Letter by Grove and Kristensen Regarding Article, “Randomized Assessment of Ticagrelor Versus Prasugrel Antiplatelet Effects in Patients With ST-segment–elevation Myocardial Infarction”

To the Editor:

We have read with interest the recent article regarding insufficient effect of oral antiplatelet drugs in the acute phase of ST-segment–elevation myocardial infarction (STEMI). Alexopoulos et al evaluated platelet inhibition at 0, 1, 2, 6, 24 hours, and 5 days in patients with STEMI, undergoing primary percutaneous coronary intervention. All patients were treated with heparin and aspirin and were randomized to standard loading and maintenance doses of either ticagrelor or prasugrel. The authors reported a high frequency of high on-treatment platelet reactivity at the first 3 time points and concluded that both ticagrelor and prasugrel exhibit an initial delay in the onset of platelet inhibition.

These findings concur with our recent study in a similar population of patients with STEMI, undergoing primary percutaneous coronary intervention. Our study population was pretreated with clopidogrel, and more than half of the patients had high residual platelet reactivity 4 hours after initiation of antithrombotic treatment. All oral P2Y12-inhibitors thus seem to provide suboptimal platelet inhibition in the acute phase of STEMI. As discussed by Alexopoulos et al, previous studies indicate that antiplatelet drugs have a faster onset of action in healthy individuals and patients with stable coronary artery disease, and delayed platelet inhibition in STEMI may be partly explained by impaired drug absorption.

We suggest that an increased platelet turnover in patients with STEMI may reduce the effect of antiplatelet drugs. Thrombopoiesis and the rate of platelet turnover are reflected by the amount of circulating platelets newly released from the bone marrow. An accelerated platelet turnover may affect the potency of antiplatelet drugs mainly because an increased number of immature platelets with increased hemostatic potential will circulate in the blood and an increased turnover of the circulating platelet pool counteracts the relatively short half-lives of antiplatelet drugs.

In our recent study, both residual platelet aggregation and platelet turnover indices (mean platelet volume, immature platelet fraction, and immature platelet count) were significantly increased in the acute phase of STEMI compared with a stable phase of 3 months after percutaneous coronary intervention. These findings are in line with a previous study by our group, showing that platelet turnover is increased in patients with STEMI compared with healthy individuals and patients with stable coronary artery disease.

High on-treatment platelet reactivity is a predictor of cardiovascular events in patients with STEMI, undergoing percutaneous coronary intervention, and exploring mechanisms of interindividual differences in the efficacy of antiplatelet drugs is important. We propose that an increased platelet turnover may represent such mechanism.

Disclosures

Dr Grove has received lecture fees from AstraZeneca, Bayer, Boehringer Ingelheim and Pfizer and serves on advisory boards for AstraZeneca and Bristol-Myers Squibb.

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References

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