The effect of fibrate therapy in two patients with neutral lipid storage disease with myopathy (NLSDM).

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We would like to evaluate the beneficial effects of fibrate treatment on muscle mitochondrial and cardiac function in patients with NLSDM.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON37985

Source
ToetsingOnline

Brief title
Fibrate Trail

Condition

- Heart failures
- Metabolic and nutritional disorders congenital
- Lipid metabolism disorders

Synonym
Neutral lipid storage disease with myopathy / heriditary fataccumulation disorder

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Fibrate, lipid storage, mitochondrial function, NLSDM

Outcome measures

Primary outcome

Main study parameters are the changes in mitochondrial function, cardiac,

hepatic and muscle lipid accumulation and cardiac function after treatment.

Secondary outcome

As secondary endpoints changes in insulin sensitivity is considered.

Study description

Background summary

NLSDM is a disease caused by a defect in the PNPLA2 gene encoding ATGL. Patients with NLSDM accumulate triglycerides and exhibit muscle weakness, cardiac failure and hepatosteatosis. Most of these patients die at young age due to cardiac failure. Not much is known about the underlying mechanisms, though recently it was discovered that PPAR activation in ATGL-/- mice was impaired leading to decreased mitochondrial function, lipid accumulation and cardiac failure resulting in death at young age. Activation of PPARs, by treatment with fibrates rescued the phenotype and reduced mortality rates in these mice. These findings may have a major impact for patients with NLSDM if these results can be translated to humans.

Study objective

We would like to evaluate the beneficial effects of fibrate treatment on muscle mitochondrial and cardiac function in patients with NLSDM.

Study design

Patients will be treated with fibrates during a period of 28 weeks. Baseline measurements will be performed prior to the study and after 12 and 28 weeks of treatment. Cardiac and muscular lipid accumulation, cardiac function, mitochondrial function and insulin sensitivity will be assessed during these baseline measurements.
Besides these patients, also healthy control subjects will be included in this

study. They will not recieve treatment but will only perform the baseline measurements in order to estimate the size of the effect of the treatment of the NLSDM patients.

Intervention

Patients will receive a dosage of 400mg Bezafibrate every day during 28 weeks. Control subjects will not be treated.

Study burden and risks

For all subjects:
They will come to Maastricht for baseline measurements such as a Bodpod measurement, a series of MRI/MRS scans, a clamp and a biopsy.

For the NLSDM patients:
After baseline measurements, patients will receive treatment by an endocrinologist at the Azm (dr. B. Havekes) and after 12 and 24 weeks of treatment the measurements will be repeated. The patients will eventually visit the department 15 times (day 1 screening, day 7 Bodpod, muscle strength/grip test, ultrasound and MRS; day 8 and MRS, clamp and biopsy; 9x check-up during intervention period, and after 12 and 28 weeks the measurements of day 7 and 8 will be repeated) during the 28 week study period. During these visits 3 hyperinsulinemic-euglycemic clamps, including 3 muscle biopsies, will be performed and 6 MRS-sessions will take place.

Control subjects will only visit the MUMC for baseline measurements and thus will undergo the clamp, biopsy and 2 MRI sessions only once.

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

NLSDM:
- Patients with NLSDM;Controls:
- female gender
- between 20-45 years old
- BMI between 20-30 kg/m2
- healthy (no chronic diseases)

Exclusion criteria

NLSDM:
- none;Controls:
- use of Fibrates and anti-coagulantia
- Contra-indications for MRI:
- Electronic implants such as pacemakers or neurostimulator
- Iron-containing corpora aliena in eyes or brain
- Some hearing aids and artificial (heart) valves which are contraindicated for MRS
- Claustrophobia
- Subjects, who do not want to be informed about unexpected medical findings, or do not wish that their physician is informed, cannot participate in the study.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-08-2011
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Bezalip retard
Generic name:	Bezafibrate
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	20-07-2011
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	04-08-2011
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	28-12-2011

Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	25-10-2012
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
EudraCT	EUCTR2011-001205-27-NL
CCMO	NL35884.068.11