Pituitary dysfunction after traumatic brain injury: a new challenge in neurotraumatology

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Protocol 1: To determine whether pituitary dysfunction is present at intermediate duration of follow-up after traumatic brain injuryProtocol 2: To determine whether injury to brain tissue that explains traumatic brain injury-induced pituitary…

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON30285

Source
ToetsingOnline

Brief title
Pituitary dysfunction after traumatic brain injury

Condition

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

Synonym
brain injury caused by trauma, traumatic brain injury

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

Intervention

Keyword: associated with the hormonal stress response, Functioning in daily life, Pituitary dysfunction, Polymorphisms of genes, Traumatic brain injury

Outcome measures

Primary outcome

Protocol 1: Proportion of TBI patients who display a pituitary dysfunction

Protocol 2:

a) Difference in volume of pituitary gland and hypothalamus

b) Difference in structural connectivity between hypothalamus and hypothetical

projections

c) Differences in functional connectivity in the resting state

Protocol 3: Difference in functioning in daily living as expressed by

GOS-E-score

Secondary outcome

Protocol 1:

a) Proportion of patients with a history of trauma without head injury that

have pituitary dysfunction

b) Difference in functioning in daily living as expressed by GOS-E-score

c) Difference in abnormalities going with classical pituitary dysfunction, as

assessed by a questionnaire, physical examination and cardiovascular analysis

d) Difference in scores on questionnaires on quality of life, physical,

cognitive and psychological functioning and fatigue

Protocol 2: Difference in structural cerebral defects

Protocol 3:

a) Difference in scores on questionnaires on quality of life, physical,

cognitive and psychological functioning and fatigue

b) Difference in scores on neuropsychological evaluation

c) Difference in presence of biochemical pituitary dysfunction

Study description

Background summary

Traumatic brain injury (TBI) yearly hits a large number of mainly young people. The consequences (i.e. long lasting psychocognitive and somatic limitations: posttraumatic complaints) are a large burden to patient and society. These posttraumatic complaints show hitherto unrecognized striking similarities to the signs and symptoms that occur in neuroendocrine disorders. Recent studies suggest that the prevalence of anterior pituitary dysfunction following head injury is approximately 30% of all moderate and severe TBI patients. So far sparse research has been carried out on patients with mild TBI and at intermediate follow-up (1 to 2 years), and there was a selection bias. It is not elucidated yet whether the observed pituitary dysfunction related to TBI is clinically displayed.

Actually it is assumed that pituitary ischemia is a sole pathophysiological mechanism through which TBI causes disruption of pituitary function. The involvement of the distinctive pituitary hormonal axes and the reversible pattern of pituitary dysfunction in some patients argue for other pathophysiological mechanisms. An additional mechanism could be damage to structures projecting on the hypothalamus. In that case, plasticity of brain

function and regenerative capacity after damage of brain tissue could explain the observed reversibility of pituitary dysfunction.

Another approach to predict impaired recovery after TBI is the analysis of genetic polymorphisms. TBI disturbs the functional equilibrium in the local tissue of the brain, impairing recovery. Optimal adaptation of neuro-endocrine balances is imperative for restoration of this equilibrium. Genetic polymorphisms may account for differences in the expression of the stress response of individual hormonal axes and the capacity to adapt to tissue damage associated with TBI.

Study objective

Protocol 1: To determine whether pituitary dysfunction is present at intermediate duration of follow-up after traumatic brain injury

Protocol 2: To determine whether injury to brain tissue that explains traumatic brain injury-induced pituitary dysfunction, is localized in the hypothalamo-pituitary zone and/or in the afferent (especially cortical) projections to the hypothalamus

Protocol 3: To evaluate whether polymorphisms in genes, associated with the stress response of distinctive pituitary hormonal axes, are related to clinical outcome after traumatic brain injury

Study design

Protocol 1 and 3: explorative cohort study

Protocol 2: observational study

Study burden and risks

Post traumatic complaints and psychological/physical limitations after TBI are a large burden to patiënt and society. New methods of prevention and treatment of these limitations are therefore important. Once insufficiency of the pituitary is diagnosed, it is easily treatable by hormone substitution. Actually, it has not been elucidated yet whether pituitary dysfunction could explain a major part of the clinic that is found in patients with a history of TBI at intermediate follow-up. Most factors limiting recovery, such as a disturbed cerebral metabolism in the acute phase, cannot be influenced. Hormone deficiencies in contrast can be treated within regular health care by hormone substitution therapy. A better understanding of the pathophysiological mechanisms that are involved in TBI-associated pituitary insufficiency could give rise to development of new intramural and transmural approaches in the first months after trauma with adaptations in the revalidation program.

We expect that in the group of patients whose expression of will is impaired as a consequence of their brain injury, the prevalence of pituitary dysfunction is highest, as their brain injury on the average is more serious. As their brain injury on the average is more serious, a study population excluding patients whose expression of will is impaired as a consequence of their brain injury, would not be representative for the total group of patients with moderate or severe TBI. The results of such a study would not be generalisable. Also we expect that pituitary dysfunction may contribute to maintenance of the impairment of expression of will, as we expect pituitary dysfunction to contribute to an impairment of psychological and cognitive recovery after TBI.

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. All patients who visit the emergency department with a mild, a moderate or a 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. Initial trauma occurred less than 24 hours before visiting the Emergency Department.
3. Age >= 18 years and <= 65 years

Exclusion criteria

1. Age > 65 years or < 18 years
2. No oral or written informed consent by patient or proxy
3. Pre-existent neuro-endocrine disorder
4. Instable infiltrative disease in the hypothalamus/pituitary region (eg sarcoidosis, tumour metastasis)
5. BMI >30 kg/m2
6. Pregnancy or wish for pregnancy during the study period women, lactation
7. Co-existent disease with decreased life expectancy, especially active malignant tumor
8. Chronic alcohol or drug abuse

Study design

Design

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

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2007
Enrollment:	600
Type:	Anticipated

Ethics review

Approved WMO

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	NL14996.091.06