האיגוד הישראלי לכירורגית לב וחזה
THE ISRAEL SOCIETY OF CARDIOTHORACIC SURGERY
האיגוד הקרדיולוגי בישראל
ISRAEL HEART SOCIETY
The 60th International Conference of the Israel Heart Society
in association with the Israel Society of Cardiothoracic Surgery
22-23 April 2013, ICC International Convention Center, Jerusalem

Differential impact of SSRIs on platelet response to clopidogrel: a randomized, double-blind, crossover trial.

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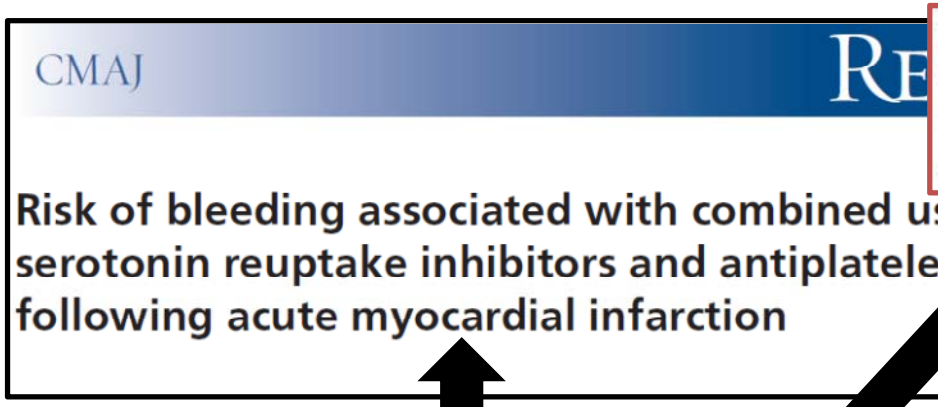
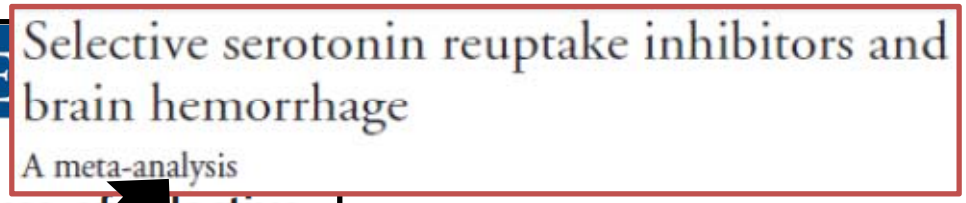
The current presentation has no conflict Of interest

Introduction

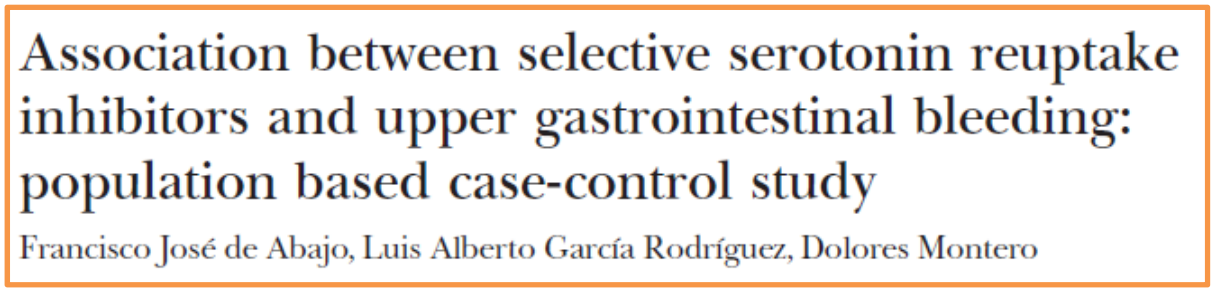
- Selective serotonin reuptake inhibitors (SSRI) are antidepressant agents that are widely used

- SSRI block serotonin reuptake by platelets, causing platelet serotonin depletion and potentially impaired platelet function





Studies have shown that use of SSRI in combination with aspirin is associated with an increased risk bleeding



CMAJ, November 8, 2011, 183(16)
Br J Clin Pharmacol / 66:1 / 76–81
BMJ Vol. 319 23 Oct. 1999
Neurology 1865–79:1862;2012

