A randomized double blind cross-over trial of the effects of low dose and high dose hydrocortisone replacement therapy on cognition, quality of life, metabolic profile and somatosensation in patients with secondary adrenal insufficiency

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hypothalamus and pituitary gland disorders
Study type	Interventional

Summary

ID

NL-OMON38411

Source
ToetsingOnline

Brief title
Hydrocortisone replacement in patients with adrenal insufficiency.

Condition

- Hypothalamus and pituitary gland disorders

Synonym
adrenal insufficiency, secondary adrenal insufficiency

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Adrenal insufficiency, Cognition, Hydrococortisone

Outcome measures

Primary outcome

The primary endpoint is cognitive performance.

Secondary outcome

The secondary endpoints are quality of life, metabolic profile and

somatosensation.

Study description

Background summary

A wide variety in HC substitution dose-regimens are considered physiological for patients with adrenal insufficiency. However, it is likely that cognition is negatively influenced by higher cortisol exposure to the brain. No studies have been performed to assess the effects of treatment regimens with a low physiological HC substitution dose on cognition in comparison to a high physiological dose. These treatment regimens should take body weight and multiple dosing into account. In addition, substitution doses should be monitored by clinical evaluation and biochemical analysis for adverse effects associated with over- or under-replacement.

We hypothesize that a low physiological HC dose results in better cognitive performance and improved metabolic profile, but in decreased quality of life with excess common somatic complaints and in increased sensitivity when compared to a high physiological HC dose.

Study objective

The aim of this study is to investigate whether a physiologically low hydrocortisone (HC) dose is better for cognition as compared to a high hydrocortisone dose. In addition, quality of life, metabolic profile and somatosensation will be described in relation to HC dose.

Study design

Randomized, double blind cross-over design.

Intervention

Patients receive either a low dose HC (0.2-0.3 mg/kg body weight) for 10 weeks followed by 10 weeks of high dose HC (0.4-0.6 mg/kg body weight) or high dose HC followed by a low dose of HC.

Study burden and risks

Burden: At baseline and after completion of both treatment arms patients will undergo neuropsychological evaluation. One week before the three visits (duration ± 4 hours) they will also fill in quality of life questionnaires.
Blood samples will be drawn before and after the test battery. The day before each visit to the hospital, patients will collect a 24-h urine collection.
During both treatment periods patients will keep a diary regarding common somatic complaints and mood.

Risks: Additional hydrocortisone dose escalation (max. of seven days per treatment arm) to prevend hypocortisolism is allowed, however not in the week preceding the hospital visit. The risk of severe hypocortisolism on study dose-regimens of HC is small and estimated to be similar to conventional treatment at the outpatient clinic.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700 RB
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700 RB

NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients with secondary adrenal insufficiency
Age >= 18 - 75 years
>= One year after tumor treatment with surgery and/or radiotherapy
On stable concomitant medications for at least six months prior to entry of study
Body weight 50-100 kg

Exclusion criteria

Inability of legal consent
Documented cognitive impairment
Drug abuse/dependence
History of psychiatric disorders
Use of anti-epileptics (e.g. carbamezapine)
Cushings disease
Type 1 or Type 2 diabetes
Current treatment for second malignancy

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-05-2012
Enrollment:	66
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	n.a.
Generic name:	hydrocortisone
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	22-11-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-12-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-06-2012
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-09-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2011-000864-82-NL
CCMO	NL35668.042.11

Study results

Date completed:	13-06-2013
Actual enrolment:	63