The adenosine receptor; a new pharmacological tool in the treatment of sepsis.

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Does antagonism of the adenosine receptor by caffeine lead to an increased LPS-induced inflammatory reaction and an increase in (subclinical) tissuedamage?Does the C34T-polymorphism of the enzyme AMP-deaminase lead to a decreased inflammatory...

Ethical review	Approved WMO
Status	Pending
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Interventional

Summary

ID

NL-OMON31085

Source
ToetsingOnline

Brief title
Adenosine in the treatment of sepsis.

Condition

- Chromosomal abnormalities, gene alterations and gene variants
- Ancillary infectious topics

Synonym
septic shock, systemic inflammation

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: ZonMW subsidie B.P.C. Ramakers (AGIKO-

project)

Intervention

Keyword: Adenosine, cytokine, inflammation, sepsis

Outcome measures

Primary outcome

- Effect on inflammation (temperature, C-reactive protein (crp), white blood

count)

- concentrations of pro- and anti-inflammatory cytokines and adenosine

- vascular (dys)function:

- effects on norepinephrine

- effects on endothelial function

- circulation endothelial cells.

- Renal failure (specific markers for tissue damage)

Secondary outcome

adenosine concentrations

Study description

Background summary

Despite maximal antibiotic and supportive therapy the moratality of septic shock remains 30-50%. Therefore new therapeutic options are needed. Pathophysiological insights are needed to explore new pharmacotherapeutic targets. The adnosine receptor is known for its anti-inflammatory actions and could therefore be a potential target in the treatment of septic shock. Stimulation of the adenosine receptor could potentially lead to a decrease in inflammation and tissue damage.

Study objective

Does antagonism of the adenosine receptor by caffeine lead to an increased LPS-induced inflammatory reaction and an increase in (subclinical) tissuedamage?

Does the C34T-polymorphism of the enzyme AMP-deaminase lead to a decreased inflammatory respons and thereby a decrease of LPS-induced tissuedamage?

Study design

doubleblind placebo controlled

Intervention

LPS (endotoxin) in three groups

1 group will be treated with caffeine, the other with placebo.

The AMPD1 group will be treated the same way as the placebo group

Study burden and risks

LPS-infusion: Intravenous injection of endotoxin (= LPS) in healthy subjects is a general accepted model to study inflammation. Worldwide thousands of volunteers had LPS injected without reports of serious adverse events or hospitalisation.

Caffeine will be infused in a concentration of 4 mg/kg. There are no health risks involved in the infusion of caffeine.

Local infusion of norepinephrine, acetylcholine and nitroprusside does not lead to systemic effects. There are no health risks involved in this infusion.

Total bloodcollection: approximately 350 ml, maximally 400 ml.

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 male volunteers (no relevant medical history, no medication)
no history of syncope
age 18-35 years
non-smokers

Exclusion criteria

History of syncope

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)

Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-07-2007
Enrollment:	33
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Acetylcholine
Generic name:	Acetylcholine
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Caffeine
Generic name:	Caffeine
Product type:	Medicine
Brand name:	Nitroprusside
Generic name:	Nitroprusside
Product type:	Medicine
Brand name:	norepinephrine
Generic name:	norepinephrine
Product type:	Medicine
Brand name:	Standard Reference Endotoxin (SRE)
Generic name:	Lipopolysaccharide
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	26-06-2007
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	EUCTR2007-002860-86-NL
CCMO	NL17473.091.07