ARTERIAL STIFFNESS IN PATIENTS WITH DUCHENNE MUSCULAR DYSTROPHY

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We aim to investigate if aortic stiffness, measured by pulse wave velocity (PWV), is present in patients with DMD and whether treatment with ACEi reduces aortic stiffness.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Heart failures
Study type	Observational non invasive

Summary

ID

NL-OMON54937

Source
ToetsingOnline

Brief title
ARTERIAL STIFFNESS IN PATIENTS WITH DUCHENNE MUSCULAR DYSTROPHY

Condition

- Heart failures
- Muscle disorders
- Neuromuscular disorders

Synonym
Duchenne muscular dystrophy

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: ACE-inhibitors, Aortic stiffness, Cardiomyopathy, Duchenne

Outcome measures

Primary outcome

Arterial stiffness of pediatric DMD patients compared to healthy controls, as non-invasively assessed with PWV measurement with the Arteriograph.

Secondary outcome

1. To investigate whether treatment with ACEi influences arterial stiffness, measured by PWV, over time in DMD patients

2. Explore the (longitudinal) relation between arterial stiffness and cardiac function in DMD patients

3. Assess the accuracy of PWV measurement using the Arteriograph versus PWV measured by cardiac MRI in DMD patients

Study description

Background summary

Cardiomyopathy in Duchenne muscular dystrophy (DMD) is frequent and characterized by progressive left ventricular (LV) fibrosis leading to dysfunction and dilatation. Factors increasing LV afterload, such as aortic stiffness, may promote LV wall stress and lead to worsening of LV function.

Little is known about the onset and course of arterial stiffness in DMD patients over time, its relation with LV dysfunction and whether this is influenced by treatment with an Angiotensin converting enzyme inhibitor (ACEi). In DMD, ACEi are first-line treatment for cardiomyopathy as studies have shown that early intervention with ACEi can favorably delay the onset and progression of LV dysfunction. Whether these favorable results are a consequence of reduced LV afterload is unknown. A meta-analysis in non-DMD patients showed that PWV is reduced by treatment with ACEi, possibly independently of its ability to reduce blood pressure.

Recently, Duchenne Care Considerations were published that propose the start of ACEi at 10 years of age. This recommended age is largely based on expert opinion and there is still debate about the optimal age for initiation of treatment. A better understanding of the course of cardiovascular changes and the influence of ACEi treatment could lead to refinement and a more individualist ACEi treatment strategy for DMD patients.

Study objective

We aim to investigate if aortic stiffness, measured by pulse wave velocity (PWV), is present in patients with DMD and whether treatment with ACEi reduces aortic stiffness.

Study design

This prospective observational study will be conducted at the LUMC.

The study has a cross sectional and longitudinal part.
• For the cross sectional part, patients will be included in the study during their annual outpatient clinic visit. Only the PWV measurement will be performed in research setting at this visit.
• The longitudinal part of this study will exist of patients that are starting with ACEi therapy versus patients and their parents that choose not to start (choice is independent of this protocol). Patients will be asked to join with an additional informed consent form. The total duration for this part of the study will be 1 year per patient. A detailed description about the procedures of this study is stated in section 8 (protocol).

Study burden and risks

There are no risks associated with the measurements in this study. The PWV measured by the Arteriograph is non-invasive and works like a regular blood pressure measurement. DMD children are familiar with this measurements due to their regular clinical care.
The entire study population will consist of children due to the manifestation of (cardiomyopathy) in DMD at young age. The extent of burden is therefore low.

Subjects will not have direct personal benefit from participating in the study. The data may however aid in detecting early manifestations of cardiomyopathy in DMD. Identifying possible risk factors (i.e. arterial stiffness) for accelerated progression may lead to new treatment strategies. These may include an evidence based age for starting treatment with ACEi and, by identifying possible non responders, a more personalized treatment strategy.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Children (2-11 years)

Inclusion criteria

Inclusion criteria for DMD patients cross sectional part:
- Age between 4-15 years
- Confirmation of the diagnosis of Duchenne Muscular Dystrophy by DNA mutation or muscle biopsy.
- Who visit the DMD-out patient clinical of the LUMC for their annual visit

Additional inclusion criteria for DMD patients longitudinal part:
- Initiation of ACEi therapy is proposed by pediatric cardiologist based on clinical decision making/the Duchenne Care Considerations.

Healthy controls:

4-12 years

Exclusion criteria

- Previous exposure to cardiac medication, including ACE inhibitors (history or current use)
- Unable to lie in supine position for echocardiography
- Impossibility to measure jugulum-symphysis distance

Healthy controls:
Any sign of history of cardiovascular disease
- Previous or current exposure to cardiac medication
- Unable to lie in supine position for PWV measurement
- Impossibility to measure jugulum-symphysis distance
- Any muscle disease

Study design

Design

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

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-06-2020
Enrollment:	56
Type:	Actual

Medical products/devices used

Generic name:	Arteriograph
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	05-03-2020
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	02-08-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	03-09-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 23048
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
Other	Nederlands trial register NL8429

Register	ID
CCMO	NL71572.058.19
OMON	NL-OMON23048