Prevention of neuropsychiatric adverse effects caused by dexamethasone: insights from a placebo-controlled trial with hydrocortisone.

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Investigate whether a low-dose of hydrocortisone (cortisol) reduces neuropsychiatric symptoms in glioma, meningioma and brain metastasis patients who are perioperatively treated with a high dose of the synthetic glucocorticoid dexamethasone,...

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

Summary

ID

NL-OMON54782

Source
ToetsingOnline

Brief title
DEXA-CORT

Condition

- Other condition
- Deliria (incl confusion)

Synonym
Psychiatric adverse effects and sleep

Health condition

Depressie, Manie, Angst, Cognitie, Slaap

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: Dexamethasone, Hydrocortisone, Psychiatric adverse effects

Outcome measures

Primary outcome

The primary parameter is neuropsychiatric adverse effects measured by the Brief Psychiatric Rating Scale (BPRS).

Secondary outcome

Secondary parameters are neuropsychiatric adverse effects measured with different questionnaires (Hospital Anxiety and Depression Scale, Altman Self-Rating Mania scale, Positive Affect Negative Affect Scale, Delirium Observation Scale); neurophysiological functioning assessed with different cognitive tests, sleep quality measured with the Leeds Sleep Evaluation Questionnaire (LSEQ) and quality of life with QLQ-C30+BN20.

Study description

Background summary

Over 800.000 individuals are treated annually in The Netherlands with synthetic glucocorticoids like dexamethasone. These drugs are life-saving but induce significant neuropsychiatric complaints in thousands of patients. Dexamethasone acts only via glucocorticoid receptors (GRs), while the endogenous hormone hydrocortisone stimulates in brain also mineralocorticoid receptors (MRs). An unwanted side effect of dexamethasone is the strong suppression of

hydrocortisone levels. This depletes brain MRs from ligand, which is known to compromise brain function. We hypothesize that co-treatment with a physiological dose of hydrocortisone will re-fill brain MRs and prevent - or reduce - psychopathology caused by synthetic glucocorticoids.

Study objective

Investigate whether a low-dose of hydrocortisone (cortisol) reduces neuropsychiatric symptoms in glioma, meningioma and brain metastasis patients who are perioperatively treated with a high dose of the synthetic glucocorticoid dexamethasone, compared to patients treated with high dose dexamethasone alone.

Study design

A randomized double-blind placebo-controlled trial.

Intervention

Patients will be randomized to hydrocortisone versus placebo, as add-on to the regular dexamethasone scheme peri-operative. Hydrocortisone/placebo will be administered orally: 2x 10 mg/day.

Study burden and risks

There are no additional risks for the study intervention. When hydrocortisone is used as substitution therapy when the own cortisol production is too low, the chance to get side effects are very small. Dexamethason causes suppression of the bodies own cortisol production. The hydrocortisone administered to the dexamethasone will restore the normal physiological cortisol levels in the body. The administered hydrocortisone should prevent the negative side effects of dexamethasone. This intervention has been performed in 1 other study of Warris et al. (2016). They tested the same principle but in pediatric patients with leukemia. They found that in children who suffered from most severe side effects, the hydrocortisone was able to reduce this. The burden for the subjects in this study is estimated to be 5 hours spread over 3 months.

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

- Cranial glioma, meningioma or brain metastasis scheduled to undergo surgery (resection)
- Minimal dose of peri-operative cumulative dexamethasone of 24mg or more in 6 days
- >=18 years
- Good clinical condition; KPS>=70
- Life expectancy >=6 months

Exclusion criteria

- Non-native speakers of Dutch or insufficient command of the Dutch language
- Patients that are unable to overview consequences of trial participation
- Patients with severe aphasia
- Patients that are not able to fill in the questionnaires because of cognitive impairments at the discretion of the physician
- Patients with psychiatric diseases or neurological deficits that interfere with the study to the judgement of treating physician

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	10-09-2019
Enrollment:	180
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Hydrocortisone
Generic name:	Hydrocortisone
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	07-01-2019
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	22-03-2019
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	03-04-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	02-05-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	15-07-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	29-11-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	17-12-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO
Date: 24-11-2021

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 17-12-2021

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 31-01-2022

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 21-03-2022

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 07-02-2023

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 13-03-2023

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	28-03-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	30-04-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 22627
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2017-003705-17-NL
CCMO	NL63350.058.18
OMON	NL-OMON22627