Long-term effects of neonatal glucocorticoid treatment on health in later life (follow-up study)

Published: 03-03-2009
Last updated: 06-05-2024

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

Summary

ID

NL-OMON33574

Source
ToetsingOnline

Brief title
Long-term effects of neonatal glucocorticoid treatment

Condition

- Other condition

Synonym
long-term effects of neonatal glucocorticoid treatment

Health condition

aandoeningen ontstaan in de perinatale periode

Research involving
Human

Sponsors and support

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

Intervention

Keyword: dexamethasone, glucocorticoids, hydrocortisone, neonatal chronic lung disease

Outcome measures

Primary outcome

The proposed study will provide data on behavioral, neuropsychological, and motor function. Secondly, basal physiological function (HPA-axis, and immune, cardio-vascular and central nervous system function), markers for cardio-vascular, renal and metabolic disease, and pain sensitivity will be evaluated. Finally, we will determine stress-induced HPA-axis, cardiovascular system and central nervous system responses. Blood cells will also be saved to isolate DNA to perform epigenetic studies in the future.

Secondary outcome

Not applicable.

Study description

Background summary

Neonatal glucocorticoid (GC) treatment, in particular dexamethasone (DEX), is used worldwide to prevent prematurely born babies from developing chronic lung disease (CLD). Despite the inevitability for clinicians to use GCs and the effectiveness of DEX to prevent CLD, recent evidence showed long-term adverse effects of neonatal DEX treatment. From our previous study we had to conclude that long-term effects of neonatal DEX treatment in children at school-age (age 7-10 years) were in line with earlier findings in animals. We observed hyporeactivity of the cardio-vascular system, autonomous nervous system, and hypothalamic-pituitary-adrenal (HPA-) axis in response to stress and an altered

immune balance. DEX-treated children had deviant neuromotor development, more often needed special education, and had a higher tendency towards aggressive and delinquent behavior, more social and emotional problems, and attention deficits than non-treated children. Interestingly, negative long-term effects were absent in children at school-age who had been treated with the equally effective hydrocortisone (HC). It is unknown what the consequences of neonatal GC treatment in humans are later in life. The gloomy picture of life-long deleterious effects of DEX, as was observed in rats embodies a strong indication for careful follow up of GC-treated children.

Study objective

The first objective is to determine the effects of neonatal GC treatment on basal behavioral and neuropsychological measures, emotion and motor development during adolescence. The second objective is to study basal physiological parameters in ex-prematures treated with glucocorticoids. HPA-axis, and immune, cardio-vascular and central nervous system function will be evaluated and diagnostic markers for cardio-vascular, renal and metabolic diseases will be screened. The effects of neonatal glucocorticoid treatment on development of increased pain sensitivity will be determined as well. The third objective will be to study whether the impaired stress-induced HPA-axis, cardiovascular and central nervous system responses in glucocorticoid-treated individuals at school-age further decrease during adolescence. For all three objectives it will be evaluated whether long term effects of neonatal DEX differ from the use of and neonatal HC treatment and whether deviations during adolescence increase compared to measurement at earlier school-age.

Study design

The proposed study is a retrospective cohort study in which cross-sectional group comparisons will be carried out. Furthermore, it is a long-term follow up study investigating the longitudinal development or possible aggravation of functional deviances due to neonatal use of glucocorticoids in prematurely born babies at risk to CLD.

Study burden and risks

All participants will be visited at home for neuropsychological testing and for filling out psychological questionnaires (2* hours). Participants will be asked to collect saliva on two consecutive mornings for the determination of the cortisol awakening response, and to perform a DEX suppression test (intake of 0.25mg DEX), for the evaluation of the negative feedback function of the HPA-axis. After 2 weeks a test day will be planned at the Wilhelmina Children*s Hospital (duration: 7 hours), which will include a: anamnesis + physical examination, pain sensitivity measured by algometer, motor development testing, questionnaires on health, emotion, and behaviour, and a standardized social

stress test. Before the stress test an i.v. line will be inserted to draw 6 blood samples, a total volume of 76 ml, and cardio-vascular functions will be measured non-invasively by an ambulatory device (Nexfin-HD). To minimize burden during the insertion of the i.v. line, lidocaine spray will be used. If requested by the participant, the parent / caretaker will be present in the same room during testing. Based on the age of the participants, the nature of the tests, and the requested time we consider the burden as acceptable and the risks associated with participation as negligible. More than half of the group already participated in the previous study on glucocorticoid treatment at school-age and the burden of the current study has hardly increased. Screening for the possibility of cardio-vascular, renal, and metabolic alterations makes participation for both the individual participants and the study group as a whole profitable. Moreover, this study may lead to early intervention and prevention of disease.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)

Adolescents (16-17 years)

Inclusion criteria

Inclusioncriteria glucocorticoid treated groups:
- Gestational age < 32 weeks
- Bronchopulmonary disease (BPD)
- Completed dexamethasone or hydrocortisone course;Referencegroup:
- Gestational age < 32 weeks
(matching for age, gender, gestational age, severity of IRDS, birth weight)

Exclusion criteria

Exclusioncriteria glucocorticoid treated groups:
- Dysmaturity
- Glucocorticoid treatment for other indication (i.e. hypotension) or incomplete course
- Intraventricular hemorrhage > grade II according to Papile
- Major congenital anomalies
- Periventricular leukomalacia
- Language barrier;Referencegroup:
- Dysmaturity
- Glucocorticoid treatment for other indication (i.e. hypotension)
- Intraventricular hemorrhage > graad II according to Papile
- Major congenital anomalies
- Periventricular leukomalacia
- Language barrier

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-04-2009
Enrollment:	240
Type:	Actual

Ethics review

Approved WMO

Date:	03-03-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL23955.041.08