Ocular vestibular evoked myogenic potentials in patients with myasthenia gravis

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Ocular neuromuscular disorders
Study type	Observational non invasive

Summary

ID

NL-OMON50285

Source
ToetsingOnline

Brief title
oVEMPs in patients with myasthenia gravis

Condition

- Ocular neuromuscular disorders

Synonym
myasthenia, myasthenia gravis

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: decrement, extraocular muscles, myasthenia gravis, oVEMP

Outcome measures

Primary outcome

1. The endpoint for objective 1 is the amount of decrement. We will investigate cross-sectionally which cut-off value results in the best combination of sensitivity and specificity by calculating a ROC curve. We will compare this cut-off value with that of Valko et al..

Secondary outcome

2. The endpoint for objective 2 is the presence of significant decrement, using the cut-off value established in objective 1 in order to calculate the specificity and sensitivity of the oVEMP test longitudinally.

3. The endpoint for objective 3 is the decrease of decrement. We will study whether decrement decreases after administration of acetylcholinesterase inhibitors (neostigmine test).

4. The endpoint in objective 4 is the reproducibility of decrement in two consecutive measurements in the same subjects.

Study description

Background summary

Myasthenia Gravis (MG) is a disease characterized by fatigable muscle weakness caused by impairments in neuromuscular transmission. Recent studies show that impaired neuromuscular transmission may be detectable in ocular muscles by measuring ocular vestibular evoked myogenic potentials (oVEMPs). These potentials are evoked by applying a short (4 ms) vibration to the forehead. The amplitude of the oVEMP declines after repetitive stimulation in patients with

impaired neuromuscular transmission (also known as a decrement), whereas it remains stable in healthy subjects. The application of the oVEMP in the diagnosis of MG is relatively new, but case-control studies show that this is an useful test, which is non-invasive and virtually without any burden for the patient.1, 2 This test holds great promise for two reasons. Firstly, it is the first test to measure neuromuscular transmission of the extra-ocular muscles, which are the most frequently affected muscles in MG, that are often involved early in the course of the disease. In about 10% of the MG patients the disease remains restricted to isolated weakness of the extra-ocular muscles. Secondly, unlike currently used tests, it does not require electrical nerve stimulation and is non-invasive as only a vibration is used to elicit the oVEMP.

Study objective

1. The primary objective of this study is to confirm the utility of the oVEMP cross-sectionally for the diagnosis of MG by reproducing the findings of Valko et al. in our cohort of MG patients and three control groups: healthy controls, controls with other neuromuscular diseases and controls with non-neuromuscular diseases that can cause diplopia. (Cross-sectional study)
2. Secondly, we want to investigate the diagnostic value of the oVEMP longitudinally in patients with myasthenia gravis in the differential diagnosis. (Longitudinal study)
3. Thirdly, we want to study whether the oVEMP decrement responds to treatment with acetylcholinesterase inhibitors. (Neostigmine study)
4. Finally, we want to study the reproducibility of the oVEMP decrement in healthy controls and patients.

Study design

A cross-sectional study will be performed on patients with MG and three control groups: healthy controls, controls with other neuromuscular diseases and controls with non-neuromuscular diseases that can cause diplopia. The aim of this cross-sectional study is to conform the utility of the oVEMP test for diagnostic use and to establish a threshold value for diagnostic use (using a ROC curve). Simultaneously a longitudinal study will be performed in patients with the clinical suspicion of MG. All patients are tested with the oVEMP test. By correlating the outcome of the oVEMP test with the final diagnosis, the clinical utility of the oVEMP test can be verified using the threshold value calculated by the cross-sectional study. Furthermore, we will perform the oVEMP test in patients before and after the administration of acetylcholinesterase inhibitors, which is already administered for diagnostic purposes in routine clinical care. Lastly, we want to study the reducibility of the outcome measure decrement, by performing the measurement twice in a subgroup of patients.

Study burden and risks

The risks associated with participation can be considered negligible and the burden can be considered minimal, because the study only involves asking the patients to look in two directions for 60 seconds and a measurement with a minimal intervention (applying non-harmful vibration to the head with a hand-held mini-shaker and a small number of skin electrodes). The intensity of the vibration is comparable with the vibration of an electrical toothbrush. In the future patients may benefit from these investigations because the newly developed tool is expected to aid in the diagnosis of MG.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Cross-sectional study (objective 1)
Patients with MG:

* Patient is legally capable
* Definitive diagnosis of MG defined as the presence of a typical history and at least one positive ancillary test,
including edrophonium testing, RNS, and serum autoantibodies (anti-acetylcholine receptor [AChR], anti-muscle specific tyrosine kinase [MuSK]).
Healthy controls:
* Healthy control is legally capable
* No diagnosis of MG
* Absence of disease that involves eye-muscle function or any other muscle disease
Controls with other neuromuscular diseases:
* Patient is legally capable
* No diagnosis of MG
* Definite diagnosis of other neuromuscular disease
Controls non-neuromuscular diseases that can cause diplopia:
* Patient is legally capable
* No diagnosis of MG
* No other neuromuscular disease
* Definite diagnosis that can cause diplopia
* Presence of diplopia
Longitudinal study (objective 2)
Patients with the clinical suspicion of MG:
* Patient is legally capable
* MG is in the differential diagnosis
* No definitive diagnosis of MG'
Neostigmine study (objective 3)
Patients who undergo an acetylcholinesterase inhibitor (neostigmine) test within routine clinical care:
* Patient is legally capable
* MG is in the differential diagnosis
* Patient undergoes neostigmine test for diagnostic purposes

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:, * Patients who are legally incapable
* Patients who are under the age of 16
* Patients with known vestibulo-cochlear disorders

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:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-10-2018
Enrollment:	136
Type:	Actual

Medical products/devices used

Generic name:	Mini-shaker - Type 4810
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	01-10-2018
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	17-07-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL65522.058.18

Study results

Date completed:	06-10-2021
Actual enrolment:	102