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

Gepubliceerd: 07-11-2011 Laatst bijgewerkt: 18-08-2022

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Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON27537

Bron
NTR

Verkorte titel
MARE study

Aandoening

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

Ondersteuning

Primaire sponsor: ZONMW
Overige ondersteuning: ZONMW

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Changes in glucose metabolism (oral glucose tolerance tests) in subjects with HME with either EXT1 or EXT2 mutation compared to unaffected control subjects.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

One measurement period.

Onderzoeksproduct en/of interventie

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

2. Synacthen test for adrenal gland function.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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).

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Parallel
Toewijzing:	Niet-gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-02-2012
Aantal proefpersonen:	600
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	07-11-2011
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL2982
NTR-old	NTR3130
Ander register	MEC AMC : 2011_339
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A