Does ATP cause Annexin A5 targeting in the human forearm?

Published: 12-11-2007
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To study the impact on intra-arterial ATP infusion on Annexin A5 targeting.

Ethical review	Approved WMO
Status	Pending
Health condition type	Arteriosclerosis, stenosis, vascular insufficiency and necrosis
Study type	Interventional

Summary

ID

NL-OMON31848

Source
ToetsingOnline

Brief title
ATP01

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
atherosclerosis, bloodvessel calcification

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 A5, atherosclerosis, ATP, phosphatidylserines

Outcome measures

Primary outcome

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

control thenar muscle at 60 and 240 minutes after Anneinx administration

Secondary outcome

To study influence of adenosine infusion and ischemic preconditioning on ATP

induced Annexin A5 targeting.

Study description

Background summary

Exposed (on the outer leaflet of the cell membrane) phosphatidylserines have been associated with inflammation and activation of the clotting cascade. Both actions are also known to play an important role in cardiovascular disease, as inflammation contributes to development of atherosclerotic plaques, and the clotting cascade participates in thrombus formation that causes acute arterial occlusion. Furthermore, phosphatidylserines may be involved in cell death during reperfusion.
ATP can cause elevation of intracellular Ca2+, what can elicit phosphatidylserine translocation. Preliminary evidence from our molecular pharmacology section suggests that ATP induces phosphatidylserine exposure on endothelial cells. In this study we investigate whether intra-arterial administration of ATP can trigger phosphatidylserine exposure in the forearm and what interventions can inhibit this action of ATP. We hypothesize that ATP is also involved in Annexin A5 targeting after ischemic exercise of the forearm. Therefore, interventions that prevent Annexin targeting in response to ischemic exercise should also prevent phosphatidylserine exposure in response to ATP.

Study objective

To study the impact on intra-arterial ATP infusion on Annexin A5 targeting.

Study design

The main study has an open label parallel randomized design. The nuclear

physician who is responsible for quantification of the Annexin A5 targeting is blinded for the subject allocation.

Intervention

intra-arterial (brachial artery, non-dominant arm) administration of ATP (100 ug/min/dl forearm volume). If this intervention results in Annexin A5 targeting, the effect of intra-arterial adenosine infusion and ischemic preconditioning will be investigated on this ATP-induced targeting

Study burden and risks

Treatment with ATP and adenosine is not expected to harm the volunteers. Administration can be discomfortable (a *pins and needle* sensation in the infused forearm), however this quickly disappears after discontinuation of the infusion. 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. Occurrence of an allergic reaction is theoretically possible upon administration of Annexin A5, however there have been no allergic reaction reported in all volunteers exposed to Annexin A5. The volunteers will not benefit directly from participating in this study.

Contacts

Public
Universitair Medisch Centrum Sint Radboud

postbus 9101
6500 HB Nijmegen
Nederland
Scientific
Universitair Medisch Centrum Sint Radboud

postbus 9101
6500 HB Nijmegen
Nederland

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
-Informed consent

Exclusion criteria

-History of any cardiovascular disease
-Hypertension (in supine position: systole > 140 mmHg, diastole > 90 mmHg)
-Diabetes mellitus (fasting glucose > 7.0 mmol/L or random glucose > 11.0 mmol/L)
-Hyperlipidaemia (fasting total cholesterol > 5.5 mmol/l or random cholesterol > 6.5mmol/L)
-Drug abuse
-Concomitant chronic use of medication
-Administration of radioactivity for research purposes with an effective dose over 5mSV, during the last 5 years
-Participation to any drug-investigation during the previous 60 days as checked with VIP check according to CRCN standard procedures

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2008
Enrollment:	51
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	adenocor
Generic name:	adenosine
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	ATP
Generic name:	ATP

Ethics review

Approved WMO

Date:	12-11-2007
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	EUCTR2007-005893-29-NL
CCMO	NL20283.091.07