Diabetes and CYP2C19 Polymorphism Synergistically Impair the Antiplatelet Activity of Clopidogrel Compared With Ticagrelor in Percutaneous Coronary Intervention-treated Acute Coronary Syndrome Patients

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Abstract

Diabetes and CYP2C19 loss of function (LOF) alleles are associated with the variable antiplatelet activity of the prodrug clopidogrel. We conducted a randomized trial (NCT03613857) to compare the combined and individualized effects of diabetes and CYP2C19 polymorphisms on the antiplatelet reactivity of clopidogrel versus ticagrelor in patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI). Patients (948, 1 year follow-up 943) were randomly allocated in a 1:1 ratio to receive either clopidogrel or ticagrelor, after PCI; patients were subdivided into 8 subgroups according to the diabetes and/or CYP2C19 allele status. The study outcomes were recurrent ACS, maximum platelet aggregation (MPA), high platelet reactivity index (PRI), and incidence of major bleeding events. Diabetic patients with LOF alleles taking clopidogrel had the highest recurrent ACS rate (6 of 33 patients) versus all other study groups ($P < 0.05$). However, both drugs had similar proportions of recurrent ACS in all other subgroups. Similarly, both PRI and MPA were significantly higher in the diabetic patients having LOF alleles and receiving clopidogrel versus all their study groups ($P < 0.05$). Nevertheless, ticagrelor caused higher rates of major bleeding versus clopidogrel ($P < 0.001$). PCI-treated ACS patients with diabetes and CYP2C19 LOF alleles are at a higher risk of recurrent ACS and high PRI/MPA, when treated with clopidogrel versus ticagrelor, but almost comparable outcomes are recorded in the absence of 1 or the 2 risk factors.

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