Introduction

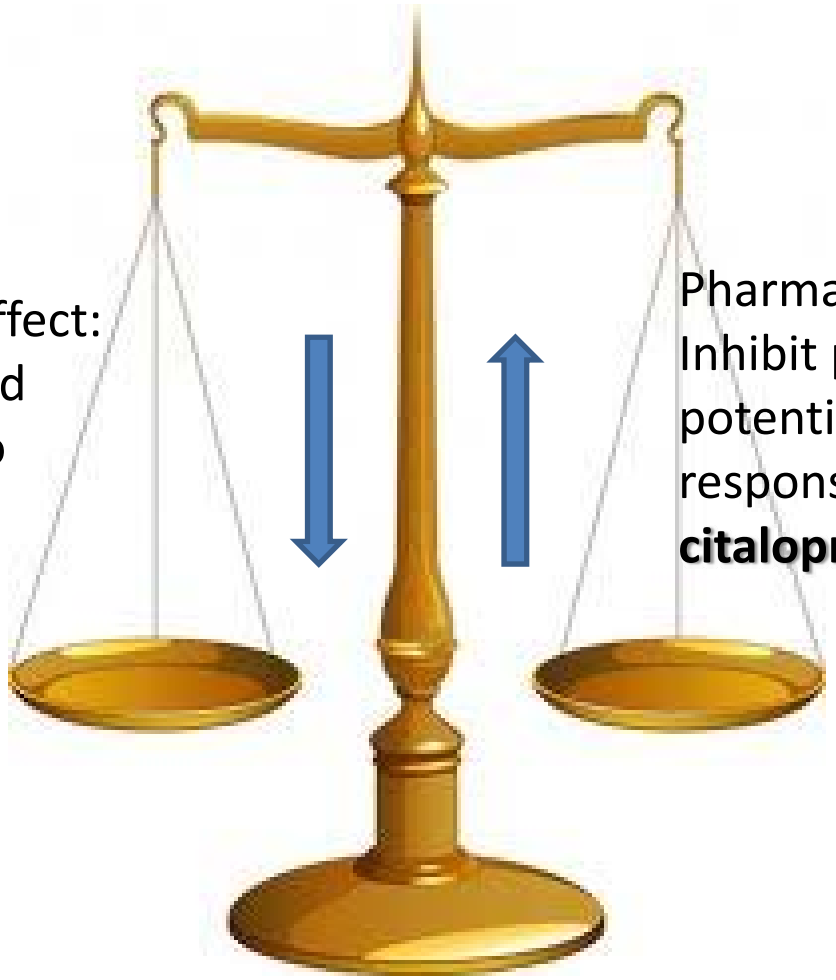
- little information is known about the interaction of SSRIs and clopidogrel

- Clopidogrel is a pro-drug undergoing active metabolism in the liver by CYP2C19

- Fluvoxamine is an SSRI and inhibitor of CYP2C19
- Citalopram is an SSRI without known effect on liver metabolism

Introduction

Pharmacokinetic effect:
Inhibit CYP2C19 and reduce response to clopidogrel
fluvoxamine



Pharmacodynamic effect:
Inhibit platelet function and potentially augment response to clopidogrel
citalopram & fluvoxamine

Aim

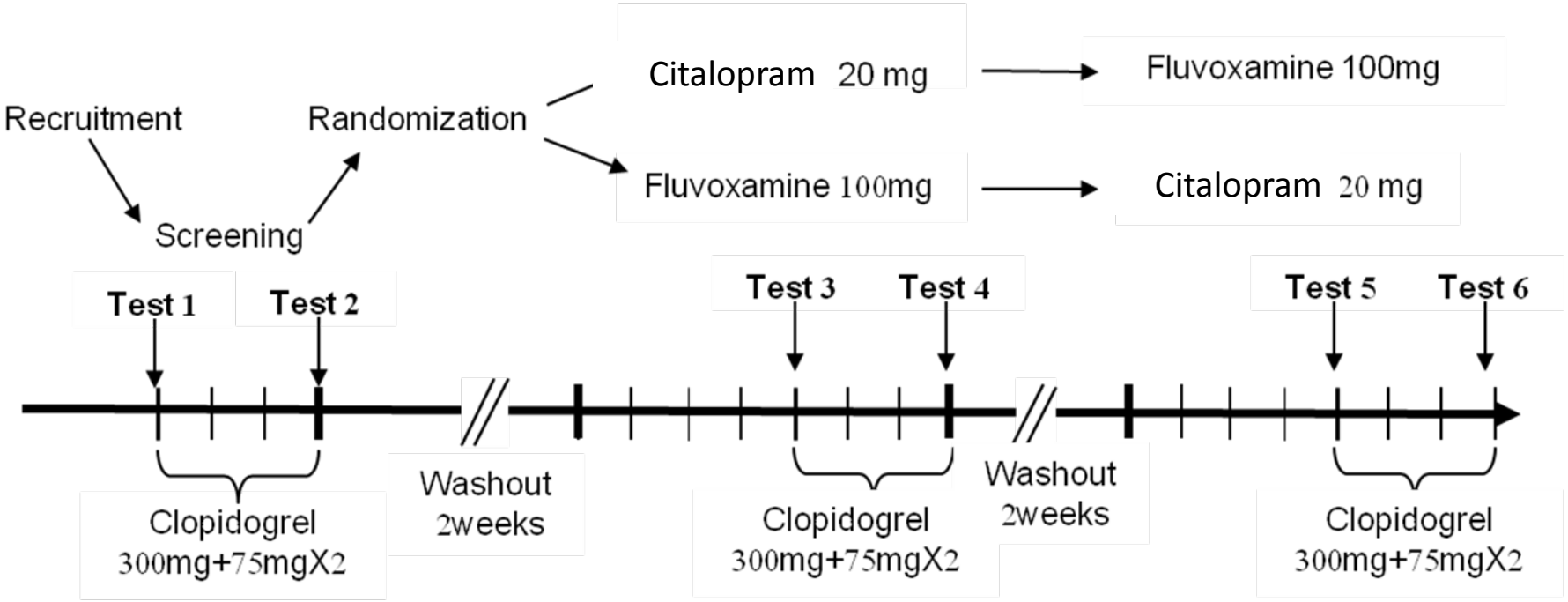
To assess the effect of two different SSRIs on platelet aggregation and on the laboratory response to clopidogrel

