Congenital central hypothyroidism plusminus ACTH or growth hormone deficiency: etiology and outcome

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Endocrine disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON47244

Source
ToetsingOnline

Brief title
CHC in the Netherlands

Condition

- Endocrine disorders congenital
- Hypothalamus and pituitary gland disorders

Synonym
absent stimulation of thyroid, Congenital hypothyroidism of central origin

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Congenital cental hypothyroidism, Congenital hypopituitarism

Outcome measures

Primary outcome

1: Mortality rate

2: Cognitive outcome: school results compared to average CITO test scores and

compared to siblings

3: DNA analysis: prevalence of Igsf1 mutations in the subgroup of children with

isolated CH-C, results of whole exome sequencing.

Secondary outcome

not applicable

Study description

Background summary

Congenital hypothyroidism (CH) can be of thyroidal or central origin. Central CH (CH-C) can be isolated or occur within the framework of multiple anterior pituitary hormone deficiency (MPHD). In the Netherlands from 1994 onwards CH-C is effectively detected by way of a unique neonatal screening strategy. This has led to a cohort of early treated children with CH-C in the Netherlands. Such a cohort of early treated children with CH-C has never been reported on and many questions still remain regarding mortality, morbidity of early treated CH-C and etiology.
By collecting data on mortality and morbidity we will provide further insight in the benefit of screening for CH-C which may lead to changes in neonatal screening programs worldwide. Most screening programs worldwide do not detect CH-C. Recently,a high percentage of developmental delay was reported in a retrospective study of late diagnosed CH-C patients (56% developmental delay) In this study also the genetic/molecular physiological background may be further unraveled.

Study objective

In this predominantly observational study all patients diagnosed with CH-C in the Netherlands between 1-1-1995 and 1-1-2015 will be traced and the following research questions will be addressed:
1) What is the mortality rate associated with early diagnosed CH-C within the framework of MPHD?
2) What is the developmental and psychosocial outcome of children with early diagnosed and treated CH-C?
3) What is the genetic/molecular physiologic background of isolated CH-C and CH-C within the framework of MPHD?

Study design

The whole cohort of children diagnosed with permanent congenital CH-C between 1-1-1995 and 1-1-2015 will be traced. The names of the pediatric endocrinologists and pediatricians caring for these children are registered by TNO Leiden. All children and their parents will be contacted through their treating doctor. The details of the Medical charts will be reviewed with respect to medical/treatment history, and growth/pubertal development. Cause of death will be well documented.
As a measure of cognitive outcome we will use school results, results of intelligence tests and results of questionnaires regarding psychosocial functioning. Permission will also be asked to retrieve school results of siblings. Siblings will also be asked to fill in questionnaires regarding psychosocial functioning. These questionnaires may be filled in at home online.

Children and their parents will be invited to visit the Academic Medical Center for an interview, physical examination and an intelligence test. A single venous blood collection will be performed for genetic analysis and, if necessary, additional endocrine laboratory investigations. Intelligence testing will also be performed in siblings. A single venous blood collection will be performed for genetic analysis and, if necessary, additional endocrine laboratory investigations.

Study burden and risks

The burden to the subjects is minimal and consists of filling in online questionnaires, one visit to the Academic Medical Center in Amsterdam for a structured interview, physical examination, intelligence test and one venous blood collection to obtain 4-10 ml blood.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Permanent congenital hypothyroidism of central origin detected by the neonatal screening between 1-1-1995 and 1-1-2015.

Exclusion criteria

Transient congenital hypothyroidism of central origin (e.g. due to (untreated) maternal Graves disease).

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-06-2017
Enrollment:	170
Type:	Actual

Ethics review

Approved WMO Date:	21-07-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-03-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-06-2017
Application type:	Amendment
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	NL48833.018.14