Inflammation in facioscapulohumeral muscular dystrophy: from patient to molecules

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We aim at investigating the interplay between DUX4 and inflammation in FSHD combining MRI imaging, histology, gene and cytokine expression.

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

Summary

ID

NL-OMON48999

Source
ToetsingOnline

Brief title
Inflammation in FSHD

Condition

- Muscle disorders

Synonym
muscular dystrophy

Research involving
Human

Sponsors and support

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

Intervention

Keyword: DUX4, FSHD, Inflammation, MRI

Outcome measures

Primary outcome

Main outcomes will be: evaluation of inflammation in muscles using MRI; differential immunohistological characterization of muscle biopsies between patients and controls; difference in genomic expression profiling and cytokine profiling on blood cells and muscle tissue between patients and controls.

Secondary outcome

Secondary objectives are:

1) Assess FSHD Severity Score

2) Evaluates muscle weakness degree by MRC grading.

3) Compare the diagnostic quality of MRI and 3D ultrasound images in order to develop future 3D US guided biopsies.

4) Compare the 3D ultrasound images of patients with already acquired 3D US of healthy volunteers in order to understand possible factor contributing to muscle weakness in FSHD.

Study description

Background summary

Facioscapulohumeral dystrophy (FSHD) is one of the most prevalent inherited myopathies and is caused by the transcriptional de-repression of DUX4, a transcription factor, in skeletal muscle, responsible for a deregulation cascade resulting in the miss-expression of several immune genes, retroelements

and germlines genes in FSHD muscle. Moreover, recent studies describe muscle inflammatory infiltrates mainly composed by CD8+ T cells in muscles showing hyperintensity features on T2-weighted short tau inversion recovery magnetic resonance imaging (T2-STIR-MRI) sequences. We wonder if and which relationship exists between DUX4 activation and muscle inflammation in FSHD and we hypothesize that DUX4 induced muscle inflammation can ultimately lead to dystrophy.

Study objective

We aim at investigating the interplay between DUX4 and inflammation in FSHD combining MRI imaging, histology, gene and cytokine expression.

Study design

The study has an explorative and observational nature and it will be perform as a case-control study involving FSHD patient and healthy controls.

Study burden and risks

A total of 40 subjects will undergo a muscle biopsy. A maximum of 100 patients will be asked to join the screening procedure: 1) complete medical history; 2) blood samples collection; 3) MRI screeing scan of shoulders, upper arm and leg; 4) 3D US of one clinically affected muscel of the leg.The screening will close with the first 25 FSHD patietns reporting a MRI-STIR positivity. There are minimal risks associated with blood sampling: bleeding, a slight risk of infection, fainting or feeling light-headed. There are no associated risk with the 3D US examination and only one affected muscle of the leg will be screened only in the patient group. Also, 25 patients will undergo an MRI guided muscle biopsy of the leg, similar to a previous approved study conducted by Drs S. Lassche (Why are FSHD muscles weak? NL35549.091.11). 15 healthy controls will be asked for a needle biopsy from the leg at the outpatient clinic of the neurology department. Complications of muscle biopsies are very uncommon and include hematoma and hypoesthesia. Therefore we classify the risk of this study as negligible.

Contacts

Public
Radboud Universitair Medisch Centrum

Reinier Postlaan 4
Nijmegen 6525 GC
NL

Scientific
Radboud Universitair Medisch Centrum

Reinier Postlaan 4
Nijmegen 6525 GC
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- > 18 year old
- Genetically confirmed FSHD
- unrelated
- with symptomatic lower limb weakness

Exclusion criteria

- Age <18
- Diabetes mellitus
- Chronic obstructive pulmonary disease
- Current malignancy
- Current use of corticosteroids
- Current use of statines
- Contra-indications for MRI-scan or muscle biopsy

Study design

Design

Study type:	Observational non 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):	13-02-2019
Enrollment:	115
Type:	Actual

Ethics review

Approved WMO Date:	01-08-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-10-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-11-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-12-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-04-2019

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL64690.091.18