Brain development after prenatal growth retardation; effects of growth hormone treatment

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Ethical review	Approved WMO
Status	Pending
Health condition type	Hypothalamus and pituitary gland disorders
Study type	Observational invasive

Summary

ID

NL-OMON30243

Source
ToetsingOnline

Brief title
brain development after prenatal growth retardation; growth hormone

Condition

- Hypothalamus and pituitary gland disorders
- Pregnancy, labour, delivery and postpartum conditions

Synonym
small for gestational age / intra uterine growth failure

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: educational grant van Pfizer,Pfizer

Intervention

Keyword: brain development, effects, growth hormone, prenatal growth retardation

Outcome measures

Primary outcome

growth and brain functioning (results of neuropsychologic tests and

neuroimaging)

Secondary outcome

relationship between results of neuropsychologic tests and results of

neuroimaging techniques

Study description

Background summary

Fetal malnutrition during the last trimester will lead to fetal growth failure, whereby the brain is spared (disproportional growth failure). Recently it has been described that infants born with a low birth weight, referred as small for gestational age (SGA) due to last trimester growth failure, display slightly reduced cognitive capacity at young adult age compared with controls born with appropriate weight. Only a small percentage of about 5-10 % remains short after the age of 4 years. Since GH treatment is considered to have a favorable effect on final height, the treatment protocol in children with SGA has been accepted and recently been operationalised. Children should be carefully monitored because they are associated with an increased risk of development of cardiovascular diseases and type 2 diabetes. Recently a Dutch research group reported that the intelligence quotients (IQ*s) of SGA- children increased on GH treatment. There are, however, methodolocical shortcomings in this study in which no controlgroup was added.These data need to be replicated in a healthy and otherwise controlled study that also starts at pre-treatment baseline.
In the present study we expect to increase understanding what the effect is of GH treatment on brain developing and functioning in SGA-children, and whether the brain is still plastic during childhood, so that GH is capable to stimulate cell proliferation neuronal outgrowth and more specific will GH influence the maturation and outgrowth of connections between the different brain areas

Study objective

Whether cognitive functions in SGA children are impaired due to inappropriate developmental outgrowth in children born with a low birth weight is unknown. This is also the case for the fact whether GH treatment from the age of 4 years is still capable to stimulate neuronal outgrowth and to increase IQ's. We expect the presented study design in which functional imaging techniques and neuropsychological assessment are combined, to increase understanding on the impact of GH therapy on higher brain functioning in children with SGA.
Therefore the 3 research questions of the study are:
1. Will growth hormone treatment in children born with a low birth weight/length with incomplete catch up growth improve brain functioning?
2. Is there a difference in brain functioning in children born with a low birth weight/length between those without and with complete catch up growth?
3. Will intra-uterine growth failure affect brain development/functioning?

Study design

The study is an open prospective controlled study in which SGA children without complete catch up growth treated with growth hormone are compared with SGA children without complete catch up growth without growth hormone treatment and with children with complete catch up growth. Also SGA children with complete catch up will be compared with children with normal prenatal growth.

Intervention

structural (only at baseline) and functional MRI*s, MEG and extensive neuropsychologic testing as described below will be performed at baseline, after one year and three years in both groups A and B.
SGA patients older than 6 years of age, with incomplete catch-up growth with the indication of GH treatment, will be followed on neuropsychologic functioning. Structural and functional MRI*s, MEG and extensive neuropsychological testing will be performed only at start of the study in groups C and D

Study burden and risks

International literature reports on fMR-imaging and MEG-recording from the age of 5 years and older. Appropriate preparation, training, supervising and extended instruction on procedures before real testing are requisite. For these purposes we intend to train children using colored plastic tubes to mimic the small and close situation of the scan apparatus. During practising, the children will be exposed to the noise of the fMRI/MEG as well. Furthermore, an experienced pediatrician as well as a well-trained psychologist will supervise and evaluate the situation. When the child is not able to perform the investigations, the study procedure will be discontinued. When the first investigation of the study fails in a patient/control, the patient is

considered as drop out and a new patient/control will be recruited.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

Indications for GH treatment is based on the protocol as described by the dutch Working group on Growth Hormone
inclusioncriteria for group A (SGA-short; without GH treatment):
- Birth weight or birth length below *2 SD adjusted for duration of pregnancy.
- Present height below *2.5 SD and below minus 1 SD target height-SDS.
- Calendar age between 4 and 6 years.
- No evidence of catch up growth during the preceding year.
- Children are under regular control by pediatrician, but do not choose to be treated with GH
;Inclusion criteria group B: (SGA-short; with GH treatment)
This is a patient population who meet the criteria for SGA-short, (see inclusion criteria group

a) and are willing to be treated with GH. ;Inclusion criteria group C (SGA-normal height):
- Birth weight or birth length below *2 SD adjusted for duration of pregnancy.
- Present height above -2.0 SD and above minus 1 SD of target height -SDS.
- Calendar age between 4 and 6 years.;Inclusion criteria group D (AGA-normal height):
- Normal birth weight/length adjusted for duration of pregnancy
- Present height above *2 SD for age and within target range (TH plus and minus 2 SD)
- Calendar age between 4 and 6 years.;inclusion criteria for group E (SGA-short; with GH treatment):
- Birth weight or birth length below *2 SD adjusted for duration of pregnancy.
- Present height below *2.5 SD and less than 1 SD below target height-SDS.
- Calendar age above 6 years.
- No evidence of catch up growth during the preceding year.
- Children are under regular control by pediatrician, are willing to be treated with GH

Exclusion criteria

Dysmorphic criteria or a known syndrome (except for Silver Russell syndrome)
Skeletal dysplasia
Serious complications in the neonatal period
Other diseases, responsible for growth failure
Medication influencing growth
Psychomotor retardation
Prematurity < 35 weeks

Study design

Design

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

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2007
Enrollment:	110

Type:	Anticipated

Ethics review

Approved WMO	
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL14356.029.06