Does short dipyridamole administration induce protection against ischemia-reperfusion injury?

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The purpose of this project is to explore whether a short treatment with dipyridamole (2.5 days; i.e. 5 capsules) can reduce ischemia-reperfusion injury in the forearm.

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

Summary

ID

NL-OMON31190

Source
ToetsingOnline

Brief title
dipy003

Condition

- Coronary artery disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
infarction, ischemia reperfusion injury

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: annexin scintigraphy, dipyridamole, ischemia reperfusion injury

Outcome measures

Primary outcome

Percentage difference in radioactivity (counts/pixel) between experimental and

control thenar muscle at 60 and 240 minutes after reperfusion.

Secondary outcome

nvt

Study description

Background summary

A 7 day treatment of dipyridamole has been proven to reduce targeting of Annexin A5 in responses to ischemic exercise, indicating protection against ischemia-reperfusion injury in humans (pharmacological preconditioning). Dipyridamole increases the endogenous adenosine level by inhibition of the nucleoside transporter (ENT-1). Activation of the adenosine receptor protects against ischemia-reperfusion injury. However it is uncertain whether a treatment with dipyridamole of the duration of at least 7 days is necessary to induce protection against ischemia-reperfusion injury. For clinical application of dipyridamole induced protection against ischemia reperfusion injury, in for example the setting of an elective PTCA, a treatment duration of maximum 2 to 3 days could be implementable.

Study objective

The purpose of this project is to explore whether a short treatment with dipyridamole (2.5 days; i.e. 5 capsules) can reduce ischemia-reperfusion injury in the forearm.

Study design

Randomised cross-over design, single blinded (observer main outcome parameter)

Intervention

10 Volunteers will be randomised to receive in a cross-over design a two and a half day (5 capsules) treatment with dipyridamole (Persantin retard; 200 mg twice daily) followed by 10 minutes of ischemic isometric muscle contraction of the non-dominant forearm and upon reperfusion infusion of radiolabeled Annexin A5 (Annexin scintigraphy) and Annexin scintigraphy alone.

Study burden and risks

This study will be executed at the Clinical Research Centre Nijmegen under close medical supervision. Treatment with dipyridamole is not expected to harm the volunteers. During the first days of treatment with dipyridamole, a headache may occur. Ischemic hand gripping will temporarily result in pain in the forearm. This is completely reversible upon reperfusion. Administration of radiolabeled Annexin A5 results in an effective dose of less than 5 mSv, well within the range of accepted exposure to radioactivity for human research. Participation in this research does not interfere with possible diagnostic or therapeutic procedures with X-rays of radioactivity in the future.
Occurrence of an allergic reaction is theoretically possible upon administration of Annexin A5, however there have been no allergic reactions reported in all volunteers exposed to Annexin A5.
The volunteers will not benefit directly from participating in this study.

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

male
age 18-50 years

Exclusion criteria

-cardiovascular disease
-hypertension (systole > 140 mmHg, diastole > 90 mmHg)
-hypercholesterolemia (fasting total cholesterol > 5.5 mmol/l or not fasting total cholesterol > 6.5mmol/L)
-diabetes mellitus (fasting glucose > 7.0 mmol/L or random glucose > 11.0 mmol/L)
-asthma (recurrent episodes of dyspnea and wheezing, or usage of prescribed inhalation medication: i.e. corticosteroids or B2-agonists)
-participation in any clinical drug trial during the last 60 days prior to this study.
-administration of any radioactivity for research purposes during the last 5 years prior to this study.
-concomittant medication

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Crossover
Masking:	Single blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2007
Enrollment:	10
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Persantin
Generic name:	dipyridamole
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	17-04-2007
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2007-001909-26-NL

Register	ID
CCMO	NL17415.091.07