



Platelet Protection Using the Glycoprotein IIb/IIIa Inhibitor Tirofiban in a Patient with Heparin Induced Thrombocytopenia Undergoing Aortic Valve Replacement Requiring Cardiopulmonary Bypass

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Introduction:

Heparin induced thrombocytopenia (HIT) is a serious clinical scenario that occurs with the administration of unfractionated heparin (UFH) and to a lesser extent with low molecular weight heparin (LMWH). HIT has a high incidence of morbidity and mortality particularly in patients undergoing cardiac surgery. HIT patients spontaneously generate antibodies against heparin bound to platelet factor 4 (PF4) with the subsequent formation of antibody-antigen complexes which result in platelet activation and thrombin generation. This physiological sequence of events elicits a significant decrease in platelet count with a simultaneous increase in thromboembolic events including venous thromboembolism (VTE), pulmonary embolism (PE), stroke or myocardial infarction (MI). Hence the following dilemma:

- Patients undergoing cardiopulmonary bypass (CPB) procedures require full anticoagulation using UFH.
- This is not the optimal therapeutic strategy for patients with HIT
- It is possible that the anti-glycoprotein IIb/IIIa (GPIIb/IIIa) agents may prove suitable for managing these patients.
- Indeed, studies have demonstrated that tirofiban is a safe adjunctive therapy in the management of CPB patients with HIT.

Methods:

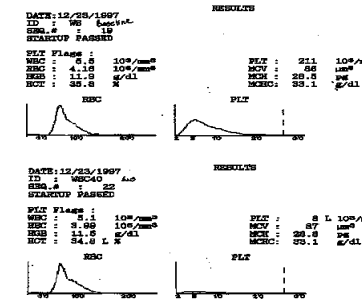
An 84-year-old female was admitted for severe aortic stenosis requiring aortic valve replacement at the University of Michigan Medical Center. Previously

diagnosed with HIT, the patient had no residual circulating HIT antibodies against platelets (via EIA, GTI Inc. Brookfield, WI). In an effort to protect the patient's platelets and thereby prevent HIT, it was decided to administer the short-acting GPIIb/IIIa antagonist tirofiban (Aggrastat). Anticoagulation during CPB was achieved with standard UFH dose of 300 units/kg to maintain an ACT of 480 seconds or greater. A loading and infusion dose of tirofiban 10µg/kg and 0.15µg/kg/min was administered prior to UFH. Tirofiban infusion was stopped 30 minutes prior to the termination of CPB.

The patient was evaluated for both platelet count and function using the FDA approved Plateletworks™ (Helena Point of Care, Beaumont, Texas) peri-procedurally.

This system uses traditional electronic impedance principles. In brief, a reference platelet count is performed on 1 mL of fresh whole blood in a Plateletworks™ tube containing K₃-EDTA as the anticoagulant. This process is repeated with a second 1mL sample of fresh whole blood in a Plateletworks™ tube containing both citrate and 20µM ADP. Platelets associate and aggregate in the presence of ADP. As the aggregated platelets exceed the threshold limitations for platelet size, they are no longer counted as individual platelets. The ratio of the platelet count between the ADP and reference tubes is calculated as percent platelet aggregation. Results are available within four minutes. Seven other blood parameters are also provided (a sample tracing of the data are shown in Figure 1).

Figure 1:
Sample tracing -
Platelet works



Results:

The data for platelet function and count are shown in Figure 2. Trends of platelet count and function are shown in Figures 2a and 2b respectively

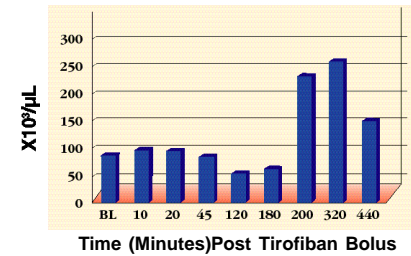


Figure 2a:
Platelet count

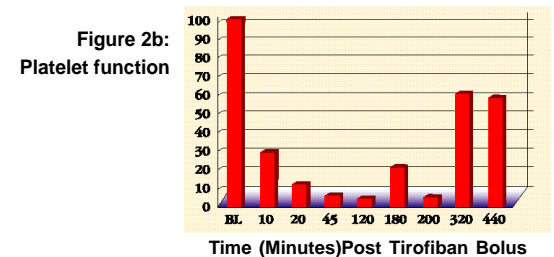


Figure 2b:
Platelet function

Platelet aggregation was reduced to approximately 12% 20 minutes post-tirofiban bolus (see Figure). Platelet function remained low throughout the procedure even after the tirofiban infusion was stopped. Indeed, recovery of platelet function (~60% aggregation) was not observed until two hours post procedure.

As a result of CPB, at two hours into the procedure the patient became hemodiluted and experienced a drop in platelet count to 53x10⁹/µL. Platelets (five packs) were transfused post-bypass and the count significantly increased (to 231x10⁹/µL). An additional five platelet packs were administered at two hours post procedure. At two and four hours after CPB, the platelet function approached baseline, pre-procedural levels.

Conclusion:

- HIT patients undergoing cardiac surgery may be optimally anticoagulated using adjunct tirofiban therapy.
- Platelet count and function may be easily measured in whole, non-anticoagulated blood using the platform described.
- Although other agents are currently being evaluated for their potential use in HIT management, the short-acting anti-GPIIb/IIIa agents tirofiban and eptifibatide should be considered as an alternative approach to anticoagulation management in these patients.