Recognition of congenital heart defects caused by CHD7 gene mutations

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Congenital cardiac disorders
Study type	Observational invasive

Summary

ID

NL-OMON34693

Source
ToetsingOnline

Brief title
CHD and CHD7

Condition

- Congenital cardiac disorders
- Cardiac and vascular disorders congenital

Synonym
congenital heart defects

Research involving
Human

Sponsors and support

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

Intervention

Keyword: CHARGE, CHD7, Congenital heart defect

Outcome measures

Primary outcome

The absolute number of mutations found in the CHD7 gene and the co-existing

medical problems in patients in whom a CHD7-mutation is found.

Secondary outcome

not applicable

Study description

Background summary

CHARGE syndrome occurs in at least 1 in 10,000 newborns. The most important features are Coloboma of the eye, Heart defect, Atresia of the choanae, Retardation of growth and/or development, Genital abnormalities, Ear abnormalities and deafness. Up to 80% of children with CHARGE syndrome have a congenital heart defect (CHD).
In 2004, we identified CHD7 as the causative gene for CHARGE syndrome. The mutation detection rate varies from 65% in patients suspected of having CHARGE syndrome to over 90% in those with typical CHARGE syndrome. The syndrome has a very broad clinical spectrum; the occurrence of the main symptoms varies considerably, even in patients with a proven CHD7 mutation. Since the discovery of the CHD7 gene, it has become clear that predominantly severe mutations cause the full clinical spectrum of CHARGE syndrome. However, an increasing number of CHD7 mutations are being identified in patients with a milder phenotype and some in children with a heart defect but not typical CHARGE syndrome. Thus the clinical diagnosis of patients with CHD7 mutations can be difficult in early infancy. There are two reasons why it is important to identify CHD7 mutations in these children. Firstly, their paediatrician can be informed about the risk of co-morbidity, e.g. visual, hearing, balance, kidney function, growth and puberty development. Timely recognition of co-existing problems can improve intervention and therapy. Secondly, information about the aetiology of the heart defect is relevant for the recurrence risk. At this moment clinical data of a unique group of over 300 patients in whom a CHD7 mutation has been found are collected to delineate the occurrence and types of CHDs found in these children (pilot study). In the current study we hypothesise that CHD7 mutations

may be present in patients with a CHD without initial suspicion of CHARGE syndrome.

Study objective

Our primary objective is to identify the patients with congenital heart defects in whom CHD7 mutation detection is needed. Secondly we want to identify the co-existing medical problems in children with a congenital heart defect due to a CHD7 mutation.

Study design

We will perform analysis of the CHD7 gene and collect the clinical data of selected patients. If a mutation in CHD7 is found, the patients will have a once only physical examination by the researcher.

Study burden and risks

The DNA of the patients with CHDs is already available and was collected for previous research projects or for the purpose of a diagnostic test. If the amount of DNA appears to be insufficient, the patient/parents will be asked for a sputum sample. So patients wil not undergo invasive procedures.
We fully realise that finding a CHD7 mutation may not only be a relief for the patient and his/her parents and important for clinical follow-up and recurrence risk, but it may also give rise to uncertainty and fear. Genetic counselling and written information will be offered to all patients/parents, as well as to their doctors, to explain the implications of the CHD7 mutation. Monitoring at the UMCG*s multidisciplinary outpatient clinic for children with CHARGE syndrome will be offered (see www.umcg.nl/patienten/polis/chargepoli).

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
9700 RB Groningen
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
9700 RB Groningen
NL

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 already available at the department of Genetics of the UMCG or a cohort of children with CHD of the department of Paediatric Cardiology of the RUNMC who
1.have a congenital heart defect that fits the spectrum of congenital heart defects found in patients with a CHD7-mutation.
2.have at least one other feature of CHARGE syndrome
3.do not have another known cause of their congenital heart defect

Exclusion criteria

- Patients with an already identified (genetic) cause of their congenital heart defect.
- Patients who do not want to be informed about the result of the CHD7 analysis

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):	29-11-2010
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO

Date:	23-04-2010
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	NL31499.042.10