Visualisation of coronary arteries for the analysis of premature atherosclerosis in patients with adult-onset growth hormone deficiency

Published: 15-09-2006
Last updated: 14-05-2024

Hypothesis:1. Patients who suffer from a hypopituitarism and an adult-onset growth hormone deficiency (AGHD) express more atherosclerotic disease in the coronary system (compared with a historically formed control subjects, present as a database in...

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

Summary

ID

NL-OMON30113

Source
ToetsingOnline

Brief title
Coronary atherosclerotic disease in GHD patients

Condition

- Coronary artery disorders
- Hypothalamus and pituitary gland disorders

Synonym
growth hormone deficiency

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: independent research grant,Pfizer

Intervention

Keyword: adult-onset GH deficiency, coronary visualization, GH intervention, pro-atherogenic phenotype

Outcome measures

Primary outcome

1. Presence of atherosclerotic disease in the coronary system (scored in an

established (blinded) protocol as the level of stenosis within coronary

segments and the level of intracoronary calcium)

Secondary outcome

Secondary outcome measurements

1. level of antioxidant capacity from HDL fractions

2. level of metalloproteinases and its inhibitors in circulation

3. capacity from endothelial progenitor cells to differentiate and to adhere.

Study description

Background summary

Patients with a hypopituitarism (and a growth hormone deficiency) are probably prone for an increased cardiovascular mortality. As a feature of premature cardiovascular disease in these patients, the intima media thickness (IMT) from carotid arteries is found to be increased. Additionally, a proatherogenic phenotype (such as a dyslipidemia, increased levels of pro-inflammatory markers and a protrombogenic profile) is present. After start of recombinant human growth hormone substitution, the intima media thickness is reduced already after 6 months of treatment (sic!). This decrease in atherosclerotic burden is

remarkable (but shown by two independent research groups) and needs therefore additional analysis.

Study objective

Hypothesis:

1. Patients who suffer from a hypopituitarism and an adult-onset growth hormone deficiency (AGHD) express more atherosclerotic disease in the coronary system (compared with a historically formed control subjects, present as a database in the cardiology department from the UMC Utrecht)
2. Atherosclerotic disease in the coronary system wil be in regression after one year substitution with recombinant human growth hormone (in line with previously published results with regard to carotid IMT)
3. Patients with a hypopituitarism and AGHD display additional proatherogenic mechanisms: 2.1 disturbances in antioxidant capacity of the high-density lipoprotein (HDL) fraction, 2.2 disturbances in the differentiation of endothelial progenitor cells with a less capacity to repair damaged endothelium, 2.3 an increase of metalloproteinases as part of the pro-inflammatory profile in circulation .

Study design

After inclusion in the study, patients will have a multi-slice coronary CT scan to analyse atherosclerotic burden in the coronary system. In additional, additional venous blood will be collected to analyse the different questions as mentioned under hypothesis 3. Both multi-slice coronary CT scan and venous blood collection will be repeated after one year GH substitution (substitution of GH is part of regular care). The obtained results will be analysed in a transectional analysis (concerning multi-slice coronary CT scan before GH substitution) and as an effect of GH intervention.

Intervention

Patients will be treated with recombinant GH (daily dosage titrated upon plasma IGF-1 levels; adjusted for sex and age) in line with international consensus guidelines (regular care)/treatment)

Study burden and risks

The efforts will consist of two additional visits in one year to the UMC Utrecht to have a multi-slice coronary CT scan and a venous blood puncture. The efforts are therefore reduced at a minimum level. The risks are quite minimized because no experimental methods are used. All techniques are part of daily patient care. An emotional burden may exist in the knowledge of atherosclerotic burden. However, patients could indicate a "not want to know

teh results". On the other hand, a pronounced expression of atherosclerotic disease could give rise to addional care with a focus on prevention of cardiovascular morbidity (such as life style adaptation and reduction of present cardiovascular risk factors)

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

1. Biochemically proven GH deficiency
2. Age between 35 and 60 years
3. GH deficient within half a year of neurosurgical procedure or GH deficient at least 5 years
4. Optimal substitution of other hormones

Exclusion criteria

1. BMI >30
2. Positive history of myocardial or valve or coronary disease or symptoms that suggest coronary disease (chest pain in rest or during exercise)
3. Rhythm disturbances
4. Moderate or severe pulmonary disease
5. Impairment in renal function (Creatinin clearance < 60 ml/min)
6. Positive family history of primary dyslipidemia
7. Positive family history from premature cardiovascular disease
8. Positive family history of diabetes type II
9. Allergy for contrast
10. Claustrophobia

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2006
Enrollment:	30
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Genotropin
Generic name:	somatropin/recombinant growth hormone
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	06-10-2006
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
EudraCT	EUCTR2006-001574-24-NL
CCMO	NL11803.091.06