Metabolic derAngements in heReditary multiple Exostoses (HME) subjects with either heterozygous EXT1 or EXT2 mutations; a clinical cohort study (MARE study)

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We would like to study whether aberrant heparansulfate synthesis in HME subjects leads to impaired glucose metabolism, dyslipidemia and subsequent increased cardiovascular risk as well as impaired adrenal gland function when compared to unaffected...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metabolic and nutritional disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON37615

Source
ToetsingOnline

Brief title
MARE study

Condition

- Metabolic and nutritional disorders congenital
- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
adrenal insufficienty, diabetes mellitus

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: ZONMW (veni beurs dr M. NIeuwdorp)

Intervention

Keyword: adrenal gland insufficiency, EXT mutations, hereditary multipele exostoses, type 2 diabetes meliitus

Outcome measures

Primary outcome

Changes in glucose metabolism (oral glucose tolerance tests) in subjects with

HME with either EXT1 or EXT2 mutation compared to unaffected control subjects.

Secondary outcome

Changes in cardiovascular risk (lipidprofile and ECG changes) in subjects with

HME with either EXT1 or EXT2 mutation compared to unaffected control subjects.

Changes in adrenal gland function (synacthen test) in subjects with HME with

either EXT1 or EXT2 mutation compared to unaffected control subjects.

Study description

Background summary

EXT-1 or EXT-2 genes are of pivotal importance in normal organ and skeleton development due to their role in heparansulfate synthesis, a sugar chain present in all human cells .Hereditary multiple exostoses (HME) is a clinical syndrome comprising lifelong risk of development of cartilage/bone tumor formation and therefore are regularly checked at the OLVG orthopaedic outpatient clinic . Previous research from our group has shown that HME subjects are characterized by impaired insulin secretion, a hormone involved in glucose metabolism. Moreover, we found that mice with EXT1 or EXT2 heterozygous mutations (eg murine model of human HME) are characterized by dyslipidemie/fasting hypertriglyceridemi due to impaired cholesteroluptake in the liver. Moreover, we gathered evidence that heparansulfates are implicated in normal adrenal function, a gland that synthesizes cortisol. In order to

investigate whether these findings hold true for HME subjects with either EXT1 or EXT2 mutations or unaffected familiy member, we would like to execute this study.

Study objective

We would like to study whether aberrant heparansulfate synthesis in HME subjects leads to impaired glucose metabolism, dyslipidemia and subsequent increased cardiovascular risk as well as impaired adrenal gland function when compared to unaffected family members.

Study design

observational study with functional (oral glucose tolerance test and synacthen) tests

Study burden and risks

Despite a minimal risk of short term hypotension upon synacthen bolus infusion, no sideeffects are expected. Moreover, we believe that the outcome of these three studyquestions regarding glucose tolerance, cardiovascular risk and adrenal gland function categorized to EXT1 or EXT2 genotype renders usefull l information for phenoptype and clincal stastus of subjects with HME. Moreover, we think that these results provide pathophysiological information about glucose tolerance, cardiovascular risk and adrenal gland function in the general population. Therefore we think that the benefits of this study outhweight the minimal conveyed risk.

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

*Age between 18 and 70 years
*Clinical diagnosis of Hereditary Multipele Exostoses (HME) with/without proven EXT1/EXT2 mutation (patient) OR unaffected family member (control)
*Written informed consent

Exclusion criteria

* History of psychiatric disease (psychosis)
* Pregnancy or female participants at childbearing age not using adequate anticonception (due to synacthen infusion)

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-07-2012
Enrollment:	400
Type:	Actual

Ethics review

Approved WMO

Date:	23-02-2012
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	NL38725.018.12
Other	NTR 10510