Impact of the type of acute coronary syndrome on the pharmacodynamic response to P2Y12 inhibitors in the acute and maintenance phase of therapy

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Topic(s):
Thrombosis, Platelets, and Coagulation

Citation:
Funded by Instituto de Salud Carlos III through the project PI13/01012 (co-funded by European Regional Development Fund, ERDF, a way to build Europe)

Background: The presence of an acute coronary syndrome (ACS) is per se a predictor of reduced responsiveness to clopidogrel; in particular, patients with ST-elevation myocardial infarction (STEMI) have impaired clopidogrel-induced platelet inhibition than those with other forms of ACS. However, the impact of the type of ACS on the pharmacodynamic efficacy of more potent P2Y12 antagonists such as prasugrel or ticagrelor has not been fully elucidated to date.

Purpose: To assess the impact of the type of ACS on platelet inhibition mediated by P2Y12 receptor antagonists in the acute and the maintenance phase of therapy in a contemporary cohort of ACS patients undergoing percutaneous coronary intervention (PCI).

Methods: Substudy of a prospective, national, multicentre, pharmacodynamic registry conducted in a population of ACS patients undergoing PCI and treated with dual antiplatelet therapy including aspirin and a P2Y12 inhibitor as per clinical indication. Patients were classified according to the ACS diagnosis into groups: a) STEMI, b) non-ST-elevation ACS (NSTEACS), c) unstable angina (UA), and d) other (excluded from the present analysis). Platelet function tests (PFT) were performed at day 1 and day 30(±5) after PCI and included: 1) VerifyNow P2Y12 assay, expressed as P2Y12 reaction units (PRUs); 2) Vasodilator-stimulated phosphoprotein (VASP) assay; and 3) Multiple electrode aggregometry (MEA).

Results: A total of 965 patients (372 with STEMI, 395 with NSTEACS and 198 with UA) were included in the present substudy. At day 1, the proportions of patients with each type of ACS according to the P2Y12 inhibitor received were: 1) clopidogrel (n=317): STEMI 35,0%, NSTEACS 34,4% and UA 30,6%; 2) prasugrel (n=192): STEMI 70,3%, NSTEACS 17,7% and UA 12,0%; 3) ticagrelor (n=456): STEMI 27,6%, NSTEACS 55,3% and UA 17,1%. A statistically significant reduced platelet inhibition, measured with the VerifyNow system, was observed in STEMI patients compared with the other forms of ACS in patients receiving clopidogrel (STEMI: 217,3 ± 8,1, NSTEACS: 157,1 ± 7,9 and UA: 164,9 ± 8,6 PRUs; p for STEMI vs. NSTEACS <0,001 and p for STEMI vs. UA <0,001) and ticagrelor (STEMI: 57,7 ± 3,8, NSTEACS: 45,2,1 ± 2,6 and UA: 40,6 ± 4,9 PRUs; p for STEMI vs. NSTEACS 0,008 and p for STEMI vs. UA 0,007), while a numerical trend towards greater platelet reactivity in STEMI compared to UA was observed in subjects receiving prasugrel (Figure). Remarkably, at day 30, no significant differences on platelet inhibition were observed according to the ACS type with any of the P2Y12 inhibitors. Similar results were observed with MEA and VASP assays.
Conclusions: Patients presenting with STEMI have impaired platelet inhibition mediated by P2Y12 antagonists compared to other types of ACS during the acute phase of therapy, whereas no difference is observed during the maintenance phase of treatment.