The role of inflammation in the pathogenesis of cardiovascular morbidity in patients with acromegaly

Published: 07-12-2015
Last updated: 19-04-2024

Primary Objective: To examine comprehensively the role of inflammation in the pathogenesis of CV complications in acromegaly. This will be done by exploring the inflammatory and metabolic profiles of patients with acromegaly and correlating these...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hypothalamus and pituitary gland disorders
Study type	Observational invasive

Summary

ID

NL-OMON45957

Source
ToetsingOnline

Brief title
Inflammation and cardiovasculair morbidity in acromegaly

Condition

- Hypothalamus and pituitary gland disorders

Synonym
Acromegaly

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: IPSEN farmaceuticals

Intervention

Keyword: acromegaly, cardiovascular, inflammation

Outcome measures

Primary outcome

Main study parameters/endpoints: circulating inflammatory markers, metabolic parameters and CV parameters, effects of GH, IGF-1 and oxLDL on immune cells in vitro

Secondary outcome

Vascular ultrasound measurements (IMT, PWV and FMD). Muscle morphometry and inflammatory and metabolic profile. Whole genome analysis. Gut and mouth microbiome. Epigenetic profiles. Urine-analysis.

Study description

Background summary

Acromegaly is caused by an excess of growth hormone (GH), which stimulates the secretion of insulin-like growth factor-1 (IGF-1). Patients are characterized by a long-term increase in cardiovascular (CV) morbidity. The pathogenesis of these complications is not completely elucidated. Recent studies link CV diseases to inflammatory processes and it is suggested that CV morbidity in acromegaly might be due to effects of IGF-1 and/or GH on the immune system. However, the inflammatory profile of acromegaly patients is largely unknown and results of previous studies are conflicting.
We hypothesize that prolonged exposure to GH and IGF-1, induces activation of innate immune responses, which might contribute to the long-term CV morbidity in acromegaly.

Study objective

Primary Objective: To examine comprehensively the role of inflammation in the pathogenesis of CV complications in acromegaly. This will be done by exploring the inflammatory and metabolic profiles of patients with acromegaly and correlating these profiles with clinical parameters of atherosclerosis and CV

risk factors;

Secondary Objectives:
To investigate the role of GH/IGF-1 exposure on epigenetic reprogramming of the monocytes in patients with acromegaly.
To investigate in vivo vascular imaging parameters as measure of vascular inflammation and the presence of atherosclerotic disease.
To investigate inflammatory markers and metabolic characteristics in muscle in order to elucidate the molecular and metabolic mechanisms governing this process.
To investigate the contribution of genetic factors to CV morbidity in patients with acromegaly by performing whole genome association studies.
To investigate the correlation between the gut and mouth microbiome and the CV morbidity in patients with acromegaly.

Study design

investigator initiated, single-center explorative cross-sectional and partly prospective study at the Radboudumc Nijmegen.

Study burden and risks

All patients (N=160) and controls (N=80) will undergo venapunction; they will provide stool, urine (in some cases) and perform an oral swab themselves. Of these 160 patients, a selected group of patients (N=60), including patients with active acromegaly and patients with controlled acromegaly (either surgically cured or biochemically controlled by use of medication), and 30 controls will also undergo non-invasive vascular ultrasound measurements. The untreated patients from the previous selected group will be included in a prospective sub-study. In this prospective part of the study, the newly diagnosed patients with (active) acromegaly will also undergo muscle biopsies (N=20). The described procedures are associated with no (cross sectional part) or minor risks (prospective part) and represent a low burden to subjects. Temporary (4 weeks) cessation of statin therapy is not expected to be harmful to the participants. There are no direct benefits for the patients participating in the study. However on the large scale, future patients with acromegaly might benefit from the knowledge accumulated in this study, particularly if the study identifies inflammatory pathways that could be targeted in these patients in addition to treatment that reduces GH/IGF-1 production.

Contacts

Public

Radboud Universitair Medisch Centrum

Geert Grooteplein-Zuid 8
Nijmegen 6525GA
NL
Scientific
Radboud Universitair Medisch Centrum

Geert Grooteplein-Zuid 8
Nijmegen 6525GA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Biochemically confirmed diagnosis of acromegaly by an increased IGF-1 level (e.i. mean > 2 standard deviations (SD) for age and sex) and an insufficient suppression of serum GH levels (e.i. GH *1 mU/l) during an oral glucose tolerance test (OGTT).

Exclusion criteria

Excluded from participation in this study will be subjects who are/have:
* Mentally incompetent;
* Pregnant or breastfeeding;
* Inadequately supplied, unstable or untreated hormonal deficiencies;
* Known inflammatory or infectious diseases or an immunosuppressive status;
* Using hormonal therapy: hormonal contraceptives (42) or hormonal substitution therapy (only applicable for the subgroups of patients);
* Using medication interfering with adiponectines, such as thiazolidinediones;
* Severe comorbidities: active malignancy (except for basal cell carcinoma), serious

psychiatric pathology;
* A systolic blood pressure *160 mmHg and/or a diastolic blood pressure *100 mmHg;
* Known untreated or unstable diabetes mellitus or ischemic cardiovascular disease;
* A self-reported alcohol consumption of >21 units per week.

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):	04-02-2016
Enrollment:	240
Type:	Actual

Ethics review

Approved WMO Date:	07-12-2015
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-01-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-03-2017

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-06-2017
Application type:	Amendment
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	NL54983.091.15