Inflammation and cardiovascular morbidity in acromegaly

Gepubliceerd: 26-01-2016 Laatst bijgewerkt: 18-08-2022

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.

Ethische beoordeling	Positief advies
Status Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON27425

Bron NTR

Verkorte titel AcroInflam

Aandoening

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

Ondersteuning

Primaire sponsor: Radboudumc Nijmegen **Overige ondersteuning:** Ipsen Pharmaceuticals

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

To examine comprehensively the role of inflammation in the pathogenesis of CV

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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;

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

cross-sectional part: 1 timepoint.

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

Onderzoeksproduct en/of interventie

none

Contactpersonen

Publiek

Afdeling Algemene Interne Geneeskunde; Sectie Endorciene Ziekten

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Wetenschappelijk

Afdeling Algemene Interne Geneeskunde; Sectie Endorciene Ziekten

Thalijn Wolters Geert Grooteplein 8; huispost 471

Nijmegen 6525 GA The Netherlands tel: 024-3614599

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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 \geq 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).

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- 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. \leq 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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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 \geq 160 mmHg and/or a diastolic blood pressure \geq 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;

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- 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

Onderzoeksopzet

Opzet

Туре:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Anders
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nodorland

Nederland	
Status:	Werving gestart
(Verwachte) startdatum:	04-02-2016
Aantal proefpersonen:	240
Туре:	Verwachte startdatum

Ethische beoordeling

Positief advies Datum: Soort:

26-01-2016 Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL5561
NTR-old	NTR5682
Ander register	NL54983.091.15 : CMO2015-2023

Resultaten