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

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON27537

Source
NTR

Brief title
MARE study

Health condition

hereditary multiple exostsoses (HME), glucose tolerance, dyslipidemia, ECG, adrenal function diabetes mellitus type 2

Sponsors and support

Primary sponsor: ZONMW
Source(s) of monetary or material Support: ZONMW

Intervention

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

1. Changes in cardiovascular risk (lipidprofile and ECG changes) in subjects with HME with either EXT1 or EXT2 mutation compared to unaffected control subjects;

2. 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

To relate clinical phenotype of subjects with Hereditary Multipele Exostoses to EXT genotype in relation to:

1. Glycemic control (HbA1c, fasting glucose and insulin, OGTT and HOMA-r);

2. Cardiovascular risk profile including baseline ECG, dyslipdemia (fasting lipid profiles) and microalbuminuria;

3. Adrenal gland function (synacthen test).

We will study subjects with hereditary multiple exostoses (HME) who are frequently seen at the outpatient clinic of orthopaedic surgery at the OLVG. Patients as well as unaffected family members will be contacted by mail one month before their regular visit to treating physician dr Ham/dr van der Zwan for their consent to participate in these clinic study and to arrive at the OLVG fasted. All studies/measurements will be performed at the OLVG.

Study objective

A recent Genome Wide Association Study (GWAS) identified novel risk loci for type 2 diabetes including EXT-2. This gene codes for exostosin, which is an enzyme involved in the elongation of heparan sulfate, a glycosaminoglycan present in all cells throughout the human body. Patients with EXT-1 and EXT-2 mutations are phenotypically characterized by the hereditary

multiple exostoses/ multiple osteochondromas (HME/MO) syndrome, an autosomal dominant syndrome causing multiple epiphysial bone tumors due to a reduction in heparan sulfate synthesis. Thus, these subjects are solely seen in the orthopaedic outpatient clinic. However, preliminary data show that mice with identical EXT mutations are also characterized by insulin secretion problems and anatomic smaller pancreas, dyslipidemia and adrenal insufficiency. This is most likely induced due to impaired heparan-sulfate orchestrated organ development and cell to cell signalling.

Study design

One measurement period.

Intervention

1. Orale glucose tolerance test (OGTT) for glucose disposal;

2. Synacthen test for adrenal gland function.

Contacts

Public
AFDELING INWENDIGE GENEESKUNDE AMC
MEIBERGDREEF 9, KAMER F4.159.2
M. Nieuwdorp
Amsterdam 1105 AZ
The Netherlands
+31 (0)20 5666612
Scientific
AFDELING INWENDIGE GENEESKUNDE AMC
MEIBERGDREEF 9, KAMER F4.159.2
M. Nieuwdorp
Amsterdam 1105 AZ
The Netherlands
+31 (0)20 5666612

Eligibility criteria

Inclusion criteria

1. Males/females aged between 18 and 70 years;

2. Clinical diagnosis of Hereditary Multipele Exostoses (HME) with/without proven EXT1/EXT2 mutation (patient) OR unaffected family member (control);

3. Able to provide written informed consent.

Exclusion criteria

1. History of psychiatric disease (psychosis);

2. Malignancy with limited lifespan;

3. Pregnancy or female participants at childbearing age not using adequate anticonception (due to synacthen infusion).

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2012
Enrollment:	600
Type:	Anticipated

Ethics review

Positive opinion

Date:	07-11-2011
Application type:	First submission

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
NTR-new	NL2982
NTR-old	NTR3130
Other	MEC AMC : 2011_339
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A