Residual effects of Cushing*s syndrome after long term remission: Impact on adipose tissue, insulin resistance, exercise intolerance and increased risk of cardiovascular disease.

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To identify some of the mechanisms in patients in remission of Cushing*s syndrome that contribute to the persistence of visceral obesity, systemic inflammation, insulin resistance, sarcopenia, a low muscle oxidative capacity and increased risk of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Endocrine and glandular disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON37749

Source
ToetsingOnline

Brief title
Residual effects of Cushing*s syndrome

Condition

- Endocrine and glandular disorders NEC
- Musculoskeletal and connective tissue disorders NEC
- Vascular disorders NEC

Synonym
Hypercortisolism

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Cushing, Long-term, Remission, Syndrome

Outcome measures

Primary outcome

- Physical fitness measured with an incremental cycling exercise test to exhaustion (VO2max-test).

- Brachial %FMD levels as a marker of conduit artery endothelial function, NO-mediated endothelium-(in)dependent vasodilation of the forearm resistance arteries.

- Mitochondrial and capillary density, eNOS levels and eNOS phosphorylation, NADPH oxidase activation, total JNK activity levels and expression of IKK* in skeletal muscle cells.

- Amount of cytokines, adipokines and their mRNA and macrophage infiltration in subcutaneous fat tissue.

Secondary outcome

-

Study description

Background summary

Cushing*s syndrome is the combination of signs and symptoms caused by

prolonged and inappropriately high exposure of tissue to glucocorticoids. Chronic hypersecretion of cortisol causes central obesity, systemic hypertension and glucose intolerance, sequentially leading to an increase in cardiovascular morbidity and mortality in the active phase of the disease. Patients in remission of CS remain to have a markedly impaired QOL and there are multiple clear indications in literature that the increased cardiovascular risk profile persists, even after long-term remission. However, all studies are performed with small numbers of patients and results are contradictory. Furthermore, the underlying mechanisms are poorly identified although there are indications that persistence of visceral obesity, systemic inflammation, insulin resistance, sarcopenia and a low muscle oxidative capacity play a role.

Study objective

To identify some of the mechanisms in patients in remission of Cushing*s syndrome that contribute to the persistence of visceral obesity, systemic inflammation, insulin resistance, sarcopenia, a low muscle oxidative capacity and increased risk of cardiovascular disease in order to be able to target future treatment strategies towards correction of these mechanisms.

Study design

This study is a cross-sectional matched case-control study.

Study burden and risks

Subjects will visit on three separate occasions. On the first visit an exercise tolerance test will be performed. On the second visit a FMD-test and an invasive vascular measurement will be performed. On the third visit muscle biopsy and subcutaneous fat aspiration will be performed. The nature and extent of burden and risks associated with the different tests are extensively described in paragraph 10.3.

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

- Subjects should be over 18 years old with the ability to read and comprehend the Dutch language
- Patients should be successfully cured for at least five years. Current remission should be confirmed by a recent 1mg dexamethasone suppression test

Exclusion criteria

- GH deficiency (This should be ruled out by an insulin tolerance test or an arginine/GHRH test) unless GH is properly supplemented (IGF-1 * 2)
- Serious co-morbidity (i.e. terminal malignancy, serious psychiatric pathology)
- Pregnancy
- Known diabetes mellitus
- Use of medication interfering with the cardiovascular system (ACE inhibitors, calcium antagonists, angiotensin II receptor antagonists) or adiponectins (thiazolidinediones)
- Severe cardiopulmonary disease as stated in the 2001 American heart association and 2002 American college of cardiology/American heart association guidelines
- Orthopedic and/or neurological diseases that impair exercise

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):	01-09-2012
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO

Date:	11-07-2012
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
CCMO	NL39893.091.12