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Meeting abstract

Calcium channel blockers reduce the antiplatelet effect of clopidogrel

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Background

Clopidogrel is activated by CYP3A4 which also metabolizes calcium channel blockers of the dihydropyridine class. Due to the known CYP3A4 inhibition by calcium channel blockers, we hypothesized that there might be a drug-drug interaction between clopidogrel and dihydropyridines in patients with coronary artery disease.

Materials and methods

Responsiveness to clopidogrel was assessed by the vasodilator stimulated phosphoprotein (VASP) phosphorylation assay and aggregometry in 200 patients with coronary artery disease undergoing percutaneous coronary intervention.

Results

The platelet reactivity index (PRI in the VASP assay, normal range 69–100%) was higher in patients on both clopidogrel and calcium channel blockers (61%) as compared to patients on clopidogrel without calcium channel blockers (48%). The absolute difference was 13% (95%CI: 6–20%; p = 0.001) and the relative difference approached 21%. A reduced effect of clopidogrel (PRI >69%) was seen in 40% of patients with concomitant calcium channel blocker treatment compared to 20% without (χ^2-test: p = 0.008). Intake of calcium channel blocker remained an independent predictor of reduced platelet inhibition by clopidogrel after adjustment for cardiovascular risk factors. This corresponded to an increased platelet aggregation of similar magnitude (p < 0.05) and was associated with adverse clinical outcome. *In vitro* incubation with calcium channel blockers (nimodipine, verapamil, amlodipine and diltiazem) did not alter the PRI or the ADP-induced platelet aggregation of patients on clopidogrel. This indicates that the negative effect occurs *in vivo*, conceivably at the level of the CYP3A4 cytochrome.

Conclusion

Co-administration of calcium channel blockers is associated with a decreased platelet inhibition by clopidogrel.