Systematic Multimodal Approach for Biomarkers And Bulbar assessments In Early-diagnosed SMA

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The goal of this research project comprises two important components1) To determine the motor unit number from the CMAP scan at time of diagnosis correlates with treatment efficacy2) To establish the usefulness of the changes in motor unit number...

Ethical review	Approved WMO
Status	Pending
Health condition type	Neuromuscular disorders
Study type	Observational non invasive

Summary

ID

NL-OMON57032

Source
ToetsingOnline

Brief title
SMA BABIES

Condition

- 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: VENI

Intervention

Keyword: Biomarker, EMG, SMA, therapy effect

Outcome measures

Primary outcome

Motor unit number at the median nerve

Secondary outcome

Motor unit number at the tibial nerve

Motor unit size

Ratio between small and large motor units

Motor unit curve pattern (smooth vs gapped)

Study description

Background summary

SMA is a monogenetic disease based on a homozygous deletion of SMN1 which results in motor neuron degeneration with progressive muscle weakness. Despite the monogentic background, SMA shows a wide clinical variability with 60% of children never able to sit if untreated (SMA type 1) and 10% learning to walk and only having milde proximal muscle weakness through life. (SMA type 3).
The perspective of infants with spinal muscular atrophy(SMA) has changed dramatically with the discovery and implementation of gene-targeting therapies and the inclusion of SMA in the Dutch newborn screening program. Treatment is effective and timing is key (=earlier treatment is better), but still, outcome is quite variable and cure incomplete.
Diagnosis of SMA through newborn screening results in a diagnosis in asymptomatic children. There are currently no markers to predict the clinical phenotype of SMA, and prediction of treatment effect is limited. Counseling of parents is therefor quite difficult.
CMAP scan determines the number of (viable) motor units. Motor unit estimation in previous studies in symptomatic patients have shown dramatic changes in the first weeks of live in severely affected (type 1) patients, with already altered motor unit number early on. Motor unit number is correlated with disease severity in SMA types 1, 2 and 3. CMAP scan analysis is feasible in infants, but was not tested before in newborns with SMA.

We hypothesis that motor unit number at time of diagnose coudl differentiate between asymptomatic patients at the wide ends of the disease severity spectrum: severe SMA (50% of all patients) and late-onset SMA (10% of patients). In these particular cases treatment perspectives and follow up might be significantly different, and prediction of these patients will improve counselling and might alter treatment discissions.

Study objective

The goal of this research project comprises two important components
1) To determine the motor unit number from the CMAP scan at time of diagnosis correlates with treatment efficacy
2) To establish the usefulness of the changes in motor unit number and CMAP scan parameters over time as a therapeutic biomarker for treatment efficacy

Study design

We will perform a longitudinal study:
Part One: search of therapeutic biomarker at time of diagnosis c.q. at start of treatment
• Determine the motor unit number, size or pattern (large cs small) by CMAP scan at time of diagnosis and its relation to treatment efficacy
Part Two: search of therapeutic biomarker over time after treatment
• Determine the change of motor unit number, size or pattern (large cs small) by CMAP scan during treatment in relation to treatment effect.
Assessments will be done at diagnosis c.q. at start of treatment (age 7-14 days), age 4-6 months (4 months after treatment) and age 18 months

Study burden and risks

Minimal burden and risks

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Babies and toddlers (28 days-23 months)
Newborns

Inclusion criteria

Homozygous deletion of SMN1 detected by the national newborn screening program
Treatment-naïve concerning SMN- modulating therapies
Given oral and written informed consent by the legal representative; legal representative are able to understand the Dutch language and information adequately

Exclusion criteria

Comorbidities that interfere with performing EMG (CMAPscan)
Strong apprehension against the performance of EMG

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-07-2024
Enrollment:	70
Type:	Anticipated

Ethics review

Approved WMO

Date:	03-10-2024
Application type:	First submission
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

No registrations found.

In other registers

Register	ID
CCMO	NL86249.041.24