Methods

- Randomized, double-blind, crossover study comparing the antiplatelet effects of clopidogrel with and without fluvoxamine and citalopram in 15 healthy volunteers

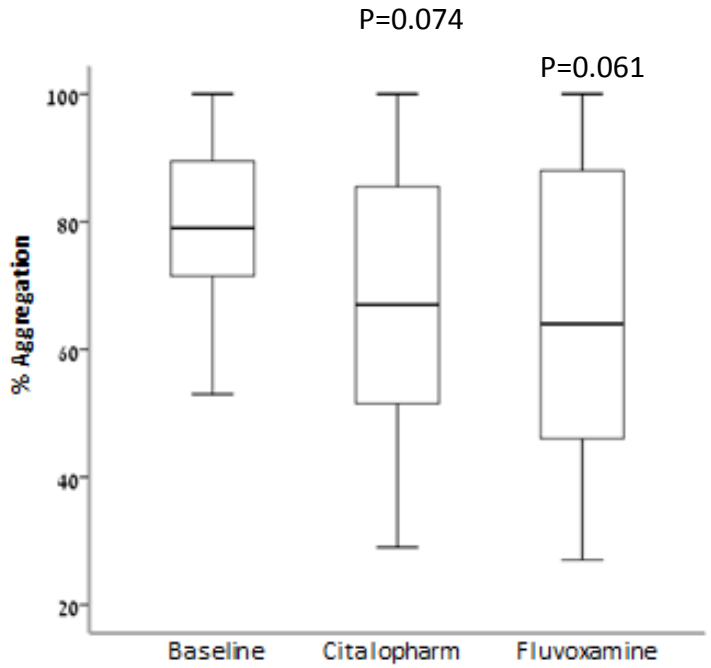
- Clopidogrel responsiveness was assessed by Light Transmittance Aggregometry (LTA) with 10μmol/L ADP and by vasodilator-stimulated phospho-protein (VASP) phosphorylation, a measure of P2Y12 receptor reactivity.

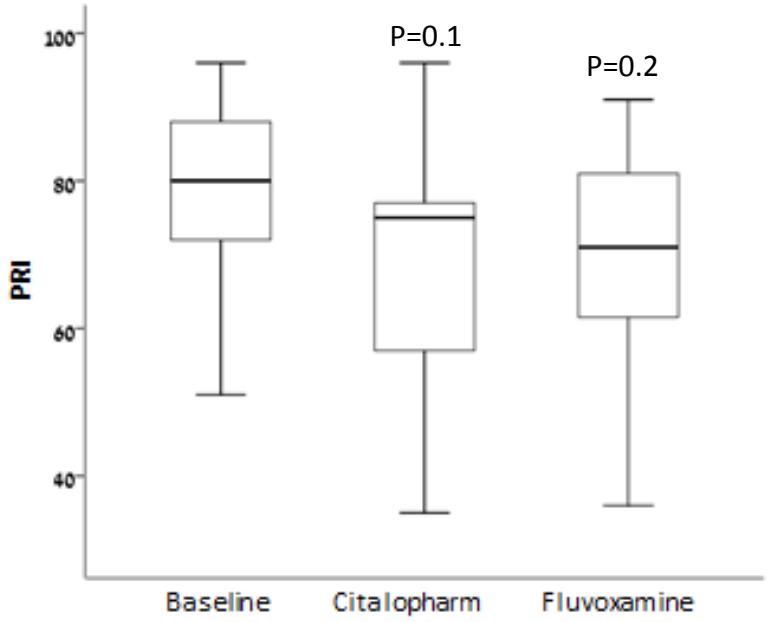
Study design:



