Unraveling genetic causes of congenital multiple pituitary hormone deficiencies

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To find new genes causing congenital MPHD associated with the characteristic MRI abnormalities of ectopic posterior pituitary gland and absent/thin pituitary stalk.

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

Summary

ID

NL-OMON38016

Source
ToetsingOnline

Brief title
MPHDgenes

Condition

- Endocrine disorders congenital
- Hypothalamus and pituitary gland disorders

Synonym
Congenital multiple pituitary hormone deficiency (MPHD); congenital hypopituitarism

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Stichting tot Steun Emmakinderziekenhuis

Intervention

Keyword: congenital hypopituitarism, ectopic posterior pituitary, whole exome sequencing

Outcome measures

Primary outcome

Detection of genes causing congenital MPHD in patients with an ectopic

posterior pituitary gland and absent or thin pituitary stalk.

Secondary outcome

Understanding of the molecular and cellular mechanisms leading to congenital

MPHD in patients with an ectopic posterior pituitary gland and absent or thin

pituitary stalk.

Increase our understanding of pituitary development in man.

Study description

Background summary

Congenital multiple pituitary hormone deficiency (MPHD) is a rare disorder with an estimated incidence of 1 in 25,000 newborns. In contrast to most neonatal screening programs worldwide, the Dutch neonatal screening program is able to effectively detect neonates with this disorder.
In a previous large nationwide study our group showed that patients with congenital MPHD show characteristic abnormalities on MRI of the hypothalamic/pituitary region: ~75% have an ectopic posterior pituitary gland (located in the floor of the third ventricle instead of in the sella turcica) and an absent or thin pituitary stalk.
Although there has been much progress in the understanding of the embryonic development of the anterior pituitary gland in terms of cell types and genes involved, less than 5% of cases of congenital MPHD can be explained by mutations in these genes. Since in most neonates with congenital MPHD the anterior pituitary gland is not absent we hypothesize that the cause of MPHD is not defective anterior pituitary gland development, but defective development (or outgrowth) of the pituitary stalk and posterior pituitary gland and that this defective development likely has a genetic cause.
The detection of genes causing congenital MPHD in patients with an ectopic

posterior pituitary gland and absent or thin pituitary stalk will enhance the understanding of the molecular and cellular mechanisms leading to congenital MPHD and also increase our understanding of pituitary development in man. Modern molecular studies using next generation techniques searching for variants in DNA derived from an affected individual and that from his/her parents, usually allow finding the causative gene.

Study objective

To find new genes causing congenital MPHD associated with the characteristic MRI abnormalities of ectopic posterior pituitary gland and absent/thin pituitary stalk.

Study design

Observational study with invasive measurements

Study burden and risks

There is no benefit of participating in this study for the participants. There is a group benefit as the study will provide further insight in the genetic causes of congenital MPHD.
The risks of this study are minimal for the participants. The burden is limited to a single visit to the AMC and a single blood sampling.

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

Patients with congenital MPHD, a pituitary MRI image consisting of an ectopic posterior pituitary gland and an absent or thin pituitary stalk. Parents of abovementioned patients. Parents must be able to read and understand the written information.

Exclusion criteria

None

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):	24-04-2014
Enrollment:	60

Type:	Actual

Ethics review

Approved WMO Date:	04-02-2014
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	NL47088.018.13