Heparin-Induced Thrombocytopenia and Cardiac Surgery: Can We Do It All With Cangrelor?

To the Editor

We read the case report on the use of cangrelor (Kengreal; Chiesi, Cary, NC) in a patient with a suspected heparin-induced thrombocytopenia (HIT) undergoing cardiopulmonary bypass (CPB).¹

The authors stated that the VerifyNow P2Y₁₂ test (Instrumentation Laboratory, Bedford, MA) was used to monitor platelet inhibition by cangrelor. The P2Y₁₂ reaction unit (PRU) below 180 was deemed to be sufficient platelet inhibition (normal reference range: 182–376 PRU). The authors reported that the initial PRU of 115 after the loading of 30 µg/kg cangrelor, but the PRU of 252 during CPB, indicated a return of platelet aggregation despite the continuous infusion at 4 µg/kg/min. We would like to make several precautionary statements about monitoring the effect of cangrelor using VerifyNow during CPB.

First, the target platelet inhibition of PRU below 180 is based on the outcome data in the drug-eluting stent studies,² but mild to moderate platelet inhibition may not be adequate to obliterate intense platelet activation via FcγRIIa receptor stimulation by HIT antibodies. Previous experiences on CPB and the use of tirofiban, a glycoprotein IIb/IIIa inhibitor, report more extensive inhibitions of adenosine diphosphate (ADP)-induced platelet aggregation (residual 10% aggregation versus 82% at baseline).³ Second, the use of the VerifyNow test during CPB is not recommended because there is a significant hematocrit fluctuation. The VerifyNow system uses a turbidimetric aggregation detection, and lower hematocrit levels during CPB can falsely elevate PRU values.⁴ This may potentially lead to overdosing of cangrelor during CPB due to falsely

high platelet aggregability due to low hematocrit. In their case report, post-CPB platelet aggregation was actually higher than the baseline (361 vs 341 PRU), but it is plausible that platelet aggregability was actually decreased after CPB in this patient who required platelet transfusion. Alternative platelet function testing such as whole blood impedance aggregometry may be preferable in the case of hemodilution.

In summary, a reversible P2Y₁₂ inhibition with cangrelor with heparin during CPB is a promising anticoagulation strategy in an HIT patient. However, before its widespread use, more preclinical data should be evaluated to determine the optimal dosing, extent of platelet inhibition, and platelet function monitoring during CPB. ■

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REFERENCES

1. Girgis AM, Golts E, Humber D, Banks DA. Successful use of cangrelor and heparin for cardiopulmonary bypass in a patient with heparin-induced thrombocytopenia and end-stage renal disease: a case report. *AA Pract.* 2019;13:10–12.
2. Michelson AD, Bhatt DL. How I use laboratory monitoring of antiplatelet therapy. *Blood.* 2017;130:713–721.
3. Koster A, Kukucka M, Bach F, et al. Anticoagulation during cardiopulmonary bypass in patients with heparin-induced thrombocytopenia type II and renal impairment using heparin and the platelet glycoprotein IIb-IIIa antagonist tirofiban. *Anesthesiology.* 2001;94:245–251.
4. Kakouros N, Kickler TS, Laws KM, Rade JJ. Hematocrit alters VerifyNow P2Y₁₂ assay results independently of intrinsic platelet reactivity and clopidogrel responsiveness. *J Thromb Haemost.* 2013;11:1814–1822.

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