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Impact of Citalopram and Fluvoxamine on Platelet Response to Clopidogrel, a Randomized, Double-blind, Crossover Trial

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Background:
Selective serotonin reuptake inhibitors (SSRI) are widely used antidepressant agents. Studies have shown that use of SSRI in combination with aspirin or warfarin is associated with an increased risk bleeding, while little information is known about the interaction of SSRIs and clopidogrel. Fluvoxamine and citalopram are both SSRIs and while fluvoxamine is an inhibitor of CYP2C19 and thus might reduce the efficacy of clopidogrel, the effect of citalopram on liver metabolism is unknown.

Aim:
The aim was to assess the effect these two different SSRIs on platelet aggregation and on the laboratory response to clopidogrel.

Methods:
A randomized, double-blind, crossover study in 15 healthy volunteers comparing the antiplatelet effect of clopidogrel with and without fluvoxamine or citalopram .The response to clopidogrel was assessed by Light Transmittance Aggregometry with10µmol/L ADP and by vasodilator-stimulated phosphoprotein (VASP) phosphorylation, a measure of P2Y12 receptor reactivity.

Results:
Mean baseline platelet aggregation was 80.1%±3.4 and reduced to 23.5% after treatment with clopidogrel. Both fluvoxamine and citalopram had modest effect on platelet reactivity (65.8%±6.4, p=0.06 vs. baseline and 67.3%±6.3, p=0.07 vs. baseline respectively). Laboratory response to clopidogrel was significantly better in the presence of citalopram as compared to fluvoxamine both in aggregometry (23.4%±3 vs. 32.3%±4.2, p=0.04) and VASP phosphorilation (35.9%±4.2 vs. 52.7±5.1, p=0.02).

Conclusion:
Fluvoxamine attenuate the laboratory response to clopidogrel, probably through inhibition of the CYP2C19, while citalopram does not affect this response. Since SSRIs are commonly used in patients after coronary syndromes and interventions, clinicians should be aware of these drug interactions and guide the selection of the appropriate antidepressant agent according to its pharmacodynamic properties and the cardiovascular risk.