACT (s)	129	336	344	310	251	197	160	145	130	104

ACT – Activated clotting time; Bivalirudin was stopped at 90 min

anticoagulants are lepirudin, argatroban, danaparoid and bivalirudin.[2,3] The problem with these drugs is excessive bleeding.[3]

Bivalirudin is a 20 amino acid synthetic peptide that directly inhibits thrombin reversibly, with a more predictable dose response, and has a short half-life (25 min). It is metabolised mainly by poteolytic cleavage and avoids the need of protamine, which is highly antigenic. For anticoagulants to work effectively and safely during cardiac surgery, they must have a rapid onset of action, maintain a desired level of anticoagulation and allow haemostasis once discontinued. Previous on- and off-pump series have suggested that bivalirudin fulfils all these requirements.[3-6] Avoidance of blood stasis (as it is metabolised by thrombin, which could lead to local reduction in anticoagulant) and attention to the intraoperative medical management of patients is critical for successful use of bivalirudin.[3,4]

Our case was in the high-risk category according to pre-test probability scoring for HIT, which warranted use of alternative anticoagulants in place of heparin.[2] We have pre-emptively used bivalirudin as an alternative to heparin for anticoagulation, which was not associated with increased risk of bleeding.[7] It can be used safely to prevent the fatal sequel of HIT, which is still an underdiagnosed condition in the Indian scenario.

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REFERENCES

1. Franchini M. Heparin-induced thrombocytopenia: An update. Thromb J 2005;3:14.
2. Keeling D, Davidson S, Watson H. The management of heparin-induced thrombocytopenia. Br J Haematol 2006;133:259-69.
3. Warkentin TE. Anticoagulation for cardiopulmonary bypass: Is a replacement for heparin on the horizon? J Thorac Cardiovasc Surg 2006;131:515-6.
4. Dyke CM, Smedira NG, Koster A, Aronson S, McCarthy HL 2nd, Kirshner R, *et al*. A comparison of bivalirudin to heparin with protamine reversal in patients undergoing cardiac surgery with cardiopumonary bypass: The EVOLUTION-ON study. J Thorac Cardiovasc Surg 2006;131:533-9.
5. Smedira NG, Dyke CM, Koster A, Jurmann M, Bhatis DS, Hu T, *et al*. Anticoagulation with bivalirudin for off-pump coronaryartery bypass grafting: The results of the EVOLUTION-OFF study. J Thorac Cardiovasc Surg 2006;131:686-92.
6. Koster A, Dyke CM, Aldea G, Smedira NG, McCarthy HL 2nd, Aronson S, *et al*. Bivalirudin during cardiopulmonary bypass in patients with previous or acute heparin-induced thrombocytopenia and heparin antibodies: Reults of the CHOOSE-ON trial. Ann Thorac Surg 2007;83:572-7.
7. Dyke CM, Koster A, Veale JJ, Maier GW, McNiff T, Levy JH. Pre-emptive use of bivalirudin for urgent on-pump coronary artery bypass grafting in patients with potential heparin-induced thrombocytopenia. Ann Thorac Surg 2005;80:299-303.

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