Results

Fluvoxamine and citalopram had modest effect on platelet reactivity at baseline



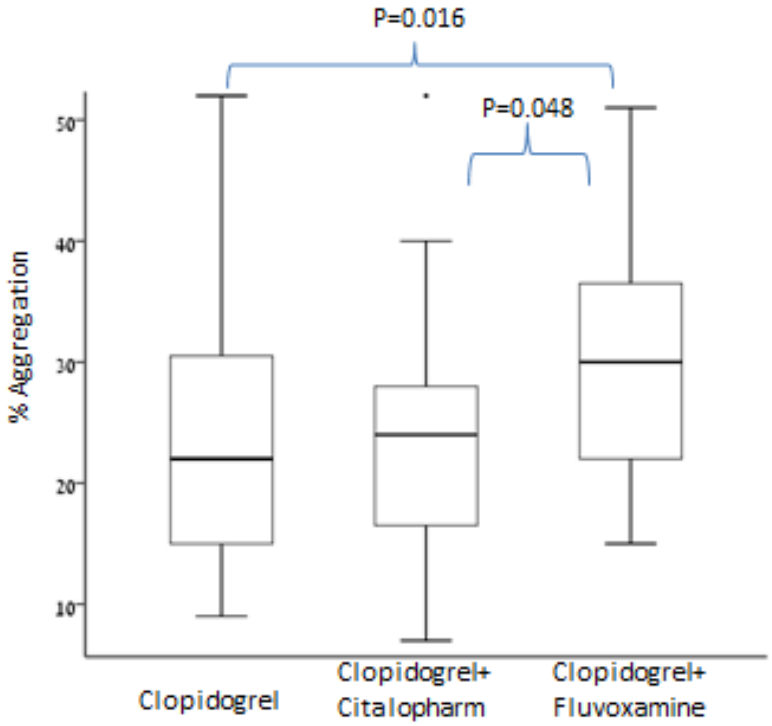


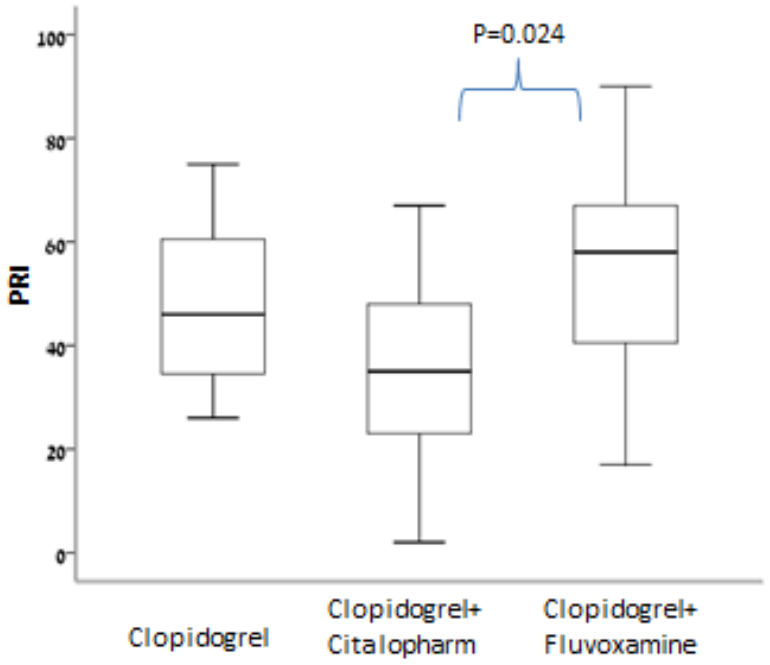
Results

Laboratory response to clopidogrel was significantly better in the presence of citalopram compare to fluvoxamine in both methods

LTA: 23.4%±3 vs. 32.3%±4.2

VASP: 35.9%±4.2 vs. 52.7±5.1





Conclusions & Practical Implications:

- 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 pharmacological properties and the cardiovascular risk.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