Inflammation and cardiovascular morbidity in acromegaly

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON27425

Source
Nationaal Trial Register

Brief title
AcroInflam

Health condition

acromegaly, acromegaly, inflammatie, inflammation, hartvaatziekten, cardiovasculaire ziekten, cardiovascular disease

Sponsors and support

Primary sponsor: Radboudumc Nijmegen
Source(s) of monetary or material Support: Ipsen Pharmaceuticals

Intervention

Outcome measures

Primary outcome

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

Secondary outcome

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 systemic and vascular inflammation as well as fat infiltration;

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 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

Prolonged exposure to supraphysiological levels of GH and/or IGF-1 induces activation of innate immune responses, which might contribute to the long-term CV morbidity in acromegaly patients.

Study design

cross-sectional part: 1 timepoint.

Prospective part: diagnosis (t=0); t = 6 months; t = 15 months

Intervention

none

Contacts

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Eligibility criteria

Inclusion criteria

In general: Subjects should be at least 18 years old and mentally competent

Acromegaly patients (group A; N = 160):

Limited protocol only: group A1 (N = 100)

- Patients with a history of a biochemically confirmed diagnosis of acromegaly by an increased IGF-1 level (e.i. > 2 standard deviations (SD) above the mean 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).

Extensive protocol (group A2-A4; total N = 60), all also part of group A)- Subgroups of patients
Biochemically confirmed diagnosis of acromegaly as stated above. In addition:

- Untreated patients (group A2; N = 20)
Patients with untreated, active acromegaly (e.i. an increased IGF-1 level and an insufficient suppression of serum GH levels during an oral glucose tolerance test (OGTT).

- Cured patients without hormonal deficiencies or use of hormonal substitution therapy (group A3; N = 20)
Patients successfully treated by surgery or radiation therapy, as confirmed by a sufficient suppression of serum GH levels (e.i. GH <1 mU/l) during an OGTT and an IGF-1 level in the reference range for age and sex.

- Patients not cured after treatment, but currently in biochemical remission, without hormonal deficiencies or use of hormonal substitution therapy (group A4; N = 20)

o ‘Treatment’ is defined as surgery, radiotherapy or medication (somatostatin-analogues, GH-receptor antagonists and/or dopamine-agonists);

o ‘Not cured’ is defined as a patient with insufficient suppression of serum GH levels (e.i. GH ≥1 mU/l) during an OGTT after surgery or radiation therapy OR as a patient who is treated with medication alone and did not undergo radiotherapy or surgery;

o ‘Biochemically in remission’ is defined as a patient who has serum IGF-1 values in reference range for age and sex (e.i. ≤2 SD above the mean for age and sex).

Hormonal substitution therapy is defined as treatment with medication for one or more of the following hormonal deficiencies: hypothyroidism, hypogonadism, hypocortisolism or growth hormone deficiency (GHD).

Hypothyroidism is defined as a serum fT4 value below the reference range; hypocortisolism is defined as an insufficient rise in serum cortisol levels during an insulin tolerance test (ITT); hypogonadism is defined as a level of serum testosterone (in males) or estrogen (in females) below the reference range for age, sex, and menstrual status (in females). GHD is defined as an insufficient rise in serum GH levels during an ITT, or, in case of contraindications for an ITT, as an insufficient maximal GH response during an arginine/GHRH test.

Prospective part of the study (Group A2; N = 20; newly diagnosed, treatment-naive patients)
The inclusion criteria for patients participating in the prospective part are similar to the inclusion criteria of the ‘extensive protocol’, as stated above.

Controls (group B; N = 80): Healthy male and female adults from the general population who are mentally competent.

Exclusion criteria

Cross-sectional part of the study

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 statins;

• Using hormonal therapy: hormonal contraceptives (42) or hormonal substitution therapy (only applicable to the subgroups of patients undergoing the extensive protocol);

• 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.

Exclusion criteria only applicable to control subjects, in addition to above-mentioned criteria:

• Established diagnosis of the following endocrine diseases: acromegaly, GHD, hyper/hypocortisolism, hyper/hypothyroidism, hyperprolactinemia, hypogonadism.

Prospective part of the study (Group A2, N = 20; newly diagnosed, treatment-naive patients).

The exclusion criteria of the prospective part are similar to the inclusion criteria of the

‘extensive protocol’, as stated above. In addition, the following exclusion criteria apply.

Exclusion criteria for FDG-PET/CT-scanning:

• type I diabetes mellitus or fasting plasma glucose >180 mg/dl (= 10 mmol/L);

• Significant radiation exposure within the preceding 12 months;

• Insulin therapy;

• Trauma, recent surgery or recent invasive diagnostic procedures (within the last 4 weeks);

• History of a neoplastic disorder, recent chemotherapy or radiation therapy (within the last 3 months);

• Pathophysiologic disturbances and symptoms, such as diarrhea and localized pain, especially in the extremities;

• Presence of benign disease with high tissue proliferation.

Exclusion criteria for M. vastus lateralis muscle biopsy

• Anticoagulant therapy (e.g. acenocoumarol, marcoumar);

• Lidocaine allergy

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-02-2016
Enrollment:	240
Type:	Anticipated

Ethics review

Positive opinion Date:	26-01-2016
Application type:	First submission

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
NTR-new	NL5561
NTR-old	NTR5682
Other	NL54983.091.15 : CMO2015-2023

Study results