SELECTING OUTCOME MEASURES IN PAEDIATRIC MITOCHONDRIAL ENCEPHALOPATHY: A PILOT STUDY

Published: 06-06-2018
Last updated: 11-04-2024

Primary Objective:Determine the relevance, feasibility, reliability (test-retest, inter- and intra-rater) and validity of a selected set of outcome measures in children with mitochondrial encephalopathy. Secondary Objective: Determine in- and...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Inborn errors of metabolism
Study type	Observational non invasive

Summary

ID

NL-OMON45750

Source
ToetsingOnline

Brief title
SO-MITO encephalopathy

Condition

- Inborn errors of metabolism

Synonym
energy metabolism disturbance

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum
Source(s) of monetary or material Support: Stofwisselkracht

Intervention

Keyword: encepahlopathy, mitochondrial disease, outcome measures

Outcome measures

Primary outcome

Functional test (easy to difficult):

Accelerometry

Spasticity- Tardieu

Barry Albright Dystonia Scale

Gross Motor Function measure (GMFM)

9 hole peg test

10m walk or run test

Scale for the Assessment and Rating of Ataxia (SARA)

Gait measurement

6-minute walking test

30 seconds sit to stand test

Questionnaires:

Pediatric Evaluation of Disabilities Inventory * Computer Adaptive Test

(PEDI-CAT)

Pediatric Outcomes Data Collection Instrument (PODCI)

Caregiver burden scales

Newcastle Pediatric Mitochondrial Disease Scale (NPMDS; including short

physical examination)

International Pediatric Mitochondrial Disease Scale (IPMDS; including short

physical examination)

Only in young children (<2 years):

Children's Hospital Of Philadelphia Infant Test Of Neuromuscular Disorders

(CHOP-INTEND; for young children)

Alberta Infant Motor Skills (AIMS; for young children)

Secondary outcome

Demographic data (age, gender, age at diagnosis, genetic diagnosis, phenotype,

height, weight)

Study description

Background summary

At this moment, there is no cure for mitochondrial disease, but drug development is quickly progressing(1, 2). We have just completed a phase 2 trial in adults with the m.3234A>G mutation in our centre, of which the results are pending. Parallel to the execution of this trial, we are preparing for paediatric trials for which the outcomes of this pilot study are crucial.
The phenotype of mitochondrial disorders is extremely heterogeneous, even between patients with the same syndrome or genetic diagnosis and varies in time. Therefore, choosing a population and/or endpoints for these studies is exceptionally challenging. Pure mitochondrial myopathies, which are part of an ongoing validation study, are extremely rare. The majority of the children suffer most from involvement of the brain (mitochondrial encephalopathy). The clinical and genetic spectrum of mitochondrial encephalopathies varies widely, ranging from children with near-normal functional abilities to children who barely make contact to their environment (3). Besides the functional abilities, the genetic, biochemical and clinical profile also differ, almost from patient to patient (4). Common symptoms include: mental retardation, autism or autistic like spectrum, epilepsy (focal or generalized), diminished consciousness, optic neuropathies, movement disorders (extrapyramidal, pyramidal or cerebellar leading to e.g. tremors, dystonia and ataxia) and spasticity.
The clinical trials in paediatric mitochondrial disease that have been performed so far have all failed to reach their primary endpoint. Next to the possible lack of effect of the drugs evaluated, this could be due to

inappropriate study design and selection of a population which was so limited in their abilities to follow instructions that measuring outcome reliably was virtually impossible. Therefore, most of the studies that are performed by international colleagues focus on adults with mitochondrial disease, mostly suffering from a pure mitochondrial myopathy like in CPEO plus like syndromes. Although clinical research is more challenging in children, especially in those with disabilities, the Radboud Centre for Mitochondrial Medicine aims to continue its efforts to also make the paediatric studies more robust. In this study, we aim to gain more experience with the most common phenotype of mitochondrial diseases: children with mitochondrial encephalopathy.

We hypothesize that by executing these pilot studies, we will be able to only include relevant, feasible, reliable and valid outcome measures in our natural history study. The psychometric data obtained in this study will be used to select outcome measures for an international multicentre natural history study in a key-opinion leader workshop.

Study objective

Primary Objective:
Determine the relevance, feasibility, reliability (test-retest, inter- and intra-rater) and validity of a selected set of outcome measures in children with mitochondrial encephalopathy.

Secondary Objective:
Determine in- and exclusion criteria for the international multicentre natural history study, based on the experience in the pilot study

Study design

This is an observational study to test the properties of the selected instruments in the targeted patient group.

Participants will be asked to visit the outpatient clinic of the RCMM three times; the study visits will last about 5 hours. The training session, baseline measurement and re-test visit will be planned at three subsequent visits at the same time of the same day of the week (2 weeks between training and baseline and 1 week between baseline and retest). The training session is included because most of these tests are already known to be subject to learning effects. The baseline and the re-test visit are used to test the stability of the measurement over time while the condition of the child does not change (test-retest reliability). During the baseline measurement, children will be seen by two physiotherapists (inter-rater reliability) and videotaped (for intra-rater reliability). The validity of the measures will be determined by correlating to patient- and physiotherapist-rated anchors. During the measurements, relevance and feasibility will be determined, in close dialogue

with patients and their caretakers.

Study burden and risks

Participants will be asked to visit the outpatient clinic of the RCMM three times; the study visits will last about 5 hours each, but the patients will only be actively involved for less than 2 hours (lots of breaks and questionnaires for parents). The time and the program for the baseline and retest measurement will be determined at the training session. None of the measurements will be painful or hazardous to patients. We aim to study the measurement properties of these instruments in this group of patients. This study is a preparation for a clinical trial in this condition and may facilitate the proper conduction of the clinical trial in this condition. For the patient, the conduction of so many tests is without any doubt burdensome. Therefore, we reduced the number of test to to-our-opinion the absolute minimum. When discussing our protocol with a parent of a patient with a mild and a parent with a child with a mild encephalopathy, they felt that the protocol was feasible. We will make a summary of the measurements after the first measurement and at the end of the stud, when indicated answering a question from clinical care.
This study must be conducted in minors and incapacitated subjects because we assess the measurement properties of these tests in this population.

Contacts

Public
Selecteer

Geert grooteplein noord 10
Nijmegen 6500 HB
NL
Scientific
Selecteer

Geert grooteplein noord 10
Nijmegen 6500 HB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

- Genetically confirmed mitochondrial disease
- Encephalopathy (e.g. psychomotor retardation, epilepsy, abnormalities at neurological examination, etc).

Exclusion criteria

- The treating physician estimates that it is too burdensome for the patient to visit to participate in this study
- Vision problems (<50% sight)

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-04-2019
Enrollment:	20

Type:	Actual

Ethics review

Approved WMO Date:	06-06-2018
Application type:	First submission
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	NL65562.091.18