A novel method for the management of patients with heparin-induced thrombocytopenia during cardiac surgery

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Abstract

A 63-year old male patient presented with prosthetic valve endocarditis and developed heparin-induced thrombocytopenia (HIT) following heparin administration for continuous veno-venous haemofiltration. Use of cardiopulmonary bypass in patients suffering from heparin-induced thrombocytopenia is difficult and challenging. We report a novel method that allows heparin use in patients diagnosed with HIT using Multiplate platelet analyser and iloprost. Platelet function analysis is complex, poorly standardized and time consuming. Multiplate platelet analyser represents a convenient, safe, reliable and rapid system that allows the assessment of platelet dysfunction. It allows objective demonstration of platelet inhibition before administration of heparin, allowing safe establishment of cardiopulmonary bypass in patients suffering from HIT.

Keywords: Cardiopulmonary bypass • Heparin • Heparin-induced thrombocytopenia • Platelet assessment • Platelet dysfunction • Multiplate platelet analyser

INTRODUCTION

Heparin-induced thrombocytopenia and thrombosis (HITT) is an immune-mediated disorder characterized by formation of antibodies against heparin–platelet factor 4 complexes (PF4) [1]. Multimolecular complexes of heparin, PF4 and IgG form and occupy platelet Fc receptors. This results in platelet activation and thereafter activation of coagulation [1, 2]. Once these procoagulant events are triggered, the prothrombotic risk remains for days to weeks, even after heparin has been stopped [2, 3]. Patients diagnosed with HIT present technical challenges for cardiopulmonary bypass (CPB), which requires high dosages of heparin [3].

Multiplate is a newer platelet function test analyser with high sensitivity for antiplatelet drugs [3–5]. We report a novel method of iloprost use along with Multiplate analyser to ascertain that all platelets were inhibited prior to administration of heparin in a patient diagnosed with HITT. This allowed safe conduct of CPB, resulting in a good outcome following cardiac surgery. To our knowledge, this is first report of its kind on the use of Multiplate analyser in a patient diagnosed with HIT undergoing cardiac surgery.

CASE REPORT

A 63-year old male patient was admitted with prosthetic aortic valve endocarditis (aortic and mitral valve vegetations, dehiscence of aortic valve and aortic root abscess). Following admission, the patient developed acute renal failure and required renal replacement therapy. Initial blood tests revealed a platelet count of 179 × 10^3 per mm^3. During hospitalization, he developed significant drop in platelet count to 35 × 10^3 per mm^3, and heparin-induced thrombocytopenia (HIT) was confirmed by serotonin release assay. Even after stopping all forms of heparin for a week, platelet counts continued to drop (16 × 10^3 per mm^3). A multidisciplinary team (MDT) discussion was held, including discussion with teams who had experience with bivalirudin use on CPB. Our patient was likely to have significant postoperative bleeding (due to endocarditis and anticipated long CPB time). The MDT agreed that it would be easier to deal with bleeding caused by a drug (heparin), which can be easily antagonized with protamine. Besides, we have significant experience with heparin, while none of the team members had significant experience with either bivalirudin or danaparoid. A decision was taken to use heparin along with a platelet inhibitor. After induction of anaesthesia, iloprost continuous infusion was started at a dose of 4 ng/kg/min increasing to 9 ng/kg/min according to platelet function analysis using multiple electrode aggregometry (Multiplate). Once complete inhibition of platelet aggregation was demonstrated (Fig. 1), the patient was fully heparinized (heparin sodium, 300 IU/kg intravenously). During CPB, the activated coagulation time was maintained at >480 s. Centrifugal pump with non-heparin-bonded circuits was used. CPB flow was kept at 2.5 l/m² body surface area. The patient was cooled to 32°C. Cold blood cardioplegia was given 1 l at induction, and then every 15–20 min, additional cardioplegia was given both retrogradely and direct ostial.
The patient underwent redo-aortic valve replacement (23 mm, Carpentier Edwards Perimount Magna), repair of aortic root, mitral valve repair and closure of the patent foramen ovale. On termination of CPB, protamine sulphate was administered to neutralize the heparin.

In the immediate postoperative phase, the patient did not have significant bleeding and did not require blood product transfusion. No heparin was administered thereafter.

DISCUSSION

Heparin is routinely used in cardiac surgery for the establishment of extracorporeal circulation [1, 2]. As heparin cannot be used in patients with HIT, alternative options such as danaproid or bivalirudin have been suggested [3].

Our patient presented complex challenges for a redo surgery for prosthetic aortic valve endocarditis, aortic root abscess and mitral valve endocarditis in the presence of established renal failure on renal replacement therapy. The options for anticoagulation for CPB in this patient included [3, 4]:

(i) Direct thrombin inhibitors (bivalirudin).
(ii) Danaparoid (which works by inhibiting activated factor Xa).
(iii) Heparin along with a potent platelet inhibitor (iloprost).

An alternative option is to defer cardiac surgery for several weeks until HIT antibodies are not detectable [1–3]. However, with deteriorating haemodynamics with severe aortic regurgitation and mitral regurgitation, this option was not viable in our patient.

Prostacyclin analogue, iloprost, prevents platelet aggregation during CPB, and temporary platelet inhibition by iloprost could allow safe heparin administration in patients with HIT undergoing cardiovascular operations [1, 2]. However, clinicians increasingly feel the need for objective tests to demonstrate platelet inhibition before heparin administration. Heparin was used in our patient, as it was a drug that the team was most familiar with, and protamine can be used to effectively reverse heparin effect if faced with bleeding postoperatively.

For management of postoperative bleeding, currently, thromboelastography is widely available as point-of-care test [3, 4]. However, a major limitation of thromboelastography is inability to detect impairment in platelet function induced by antiplatelet agents [3–5]. Several platelet function tests have been reported. However, none of these tests are suitable for routine clinical practice [3–5]. The ‘gold standard’ test for platelet dysfunction is platelet aggregometry. However, it is an arduous and time-consuming laboratory test and not a point-of-care test [3]. The platelet function analyser PFA-100 is suitable for monitoring therapy with aspirin and as a screening test for the detection of von Willebrand syndrome [4, 5]. However, it over-estimates the prevalence of aspirin resistance, and it cannot detect platelet dysfunction due to clopidogrel administration, a commonly used antiplatelet drug in CAD patients [4, 5]. Besides, the results depend on haematocrit and platelet count, thus limiting its usefulness in patients with postoperative bleeding [4, 5].

The recently introduced point-of-care instrument, the Multiplate analyser (Multiplate®, Roche Diagnostics, Mannheim, Germany), allows objective evaluation of platelet aggregation after using agonists by detecting changes in electrical resistance in whole blood [4]. In contrast to classical aggregometry, the Multiplate analyser eliminates the need for centrifugation of plasma or adjustment of platelet concentration [3–5]. In the Multiplate analyser, the test cells are for single use, whereas the electrodes of previous models had to be manually cleaned after each use [3–5]. It is also easy to handle, and results are available within a few minutes [3–5].

CONCLUSION

The use of Multiplate represents a convenient and rapid system that allows the assessment of platelet dysfunction. Usefulness and comparability of different platelet function analysers needs further assessment in clinical practice. In our patient, the Multiplate enabled confirmation of complete platelet inhibition prior to heparinization in a patient diagnosed with HIT. It needs confirmation in larger studies before it can be advocated as a strategy for routine use in HIT patients.

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REFERENCES


