Becker Muscular Dystrophy: analysis of diversity in disease severity

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1. To investigate the possible relationship between amount of dystrophin expression and clinical severity of BMD2. To investigate the relationship between specific BMD-gene mutations and clinical severity of BMD3. To investigate possible other…

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

Summary

ID

NL-OMON35006

Source
ToetsingOnline

Brief title
Becker Muscular Dystrophy: analysis of diversity in disease severity

Condition

- Neuromuscular disorders

Synonym
Becker, muscular dystrophy

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Prinses Beatrix Fonds

Intervention

Keyword: Disease susceptibility, Dystrophin, Muscular Dystrophy, Mutation

Outcome measures

Primary outcome

1. Disease course, based on data collected from a structured medical history

and information from other treating physicians.

2. Biomarkers from blood

3. Strength and Functional Assessment

4. Muscle MRI

5. Muscle biopsy parameters

6. Echocardiography

Secondary outcome

NA

Study description

Background summary

Duchenne and Becker muscular dystrophy are X-linked inherited diseases caused by a mutation in the DMD gene, which codes for dystrophin. The dystrophin protein has an important stabilizing function in muscle tissue. Absence, as in Duchenne muscular dystrophy (DMD), or abnormal functioning of dystrophin, as in

Becker muscular dystrophy (BMD), leads to muscle damage, resulting in progressive muscle weakness, fibrosis and replacement of muscle tissue with fat.

DMD has a quite uniform disease course, with patients becoming wheelchair dependant around the age of ten to twelve and needing mechanical ventilation around the age of seventeen. BMD, on the other hand, is characterized by a disease course with a wide range of severity. Our recent study shows a variability of age of loss of ambulation between nine and sixty years, while some patients stay ambulatory throughout their entire life (unpublished data)

The factors responsible for this diversity in the clinical course of BMD are still unknown, although the amount of dystrophin expression in heart or skeletal muscle could be involved. It is likely that several additional factors play a role in determining the severity of the disease. BMD, with its wide range in clinical severity, gives an excellent opportunity to study these parameters. Identification of these molecules or pathways could help to develop supportive treatments for patients with BMD as well as DMD.

Study objective

1. To investigate the possible relationship between amount of dystrophin expression and clinical severity of BMD

2. To investigate the relationship between specific BMD-gene mutations and clinical severity of BMD

3. To investigate possible other factors involved in BMD diversity, like inflammation, a role for myofibrillar components, or muscle repair genes.

4. Search for biomarkers correlating to disease severity

5. MRI-analysis of muscle as a parameter for disease severity

6. To study the relationship between muscle weakness and severity of cardiomyopathy in BMD patients.

Study design

Cross sectional observational study. Patient data will be gathered in the course of one year. Analysis will be performed in the second year of the study.

Study burden and risks

During the stduy two invasive procedures are performed: one venapuncture to obtain blood and a conchotome muscle biopsy of the tibial muscle of the lower

leg. Both are routinely performed during a diagnostic process for muscle disease as part of our regular outpatient clinic. The risk of venapuncture is some shortlasing local pain and possible bruising.
The semi-open biopsy technique with the conchotome involves a small incision of 1-1,5 cm and biopsy taking of the muscle under local anaesthesia. The risk involves local pain during and after the procedure. There is a minimal risk for local hemorrhage, infection or blistering under the adhesive plaster used for wound closure. In over 200 of these biopsies in the LUMC the last years no hemorrhage or infection was encountered. Three patients developed a traction-related blister under the adhesive plaster, which disappeared after removel of the plaster. Pain was reported minimal to moderate, lasting a maximum of three days. Less than 1% of the patients used any analgesic drugs, like paracetamol.

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

1. diagnosis of Muscular Dystrophy, defined by:
- male gender AND
- progressive muscular weakness AND
- elevated serum CPK-levels AND
- dystrophic characteristics on muscle biopsy OR
- reduced amount of dystrophin in muscle biopsy OR
- in frame mutation in DMD gene
2. Age over 18 years

Exclusion criteria

Exlusion for MRI
- claustrophobia
- pacemaker and defibrillators
- nerve stimulators
- intracranial clips
- intraorbital or intraocular metallic fragments
- cochlear implants
- ferromagnetic implants (eg. thoracic implant for scoliosis)
- inability to lie supine during less than 60 minutes

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):	01-01-2011
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	06-08-2010
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	NL30980.058.10