Effect of combined COX-1 and COX-2 inhibition on platelet aggregation in-vivo

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To investigate whether COX-2 inhibition enhances platelet aggregation by suppression of prostacyclin formation without suppressing thromboxane formation

Ethical review	Approved WMO
Status	Pending
Health condition type	Pericardial disorders
Study type	Interventional

Summary

ID

NL-OMON30233

Source
ToetsingOnline

Brief title
Effect of COX-2 inhibition on platelet aggregation in-vivo

Condition

- Pericardial disorders
- Embolism and thrombosis

Synonym
enhanced clotting, thrombosis

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: aspirin, COX-2 inhibition, platelet aggregation, prostacyclin

Outcome measures

Primary outcome

Amount of aggregation to ADP and epinephrine before and after aspirin at some

seconds after the blood left the canula

Secondary outcome

Amount of aggregation to ADP and arachidonic acid before and after aspirin in a

whole blood aggregopmeter , at more than one hour after blood collection

Study description

Background summary

Since the pain-killer VIOXX was withdrawn from the market, september 2004, because of serious side-effects in heart patients, the mechanism of these side effects is still not clear (Wadman M - Nature 2006;441:262). A dominant hypothesis is that VIOXX and other selective COX-2 inhibitors are prothrombotic by suppressing the formation of endothelial prostaglandin which is a well-known inhibitor of platelet aggregation in-vitro, without interfering with COX-1 mediated formation of thromboxane which is a reinforcer of platelet aggregation. As a consequence, the possible prothrombotic effect of selective COX-2 inhibitors is expected to be neutralized by contamporary use of COX-1 inhibition with low-dose aspirin. The role of circulating prostacyclin and of thromboxane in the possible enhancement of aggregation by selective COX-2 inhibitors has, however, never been demonstrated.

Study objective

To investigate whether COX-2 inhibition enhances platelet aggregation by suppression of prostacyclin formation without suppressing thromboxane formation

Study design

Platelet aggregation to increasing doses of adenosine diphosphate (ADP) and epinephrine is studied in blood flowing from an antecubital vein into an

optometric device that continuously measures platelet aggregation within some seconds after the blood left the venous canula. The measurements are performed before and after intake of 500 mg aspirin.
For comparison, platelet aggregability is also tested in the conventional way, with aid of a whole blood aggregometer

Intervention

Canulation of an antecubital vein. Intake of aspirin

Study burden and risks

Burden: the experiment takes the subject about 2 hours of his time
Risk: negligible

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

healthy men

Exclusion criteria

Use of medical drugs, smoking, supersensitivity to aspirin

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2006
Enrollment:	20
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	aspirin
Generic name:	acetylsalicylic acid
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2006-006352-35-NL
CCMO	NL14760.029.06