The influence of a genetic difference in the bradykinin B1 receptor gene on the inflammatory response of bradykinin B1 receptor stimulation in human mononuclear cells.

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Main objective is to test if the pharmacogenetic profile that is associated with a decreased response to ACE inhibitor therapy influences the bradykinin B1 receptor induced inflammatory response.

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

Summary

ID

NL-OMON37396

Source
ToetsingOnline

Brief title
Genetic influence on bradykinin B1 receptor stimulation.

Condition

- Coronary artery disorders

Synonym
coronary heart disease, Heart and Vascular disease

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Bradykinin B1 receptor, Inflammation, Mononuclear cells, Single nucleotide polymorphism

Outcome measures

Primary outcome

Change in gene-expression of inflammatory genes in response to bradykinin B1 receptor stimulation in human mononuclear cells in the presence or absence of the rs12050217 minor allele.

Secondary outcome

Secondary study parameters are to test if the inflammatory response is influenced by stimulation or inhibition of other components of the RAS or kinin system and evaluation of the plasma for the presence of inflammatory cytokines and RAS hormones. In addition, genetic analysis of other SNP*s in the RAS and kinin system in relation to the inflammatory response is also a secondary measurement.

Study description

Background summary

To better predict the treatment benefit of angiotensin converting enzyme (ACE) inhibitor therapy our research group conducted a pharmacogenetic analysis of genes selected from the renin angiotensin system (RAS) and kinin system in a placebo controlled ACE inhibitor study with coronary heart disease (CHD) patients. In this study an association was discovered between treatment benefit from the ACE inhibitor Perindopril and a single nucleotide polymorphism (SNP)

in the bradykinin B1 receptor gene. The bradykinin B1 receptor is present on a large variety of cells, including endothelial cells, smooth muscle cells and leukocytes. Bradykinin B1 receptor expression is low in normal healthy tissue, but is upregulated during inflammatory events. It has been shown that receptor stimulation induces an increase in inflammatory cytokines and also that inflammatory cytokines upregulate B1 receptor expression. Use of ACE inhibitors is associated with a potentiation of the substrates for bradykinin receptors, therefore we hypothesize that the presence of the pharmacogenetic profile influences the inflammatory response to bradykinin B1 receptor stimulation. To test this hypothesis we would like to investigate in mononuclear cells, isolated from blood of healthy volunteers, if the pharmacogenetic profile earlier discovered is of influence on the inflammatory response to bradykinin B1 stimulation.

Study objective

Main objective is to test if the pharmacogenetic profile that is associated with a decreased response to ACE inhibitor therapy influences the bradykinin B1 receptor induced inflammatory response.

Study design

Single blood donation of 20 ml to isolate human mononuclear cells, in which the response to bradykinin B1 receptor stimulation will be tested.

Study burden and risks

Burden and risk for participating in the study are low, subjects are asked to donate 4 tubes of blood (20ml in total) and a few general questions are asked about age, gender and if the subjects use any medication.

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 persons within the age group of 18-60 years.

Exclusion criteria

Use of ACE inhibitors, AT1 receptor blocker or renin inhibitor.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2012

Enrollment:	44
Type:	Anticipated

Ethics review

Approved WMO Date:	02-05-2012
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
CCMO	NL38754.078.12