Platelet reactivity assessment with VerifyNow®: Substitute or complement for light transmission aggregometry?

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Platelet aggregation inhibition is mandatory for patients undergoing percutaneous coronary intervention (PCI) [1]. High on-treatment platelet reactivity is an important independent risk factor for the occurrence of thrombotic and ischemic events after PCI [2]. Some point of care platelet aggregation assays are currently used in daily practice as a substitute for more expensive and time consuming complex methods. Despite the wide use of such tests, clinical trials testing the strategy of individual tailoring based on one test result have shown no clinical benefit, being the poor correlation between assays one possible explanation. Several clinical studies with the VerifyNow P2Y12 system have proposed a cut-off value of <240 platelet reaction unit (PRU) to identify “good responders” [3,4]; however, the reasons for a PRU >240 after clopidogrel treatment are not clear, and might reflect either false positives in good responders or “true” poor responders [5]. The objective of our study was to evaluate the correlation between light transmission aggregometry (LTA) and VerifyNow P2Y12 test with emphasis on patients with VerifyNow P2Y12 PRU >240 after clopidogrel treatment.

This was a single center, observational study. Subjects with stable coronary artery disease undergoing percutaneous coronary intervention were prospectively included. Platelet responsiveness to ADP was assessed 4 h after 600 mg clopidogrel loading dose using two different tests: ADP-induced platelet aggregation by LTA (turbidimetric) in response to 4 μmol/L ADP (results are expressed as platelet aggregation percentage), and platelet reactivity assessment with the VerifyNow® P2Y12 test (Accumetrics, San Diego, CA, USA) (results are expressed as P2Y12 platelet reaction unit: PRU, and percentage inhibition index). High on-treatment platelet reactivity was defined as a 4 μmol/L ADP-induced LTA >50% [6], and a VerifyNow P2Y12 PRU >240. Statistical analyses were performed at the level of significance < 0.05 using PASW 18 (SPSS Inc, Chicago IL, USA). All patients received a loading dose of 300 mg of AAS before the procedure. Informed consent was obtained from each patient and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution’s ethics committee.

A total of 115 patients were included in the study. Of them, 81% were males, 17% had a history of diabetes mellitus, and 64% had a history of hypertension. In addition, 81% were previously treated with aspirin, 39% with clopidogrel, and 86% with proton pump inhibitors. Mean VerifyNow P2Y12 PRU was 239.4 ± 91.9, percentage inhibition index 74.8% ± 23.6%, and 4 μmol/L ADP-induced LTA 25.4 ± 14.7. VerifyNow P2Y12 PRU offered a modest correlation with 4 μmol/L ADP-induced LTA (Pearson = 0.539; p < 0.01) but superior to the one provided by the VerifyNow P2Y12 percentage inhibition index (Pearson = 0.437; p < 0.01) (Fig. 1). Receiver-operating characteristic (ROC) curve analysis demonstrated that PRU (cut-off value of >240) distinguished between patients with and without 4 μmol/L ADP-induced platelet reactivity of >50% with an area under curve [AUC] of 0.82 (p < 0.01; 95% confidence interval (CI) 0.71–0.93) with a sensitivity of 100% (95% CI; 62.9%–100%) and a specificity of 55% (46.1%–65.7%). The negative predictive value of the test was 100% (95% CI; 93.9%–100%), with a positive predictive value of 14.5% (95% CI; 6.5%–26.7%) (Fig. 2). Overall, we found 55 patients (48%) with PRU >240. Of these patients, 28 (51%) had a 4 μmol/L ADP-induced platelet aggregation between 25 and 50% and 19 (34%) between 0 and 25%. It is well known that inhibition of P2Y12-mediated platelet reactivity reduce post-procedural myocardial infarction and stent thrombosis [1]. High on treatment platelet reactivity diagnosis using VerifyNow P2Y12 is a reliable and independent measure of risk for cardiovascular events [7]. However, even in patients with this condition, intensive anti-aggregation treatment based on a measure of platelet reactivity has never been successfully proven [8,9].

Using a cut-off value of <240 PRU, VerifyNow P2Y12 was an excellent tool to screen patients as all subjects were correctly anti-aggregated.

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(4 μmol/L ADP-induced platelet aggregation <50%). Conversely, in patients with PRU >240 an additional test to confirm the high on treatment platelet reactivity should be recommended as only 14.5% of those patients had a “true” poor response to clopidogrel treatment. In our study, the percentage of patients with a high on treatment platelet reactivity defined by VerifyNow P2Y12 was 48%. Of those, more than 85% had a 4 μmol/L ADP-induced platelet aggregation <50%, highlighting the lack of accuracy of VerifyNow P2Y12 in patients with PRU >240. In conclusion, VerifyNow is an excellent tool to identify patients who are properly treated with P2Y12 receptor inhibitors; however, high on treatment platelet reactivity defined by a VerifyNow P2Y12 > 240 should be confirmed with the golden standard ADP-induced light transmission aggregometry before suggesting any treatment modification.

The authors report no relationships that could be construed as a conflict of interest.

Conflict of interest

None to declare.

References


