Activation of the innate immune system in patients with primary hyperaldosteronism

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON43020

Source
ToetsingOnline

Brief title
Innate immune activation in hyperaldosteronism

Condition

- Other condition
- Vascular hypertensive disorders

Synonym
Conn's syndrome, primary hyperaldosteronism

Health condition

bloedvataandoeningen, arteriosclerose

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Horizon 2020 grant;an European Union funding programme

Intervention

Keyword: hyperaldosteronism, inflammation, innate immune system, PET scan

Outcome measures

Primary outcome

Primary study parameter/endpoint: Vascular wall inflammation in the aorta, the

left and right carotid artery and the left and right iliac and femoral

arteries, as detected with FDG-PET scanning, according to current European

guidelines.

Secondary outcome

Secondary study parameters/endpoints:

The inflammatory/atherogenic phenotype of circulating monocytes in PA

patients.

FDG uptake in spleen and bone marrow.

Study description

Background summary

Primary hyperaldosteronism (PA) is the main cause of secondary hypertension. Patients with hypertension due to PA are at a much higher risk of stroke or myocardial infarction than patients with similar blood pressure levels due to essential hypertension. Cardiovascular events, such as stroke and myocardial infarction are caused by atherosclerosis, which is characterized by a low-grade inflammation of the vascular wall. Monocyte-derived macrophages are the most abundant inflammatory cells within atherosclerotic plaques. Preclinical studies suggest that aldosterone can induce vascular wall inflammation by activation of

the mineralocorticoid receptor (MR) on monocytes and macrophages. In this study, we aim to test the hypothesis that hyperaldosteronism is an independent determinant of vascular wall inflammation and that this is at least in part mediated through activation of the innate immune system by aldosterone.

Study objective

The primary objective of the study is to determine whether patients with PA have a higher level of arterial wall inflammation than patients with essential hypertension.

Secondary Objectives:
To determine whether circulating monocytes of patients with PA are characterized by a more pro-inflammatory phenotype compared to patients with essential hypertension.
To investigate whether ex vivo incubation of healthy donor monocytes with the pooled plasma of patients with PA induces a pro-inflammatory phenotype compared to the plasma of patients with essential hypertension. If so, to investigate is this can be prevented by co-incubation with MR antagonists.
To study whether patients with PA have increased FDG-uptake in the bone marrow and spleen.
To explore whether treatment with MR antagonists or adrenalectomy reduces arterial wall inflammation in patients with PA, if these patients indeed appear to have an increased vascular inflammation.

Study design

Observational study in patients with PA and patients with essential hypertension.

Study burden and risks

The risks associated with participation in this study are low. In total, 50 ml blood will be obtained, which will not have relevant effects. In addition, all patients will undergo a 18FDG-PET/CT. This diagnostic procedure will be performed according to standard state-of-the-art clinical procedures as define by the European association of Nuclear Medicine. Duration of the procedure: 3 hours. Procedure-related exposure to radioactivity: 4,8 mSv. Patients will not have a direct benefit from participation in the study.

If baseline measurements reveal differences in vascular inflammation between PA patients and controls with essential hypertension, Follow-up measurements will be performed. These consist of one additional venous blood sampling (50 ml of venous blood) and a second PET-CT scan using the same scanning protocol after treatment with adrenalectomy or mineralocorticoid receptor antagonists, respectively. Total procedure-related exposure to radioactivity will then be

9,6mSv, which is considered proportional to the potential future benefit that knowledge on the mechanism of the increased cardiovascular risk of patients with PA will yield.

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

Patients with PA (primary hyperaldosteronism):
- Diagnosis of PA according to current guideline
- Age >=18 yrs
- Written informed consent;Patients with essential hypertension:
- Exclusion of PA according to current guidelines
- Age >=18 yrs
- Written informed consent

Exclusion criteria

- Treatment with MR antagonists within the 4 weeks before participation
- Smoking
- Diabetes mellitus
- Previous cardiovascular events (stroke, TIA, myocardial infarction)
- Heart failure
- Auto-inflammatory or auto-immune diseases
- Use of immunomodulating drugs
- Renal failure (MDRD <45)
- BMI >35
- Previous vaccination within 3 months prior to study entry.
- Current infection or clinically significant infections within 3 months before participation (defined as fever >38.5).

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-01-2017
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO

Date:	08-11-2016
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
CCMO	NL58835.091.16