PITUITARY DAMAGE AFTER TRAUMATIC BRAIN INJURY;
Occurrence of growth hormone deficiency at long term follow-up and the beneficial effects of growth hormone substitution on cardiovascular performance, quality of life and functional abilities

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To evaluate whether GH substitution in patients with an isolated GHD after TBI could reverse the severity of symptoms which characterize GHD.

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON30305

Source
ToetsingOnline

Brief title
Growth hormone substitution in isolated growth hormone deficiency after TBI

Condition

- Other condition
- Hypothalamus and pituitary gland disorders
- Structural brain disorders

Synonym
growth hormone deficiency after head injury, traumatic brain injury-induced growth hormone deficiency

Health condition

traumatologische aandoeningen

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W,independent research grant,Novo Nordisk

Intervention

Keyword: growth hormone deficiency, growth hormone substitution therapy, post traumatic complaints, traumatic brain injury

Outcome measures

Primary outcome

1. change in different components of the GHD syndrome, before and after GH

substitution, in patients with TBI

2. change in physical and neuro-cognitive factors, not necessarily associated

with GHD syndrome, before and after GH substitution, in patients with TBI

Secondary outcome

not applicable

Study description

Background summary

Traumatic brain injury (TBI) is a frequent cause of morbidity and mortality in young adults. Most of the patients have impaired physical and psychological

functioning. Most of these impairments cannot be explained by direct tissue damage due to trauma.
It was found recently that individuals with a TBI display pituitary insufficiency, ranging from isolated defects to multiple defects of pituitary hormonal axes. Most often an isolated defect was found in the somatotropic axes, an isolated growth hormone deficiency (in about 10% of all TBI patients). The classical syndrome of growth hormone deficiency (GHD) in adulthood is characterized by a change in body composition with an increase in intraabdominal fat (and consequently an increased risk profile for cardiovascular disease; eg. a proatherogenic lipid profile), impaired cognitive function and a decrease in Quality of Life. Interestingly, this complex of symptoms is highly similar to those which are observed among individuals after TBI. Intervention with recombinant GH in adults is a safe and experienced mode of treatment.

Study objective

To evaluate whether GH substitution in patients with an isolated GHD after TBI could reverse the severity of symptoms which characterize GHD.

Study design

intervention study with an Off-On-Off treatment design

Intervention

Patients with an isolated GHD will be evaluated at baseline (Off treatment), after 12 months recombinant GH (Norditropin Simplexx) substitution (On treatment), and 6 months after stop of GH substitution (Off treatment). The daily dosage of rGH will be titrated on plasma IGF-1 levels, adjusted for age and sex. Patients will visit the out patiënt clinic of the department of Endocrine Diseases during the period of rGH substitution.

Study burden and risks

GHD in adulthood is a well recognized clinical entity with an option for adequate treatment. Substitution with rGH, especially with actual low dose regimens, is not frequently associated with major side effects. Minor side effects consist of mild oedema of the legs and joints which could manifest the first months after start of rGH substitution. Therefore, identification of a GHD state in patients with a history of TBI indeed offers additional opportunities to improve their general condition. This study protocol only consists of regular methods which are daily practice, eg. venous puncture and completion of questionnaires (with collection of 45 ml of venous blood each visit). In order to assess cardiac performance, a transthoracal ultrasound is performed at visit 0, visit 12 months and a visit 18 months (in collaboration

with dr MJM Cramer, UMCU, the Netherlands)

Contacts

Public
Universitair Medisch Centrum Sint Radboud

Reinier postlaan 4
6500 HB Nijmegen
NL
Scientific
Universitair Medisch Centrum Sint Radboud

Reinier postlaan 4
6500 HB Nijmegen
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. The patient visits the emergency department with mild, moderate or severe traumatic brain injury. (Mild traumatic brain injury is defined as a history of impact to the head and a Glasgow Coma Scale score (GCS) 13-15 at entry in the emergency room, moderate traumatic brain injury is defined as a GCS 9-12 at entry in the emergency room, and severe traumatic brain injury is defined as a GCS <= 8 at entry in the emergency room)
2. The trauma has occurred less than 24 hours before visiting the emergency department.
3. Age >= 18 years and <= 65 years at the time of inclusion
4. Absolute growth hormone deficiency (defined as growth hormone response < 9 mE/l in the GHRH-arginine test), diagnosed within one of the protocols going with ABR form no. 14996 or

14998

Exclusion criteria

1. Age > 65 or < 18 years
2. No oral or written informed consent by patient
3. Pre-existent neuro-endocrine disorder
4. Co-existent dysfunction of pituitary axis other than the somatotropic axis
5. Instable infiltrative disease in the hypothalamus/pituitary region (eg sarcoidosis, tumour metastasis)
6. BMI >30 kg/m2
7. Primary dyslipidemia that necessitates treatment
8. Positive family history of premature cardiovascular disease
9. Overt diabetes mellitus type II (including a history of gestational diabetes mellitus)
10. Impairment in renal function (Creatinin clearance < 60 ml/min)
11. Pregnancy or wish for pregnancy during the study period, lactation
12. Retinal disease
13. History of neoplasmata
14. Co-existent disease with decreased life expectancy, especially active malignant tumor
15. Chronic alcohol or drug abuse

Study design

Design

Study phase:	4
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2007
Enrollment:	50
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Norditropin SimpleXx
Generic name:	somatropin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	06-11-2006
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	EUCTR2006-005442-37-NL
CCMO	NL14034.091.06