Inspiratory Muscle Training in Myotonic Dystrophy type 1: a pilot study.

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Primary Objective: To study in detail whether a 12-week home based personalized IMT training scheme using the POWERbreathe KHP2 in DM1 patients could result in improvement of maximum inspiratory pressure (PImax) and endurance capacity. We postulate...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Musculoskeletal and connective tissue disorders congenital
Study type	Observational non invasive

Summary

ID

NL-OMON50107

Source
ToetsingOnline

Brief title
IMT study

Condition

- Musculoskeletal and connective tissue disorders congenital
- Musculoskeletal and connective tissue disorders congenital

Synonym
Myotonic Dystrophy type 1

Research involving
Human

Sponsors and support

Primary sponsor: longziekten / centrum voor thuisbeademing
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Inspiratory muscle training, Myotone Dystrofie type 1

Outcome measures

Primary outcome

Difference in inspiratory muscle strength and endurance capacity after 12 weeks

IMT program compared with baseline.

Secondary outcome

Additional effects of IMT will be investigated on symptoms (using

questionnaires about cough, dyspnea, fatigue, quality of life), longvolumes

using spirometry, gas-exchange during the night.

Also effects on the diaphragm will be measured using ultrasound and EMG.

Study description

Background summary

Respiratory failure is the primary cause of mortality in Myotonic Dystrophy type 1 (DM1), which is mainly caused by respiratory muscle weakness. Atelectasis and pneumonia are additional risk factors for death occurring at a mean age of 54 years. Daily life activities are mainly limited due to fatigue and muscle weakness, being present in more than 90% of patients. As curative treatment is not available for DM1 patients yet, main treatment goals are to relieve complaints and to improve quality of life.
In case of the development of hypercapnic respiratory failure, current treatment option is only home mechanical ventilation (HMV), which improves gas-exchange but with variable effects on symptom relieve and unclear survival benefits. Patients often experience mask fitting problems and lack of symptom improvement which both result in decreased treatment motivation and consequently leads to insufficient or prematurely stopping of HMV. Thus, there is a need to search for new treatment modalities for DM1 patients with respiratory failure.
A new treatment modality could be training of the impaired respiratory muscles by inspiratory muscle training (IMT) to improve muscle strength or at least delay progression of respiratory muscle weakness. It seems paradoxical to

exercise affected muscles in patients with progressive muscle atrophy, but training programs of the skeletal muscles in DM1 shows in general small to moderate benefits by increasing muscle endurance, aerobic capacity, and maximal strength. Additional, muscle growth is confirmed by biopsies and imaging studies. Adverse effects of training are not described.
To our best knowledge only two small case series and one case report about IMT in DM1 patients exist, which showed improvement of respiratory muscle strength after completed training period. IMT studies are mainly performed in patients with chronic obstructive pulmonary disease, in which improvement in respiratory muscle strength and endurance capacity are found. Also in several other neuromuscular disorders positive effects of IMT are described. In neuromuscular disorders (mainly spinal muscular atrophy and children with Duchenne) improvement of endurance respiratory muscle training, and respiratory muscle strength are found. Based on these results we hypothesize that IMT training in DM1 patients will improve respiratory muscle function, which probably could prevent the development of atelectasis and pneumonia or even delay the need for HMV.

In this pilot study of ten DM1 patients, we aim to investigate primarily whether IMT on a 12-week home based personalized training schedule using a POWERbreathe KHP2 could improve respiratory muscle strength and endurance capacity. Secondary its effects on cough symptoms, pulmonary function, quality of life, respiratory muscle function (ultrasound of diaphragm) will be investigated.

Study objective

Primary Objective:
To study in detail whether a 12-week home based personalized IMT training scheme using the POWERbreathe KHP2 in DM1 patients could result in improvement of maximum inspiratory pressure (PImax) and endurance capacity. We postulate that a positive outcome of this pilot study could be defined as reaching at least 20% improvement in both PImax and endurance capacity in at least five of ten patients.

Secondary Objective(s):
Additional, we will investigate the effects of training on some clinically outcome parameters: cough and fatigue, quality of life and lung volumes. Direct effects of training on the respiratory muscle function (activity, movement and thickness of the diaphragm) will be measured by ultrasound.

Study design

This study is a single arm intervention pilot study of ten DM1 patients, investigating the effects of IMT on inspiratory muscle strength and endurance capacity.

Adult DM1 patients, who have reduced PImax and vital capacity (both <80% of predicted) without need or indication for HMV will be asked to participate for this study. Before starting a training schedule patients will undergo additional tests at baseline to measure pulmonary function (including inspiratory muscle strength and endurance capacity), ultrasound of diaphragm and symptoms based on questionnaires.
A personalized training schedule will be prepared in collaboration with a physiotherapist. Training sessions consist of 30 breaths, using a POWERbreatheKHP2, at least 10 sessions per week (5 days per week, one session in the morning and one session in the evening). One session takes circa 3-5 minutes.
Training intensity will start on 20% of baseline PImax and will be increased every two weeks during a supervised training session until 50% of baseline PImax in the final two weeks of the schedule. Data about training sessions that have been done at home are stored on the trainer (anonymized). Data of power and work of breathing per breathing session in combination with a patients* diary will be used to increase training intensity during supervised training sessions.
After 12 weeks of training all previously described tests will be tested again.

The first and last visit to the hospital will takes circa 4h to perform all investigations.
Every two weeks a supervised training session will be done in the hospital, which will take circa 30 minutes.

Study burden and risks

Benefits:
Subjects can improve their inspiratory muscle strength and endurance capacity by participating in this IMT study. If therapy will be continued afterwards these improvements could subsequently result in decrease of cough / dyspnoea symptoms and decreases the risks of atelectasis and pneumonia. The development of respiratory failure (and needs for HMV) could also be delayed

Risk assessment
Patients can experience some short term side effects like dizziness, fatigue or some myalgia due to the training sessions, which should disappear soon after the training session.
Due to the natural burden of DM1 with progressive muscle weakness a theoretical potential risk could be that muscle strength and endurance capacity will decrease instead of increase. However, in other neuromuscular disorders (Duchenne, ALS), this is not described.

Group relatedness
Indirect benefits of this study might be achieved, because at a group level we will learn more about effects of training on respiratory muscles in DM1. The

gained knowledge will help to develop future studies and new treatment modalities.

Time schedule:
The first and last visit to the hospital will takes circa 4h to perform all investigations.
Patients have to do their home training sessions daily, at least 10 sessions per week, which will take circa 10 minutes per day.
Every two weeks a supervised training session will be done in the hospital, which will take circa 30 minutes.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
- Diagnosed with DM1 (based on DNA features).
- Age >= 18 years old.
- Reduced PImax and vital capacity (both <80% of predicted).
- Able to provide feedback.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Need or indication for HMV (daytime hypercapnia, pCO2 >= 6.0 kPa)
- Inability to adequately use a POWERbreathe, for example air leak during maneuvers.
- Inability to communicate or answer questionnaires.
- Vital capacity <25% of predicted.
- Clinically unstable, for example pneumonia, decompensatio cordis
-known heart failure, defined as left ventricular ejection fraction of < 50% of predicted.

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-03-2021
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO Date:	07-04-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL72137.042.20
Other	NTR: NL8272