A genetic follow up study in Turner syndrome

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The main objective is to assess the frequency of hidden mosaicism, including Y material, in TS patients and examine the effect on: response to different GH doses and GH injection frequency regimens, aortic diameter and distensibility, congenital…

Ethical review	Approved WMO
Status	Will not start
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Observational non invasive

Summary

ID

NL-OMON34852

Source
ToetsingOnline

Brief title
Genetic follow up in Turner syndrome

Condition

- Chromosomal abnormalities, gene alterations and gene variants

Synonym
patients with 45, Patients with Turner syndrome, X.

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,nog niet bekend.

Intervention

Keyword: Fenotype, Genotype, Hidden mosaicism, Turner syndrome

Outcome measures

Primary outcome

The frequency of hidden mosaicism, including Y chromosomal material, in 45,X females. The effects of different GH regimens will be analyzed to a background of genotypic variation of the sex chromosomes and the growth hormone receptor. The clinical parameters (aortic diameter and distensibility, congenital cardiac malformations, lipid profile, final height and final height gain) are already assessed in the original studies.

Secondary outcome

not applicable.

Study description

Background summary

Turner syndrome (TS) is characterized by the partial or complete absence of the second X chromosome. Forty to sixty percent of TS patients have the karyotype 45,X. The other patients show either a mosaicism consisting of at least one cell line containing 45,X, or a structural aberration of the second X chromosome (i.e. Xp or Xq deletion, isochromosome Xq, or ring X). The majority of patients with mosaicism shows considerable tissue-specific differences in levels of X-aneuploidy. In approximately 5% of TS women, cytogenetic examination shows cells containing Y chromosomal material. Detecting Y chromosomal material is important since this is a risk factor for the development of gonadoblastoma. Around 60 to 80 percent of patients with 45,X karyotype have maternally derived X chromosomes. Specific cognitive skills, visceral adiposity and statural growth have been linked to the parental origin of the single normal X chromosome in TS. Research on the effect of having a maternally or paternally derived X chromosome on growth and other clinical features can improve quality of treatment of girls and women with Turner syndrome.

The prevalence of heterozygosity of a deletion of exon 3 in the GH receptor gene (a polymorphism; d3-GHR) in humans is approximately 25 to 32%, while homozygosity is found in 9 to 14%. It has been reported that the presence of a d3-GHR resulted in an increased responsiveness to GH therapy in short children without GH deficiency. Genotyping d3-GHR might provide a tool for a more precise understanding of the growth promoting effects of GH therapy in the individual TS patient.

Study objective

The main objective is to assess the frequency of hidden mosaicism, including Y material, in TS patients and examine the effect on: response to different GH doses and GH injection frequency regimens, aortic diameter and distensibility, congenital cardiac malformations, lipid profile, dysmorphic features and the frequency of gonadoblastoma in individuals with Y material. Other objectives are to assess the effect of paternal or maternal origin of the X chromosome and the effect of d3-GHR on the effect of GH dose and injection frequency, on final height and final height gain.

Study design

Observational study.

Study burden and risks

This non-therapeutic, observational study does not entail any known risks. The burden imposed by the study is mainly the time investment needed for coming to the hospital, the questionnaires, the clinical examination, the making of the photographs and the collecting of the different tissues. The study therefore meets the requirement of negligible risk and minimal burden. A benefit from taking part in the study is a free and detailed genetic analysis. This may be very valuable for the patients and parents or legal guardians of patients with TS.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients with Turner syndrome who have been participating in one of the following studies: MEC: GHTUR/BPD/13NL and MEC: GHTUR/BPD/12NL (the inclusion criteria of the original protocols are described in the protocol at page 14).

Exclusion criteria

The exclusion criteria are those of the original protocols: MEC: GHTUR/BPD/13NL and MEC: GHTUR/BPD/12NL ((the exclusion criteria of the original protocols are described in the protocol at page 15).

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	85
Type:	Anticipated

Ethics review

Approved WMO Date:	26-04-2010
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	NL31773.058.10