Research on the occurrence of CHARGE syndrome features and CHD7 mutations in patients with Kallmann syndrome

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To investigate the occurrence of undiagnosed CHARGE syndrome in patients diagnosed with (atypical) Kallmann syndrome and to define criteria for CHD7 analysis in patients with Kallmann syndrome.

Ethical review	Approved WMO
Status	Completed
Health condition type	Congenital and hereditary disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON31298

Source
ToetsingOnline

Brief title
Clinical overlap between CHARGE and Kallmann syndrome

Condition

- Congenital and hereditary disorders NEC

Synonym
Hall Hittner syndrome = CHARGE syndrome, hypogonadotropic hypogonadism (delayed puberty) + an/hyposmia (decreased ability to smell) = Kallmann syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: CHARGE syndrome, CHD7, clinical features, Kallmann syndrome

Outcome measures

Primary outcome

CHD7 mutation: present or absent
CHARGE features: present or absent

Secondary outcome

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Study description

Background summary

Kallmann syndrome is characterised by hypogonadotropic hypogonadism and an/hyposmia. These two clinical features are also frequently seen in CHARGE syndrome. In addition, multiple other congenital malformations can be present in CHARGE syndrome, e.g. heart, eye, renal and ear anomalies. CHARGE syndrome can be very mild and this makes it very difficult to distinguish from Kallmann syndrome.

CHARGE syndrome is caused by mutations in the CHD7 gene. Kallmann syndrome is genetically very heterogeneous and several genes are known that together account for 30% of all cases. The two most important genes are KAL1, responsible for X-linked and FGFR1 involved in autosomal dominant Kallmann syndrome.

In a pilot study we demonstrated a mutation in CHD7 in three out of 33 Kallmann syndrome patients of North-American and Japanese descent. Careful re-evaluation of these three patients showed that one of them fulfilled the clinical criteria for CHARGE syndrome. In the current study we will investigate the etiological/embryological overlap between these two syndromes.

Study objective

To investigate the occurrence of undiagnosed CHARGE syndrome in patients diagnosed with (atypical) Kallmann syndrome and to define criteria for CHD7 analysis in patients with Kallmann syndrome.

Study design

All Dutch (paediatric) endocrinologists will be addressed both by letter and at the meeting of paediatric endocrinologists (autumn 2007) about this part of the study. They will receive extensive information on CHARGE syndrome and its overlap with Kallmann syndrome. They will receive two information letters (for themselves and for the patients, E1), a medical questionairre (F1) and a consent form (E2). If the patient/his parents give consent, the questionairre and a copy of the CHD7 analysis results will be sent to Groningen for evaluation. CHD7-positive patients will be offered a visit to the outpatient clinic in Groningen.

Study burden and risks

The burden and risks associated with this study are minimal. For participation in this study a single bloodsample might be necessary. The study is beneficial for the patient and his parents.

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

Kallmann syndrome patients (both an/hyposmia and hypogonadotropic hypogonadism must be present)

Exclusion criteria

Presence of a KAL1 or FGFR1 mutation

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	06-12-2007
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO
Application type: First submission

Review commission: METC Universitair Medisch Centrum Groningen (Groningen)

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	NL19178.042.07

Study results