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Growth hormone deficiency and clotting

Submission date
07/01/2013

Recruitment status
No longer recruiting

Registration date
29/01/2013

Overall study status
Completed

Last Edited
15/05/2018

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Patients with an underactive pituitary gland (hypopituitary) on replacement hormones but not growth hormone replacement have an approximately twofold increase in mortality, mainly due to diseases of the blood vessels (heart attacks, strokes). These patients show increases in body fat, reduced muscle mass, increased blood cholesterol, difficulties handling sugar, as well as increased levels of some clotting factors. How these latter observations translate to blocking of arteries and increased vascular disease is unclear. Blocking of arteries begins with inflammation of the lining, followed by accumulation of fat in the wall of the artery resulting in a localized plaque. Later clot formation on top of the inflamed fat-filled plaque blocks the artery. We aim to comprehensively characterize risk factors for blood vessel (vascular) disease in hypopituitary patients and study the process by which these risk factors translate into vascular disease. We also aim to determine whether growth hormone replacement can reverse any documented abnormalities. The study will include patients with an underactive pituitary gland who are deficient in growth hormone, and who wish to undergo a trial of growth hormone replacement.

Who can participate?
Adults over age 18 years, and of either gender with confirmed growth hormone deficiency (GHD).

What does the study involve?
The study involves measurement of height, weight, waist and hip circumference, and assessment of body fat and muscle content (electronic scale [bioimpedence] and absorptiometry [low dose X-rays]). Blood will be taken for a number of measures of blood fat, inflammation, sugar handling, factors that make the blood more sticky, and to examine the characteristics of clots that these patients form. A measurement of the thickness of the wall of blood vessels will be made with ultrasound (sound waves), and a blood pressure monitor worn for 24 hours. Once these tests have been performed the volunteers will be started on growth hormone and the dose optimised over three months. Patients will be left on the optimal growth hormone dose for three months and then all the tests repeated.

What are the possible benefits and risks of participating?
There are no direct benefits to participating in the study. The data derived from the study will enhance our understanding of the risk of an underactive pituitary gland, how the observed abnormalities translate into vascular disease, and whether growth hormone can reverse the observed abnormalities. There are no significant risks associated with participating in the study.

The dose of X-rays used in the absorptiometry scans is equivalent to the exposure received during half a day of normal background radiation from our surroundings.

Where is the study run from?
The study is run from the Department of Endocrinology at Leeds Teaching Hospitals NHS Trust (UK).

When is the study starting and how long is it expected to run for?
The study is expected to start in April 2013 and last three years.

Who is funding the study?
Although the study is funded by Sandoz UK Limited, the study protocol and design is wholly the concept of Dr R Murray at Leeds Teaching Hospitals.

Who is the main contact?
Mrs J Lynch
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Contact information

Type(s)
Scientific

Contact name
Dr Robert Murray

Contact details
Dept of Endocrinology
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Beckett Street
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
ED12/10391

Study information

Scientific Title
Elucidation of the effects of growth hormone (GH) deficiency and GH replacement on vascular risk and clot dynamics

Study objectives
Epidemiological studies support an increased vascular morbidity and mortality in growth hormone deficient (GHD) adults though do not prove cause and effect. We hypothesize that GH deficiency is associated with an inflammatory and thrombotic environment, which translates into the observed excess vascular mortality. Furthermore, we hypothesise that GH replacement will normalize the abnormalities in the inflammatory and thrombotic pathways.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee Yorkshire & The Humber - South Yorkshire, 04/03/2013, REC ref: 13/YH/0061

Study design
Single-site cross-sectional at baseline, and thereafter incorporates longitudinal case-controlled data after routine clinical intervention with growth hormone replacement

Primary study design
Observational

Secondary study design
Cross sectional study

Study setting(s)
Hospital

Study type(s)
Screening

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Patients with hypothalamo-pituitary pathology, proven to be severely growth hormone deficient

Interventions
For patients and controls measures will be performed at baseline and repeated in the patients alone after growth hormone dose optimisation and three months on the ideal dose.

Measurements include:
1. Anthropometry
2. Body composition [bioimpedance & dual-energy X-ray absorptiometry (DXA)]
3. Conventional vascular risk factors (cholesterol, glucose handling)
4. Additional vascular risk factors (markers of inflammation, coagulation, fibrinolysis)
5. 24-hour blood pressure recording
6. Ultrasound of major arteries to examine intima-media thickness
7. Studies of clot formation and lysis

Intervention Type

Other

Phase
Not Applicable

Primary outcome measure
Turbidity analysis

Secondary outcome measures
1. Inflammatory, fibrinolytic, procoagulant markers
2. Lipids
3. 24-hour blood pressure
4. Body composition

Measurements will occur prior to commencing growth hormone replacement, and having been on a stable dose of growth hormone for three months. Measurement of body fat and muscle will be performed using an electrical scale (bioimpedence analysis) and X-ray absorptiometry. The latter uses low dose X-rays to differentiate between fat, muscle and bone. Levels of blood fats, sugar, clotting factors etc will be measured using standard laboratory assays. Rates of clot formation and breakdown will be assessed in the laboratory by measurements of changes in optical density using a spectrophotometer (measures changes in light) both at the beginning of the clotting reaction and after formation of the mature clot.

Overall study start date
01/04/2013

Completion date
01/04/2016

Eligibility

Key inclusion criteria
1. Able to give written consent
2. Adults over age 18 years, and of either gender with confirmed GHD (insulin stimulation test <3 ug/L)
3. Other hormone replacement therapy stable for at least three months

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants

140

Key exclusion criteria
1. Active malignancy
2. An acute vascular event within three months of the study
3. Any therapy other than hormone replacement
4. Serum creatinine >120 mol/l
5. Abnormal liver function tests (LFTs) [alanine transaminase (ALT) >3 fold upper limit of normal]

Date of first enrolment
01/04/2013

Date of final enrolment
01/04/2016

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
St James's University Hospital
Leeds
United Kingdom
LS9 7TF

Sponsor information

Organisation
Leeds Teaching Hospitals NHS Trust (UK)

Sponsor details
Research and Development
34 Hyde Terrace
Leeds
England
United Kingdom
LS2 9LN

Sponsor type
Hospital/treatment centre

Website

http://www.leedsth.nhs.uk

ROR
https://ror.org/00v4dac24

Funder(s)

Funder type
Industry

Funder Name
Sandoz Pharma UK Limited (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No