Fatigability in Spinal Muscular Atrophy

Published: 23-06-2014
Last updated: 15-05-2024

To determine the reproducibility and validity of specific outcome measures for skeletal and respiratory fatigability in subjects with SMA.

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

Summary

ID

NL-OMON44457

Source
ToetsingOnline

Brief title
Fatigability in SMA

Condition

- Neurological disorders congenital
- Neuromuscular disorders

Synonym
SMA, Spinal Muscular Atrophy

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Stichting Spieren voor Spieren

Intervention

Keyword: Fatigability, outcome measure, SMA

Outcome measures

Primary outcome

1) Reproducibility of fatigability tests (reliability (ICC) , measurement error (ME)

2) Construct Validity

- content validity between fatigability tests,perceived fatigue and peripheral muscle fatigue: Pearson/Spearman Correlation Coefficient

- convergent validity between fatigability tests (endurance time and delta muscle strength values) and nerve conduction study (delta compound muscle action potential) : Pearson/Spearman Correlation Coefficient

- convergent validity between fatigability tests (endurance time and delta muscle strength values), perceived fatigue (Borg scores and fatigue questionnaires) and peripheral muscle fatigue (EMG registration; Root Mean Square amplitude muscles arms/legs/respiratory)

- discriminative validity between fatigability tests SMA patients, healthy control group and patient controle group: Analysis of Variance (ANOVA)

METC-protocol: H8 Methods, H10 Statistical Analysis

Secondary outcome

Feasibility parameters

- measurement completion

- acceptability

- perceived burden

Study description

Background summary

Spinal muscular atrophy(SMA) is a disorder characterized by degeneration of the motor neuron. It has a wide range of severity, ranging from neonatal respiratory insufficiency and death (SMA type 1), inability to walk independently (SMA type 2), problems with or loss of ambulation (SMA type 3) to mild impairments in adults (SMA type 4). Fatigability, defined as the decline in performance during and after prolonged motor tasks, is a common symptom in addition to weakness. Recently, it was shown that neuromuscular junction (NMJ) dysfunction is present in 50% of patients with SMA, which may be one of the causes of fatigability. There is no curative treatment for SMA. Possible treatment options for fatigability are drugs that improve the function of the NMJ or exercise training (ET) that may reverse some of the detrimental effects of inactivity in patients with neuromuscular disorders. Intervention study design is complicated by the lack of reliable outcome measures for fatigability in patients with SMA. To test the efficacy of possible treatment strategies for fatigability in SMA patients we first need to develop reliable and of valid outcome measures to assess fatigability in SMA patients and to explore associations between fatigability and neuromuscular dysfunction

Study objective

To determine the reproducibility and validity of specific outcome measures for skeletal and respiratory fatigability in subjects with SMA.

Study design

psychometric study on reproducibility and validity

Study burden and risks

Measurements will be distributed over three different days and will take approximately 90 minutes each time. Two measurements will be performed at the participant home or at the exercise laboratory, depending the subjects* preference. One measurement (T1 figure 2) will be performed at the exercise laboratory. All subjects will perform several tests to measure skeletal and respiratory fatigability. They will undergo measurement of height, bodyweight, lung function and muscle function and fill out questionnaires about fatigue and

fatigability twice at home. The risks of these tests are negligible. Similar tests used in usual care are well tolerated in other patient groups with neuromuscular disorders.
Patients with SMA >= 12 years will be asked to undergo a short non-invasive EMG protocol with repetitive nerve stimulation (RNS) of the ulnar (hand muscle) and accessory (shoulder) nerves to document dysfunction of the neuromuscular junction. This same protocol was well-tolerated in a previous study on SMA patients performed by our research group in this hospital1 (MET_Utrecht 10-357). RNS is also frequently used in the workup of patients with neuromuscular disease. RNS is often experienced as a short prickling or itchy feeling. The protocol will be limited to 2x10 minutes which includes preparations such as attaching surface electrodes. RNS will be performed in short runs lasting 10-20 seconds. The burden of repetitive nerve stimulation can be considered as minor. Importantly, subjects will also be included if they do not want to undergo an EMG. The criteria of the Nederlandse Vereniging voor Kindergeneeskunde (Dutch association of Paediatrics) concerning research involving children will be strictly applied.
There are no direct benefits for the participants. However, being able to measure fatigability will enable researchers to develop drugs and exercise training programs aimed at this specific group of children in order to reduce fatigability and improve daily life functioning. A previous survey has indicated that patients with neuromuscular disorders including SMA give high priority to research aiming at investigating the effects of care, including training in addition to research on a potential cure

Contacts

Public
Universitair Medisch Centrum Utrecht

Lundlaan 6
Utrecht 3508 AB
NL
Scientific
Universitair Medisch Centrum Utrecht

Lundlaan 6
Utrecht 3508 AB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

1) Genetically confirmed diagnosis of SMA type 2 or type 3 or type 4 (study group) or Genetically conformed diagnosis of other neuromuscular disease without neuromuscular junction dysfunction (patient control group) or healthy subject (healthy control group)
2) Ability to follow test instructions
3) Parental informed consent/ Inform consent
4) Age 8-60 years

Exclusion criteria

- Concomitant medical problems that might intervene with the outcomes of the testing: Prior to the first test, all subjects will fill out the Preparticipation Questionnaire. This questionnaire is based on the original version designed by the American College of Sports Medicine and American Heart Association. The Dutch version is currently being used by the Child Development and Exercise Center and the Department of Cardiology during standard care procedures such as Cardio Pulmonary Exercise Testing. In the case of possible risk factors for exercise testing, the researcher will contact the medical specialist or general practitioner of the subject about the possibility to participate before the subject is included

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):	17-11-2014
Enrollment:	150
Type:	Actual

Ethics review

Approved WMO Date:	23-06-2014
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	16-09-2014
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-09-2015
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-05-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-10-2016
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	09-02-2017
Application type:	Amendment
Review commission:	METC NedMec

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: 29501
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL48715.041.14
OMON	NL-OMON29501

Study results

Date completed:	03-07-2019
Actual enrolment:	125