Influenza vaccination in patients with Myasthenia Gravis

Published: 08-08-2016
Last updated: 31-12-2024

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Ethical review	Approved WMO
Status	Completed
Health condition type	Neuromuscular disorders
Study type	Interventional

Summary

ID

NL-OMON43158

Source
ToetsingOnline

Brief title
Influenzavaccination in Myasthenia Gravis

Condition

- 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: verkregen geld voor subsidie/onderzoek

Intervention

Keyword: Flu vaccine, Influenza, Myasthenia gravis, Vaccination

Outcome measures

Primary outcome

Change in total influenza specific serum IgG titer in patients with AChR MG.

Secondary outcome

Clinical relevant change in clinical scores (2 points for MG-ADL, 3 points for

the QMG and the MG composite). Approaches to look at the clinic:

1. The mean change of the test scores of the two groups (A+B vs. C+ D)

2. The number of patients who show a clinical relevant test on one of the tests

en

compare this number of patients between the groups.

3. If a patient shows a clinical relevant change on a test, to look whether

this is also

on the other tests en compare this number of patients between the two groups

(A+B vs C+D).

- Change in autoimmune antibody titers against AChR.

- The effect of the pre-study medication (use of immunosuppressive medication)

at the immunological response.

Study description

Background summary

Myasthenia gravis (MG) is neuromuscular disorder in which functional acetylcholine receptors (AChR) become depleted at neuromuscular junction due to an antibody-mediated autoimmune attack on the neuromuscular synapse. Patients are at an increased risk of infection due to the immunosuppressive therapy, while at the same time vaccination might be less effective. Despite the common use of immunosuppressive treatment in these patients, little is known about the effectiveness and safety of vaccination in these patients. Recently a tetanus revaccination study in MG patients showed an effective response to the booster (unpublished data), without any major safety issues. We would like to further study the effect of vaccinations on MG, using the yearly influenza vaccination. Influenza is a frequently used vaccine with a well know safety profile in healthy persons, but about the effectiveness and safety in myasthenic patients little is known. Studying the influenza vaccine would give additional information compared with the tetanus revaccination. This is because it is a vaccine in which 2 of the 3 used strains are new influenza strains for the patient this season. This in contrast with the tetanus vaccine, which is a revaccination instead of a de novo vaccination.

Study objective

The main objective of this study is to investigate the effectiveness of the humeral immune response after influenza revaccination in patients with MG with acetylcholine antibodies (AChR MG). The secondary objectives are to determine if vaccination induces immunological or clinical exacerbation in patients with AChR MG.

Study design

The study is a longitudinal experimental study. Blood samples, clinical tests and questionnaires will be used. The patient and the clinician who takes the clinical tests are blinded till the end of the visit at 4 weeks. The MG-ADL at 2 and/or 3 months is open label follow-up.

Intervention

Influenza vaccine and/or placebo (NaCl 0.9%)

Study burden and risks

At the day of the vaccination (or placebo) 17.5 ml blood will be withdrawn and the clinical tests will be taken. Four weeks after the revaccination again 17.5ml blood will be withdrawn and the clinical scores will be taken. If the patient received the placebo at the first visit, they will receive the influenza revaccination, to ensure that none of the patients that participate

in the study misses the active influenza immunization. In case that the patient receives the influenza vaccine at the second visit, 17.5 ml blood will be withdrawn 4 weeks after the real immunization. Side effects of the revaccination include redness at the injection site, muscle ache and fever. These will be recorded and monitored throughout the trial. The influenza vaccine is frequently used en known for its safety. In theory the vaccine could induce a worsening of the symptoms. However, this risk is considered very low based on our experience with yearly flu vaccination and the tetanus revaccination study in MG patients.

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

1. Males and females aged above 18 years at the time of the injection.

2. Patient with ocular or generalized AChR MG and
3. A positive serologic test for AChR antibodies > 0.5 nmol/l in the past
4. Patient with prednisone dose lower than 30mg and stable (dose +/- 5mg) during the 3 months before participation; other immunosuppressive should be stable/unchanged.
5. A healthy control above 18 years at the time of injection with no immunosuppressive medication.

Exclusion criteria

1. MG patients with a severe form of MG (Grade 4 or 5 based on MGFA classification).
2. Myasthenic crisis in the last 3 months
3. Presence of a thymoma.
4. Planned thymectomy during the study period or within 12 months prior of the tetanus toxoid booster immunization.
5. Any confirmed or suspected immunosuppressive or immunodeficient condition not related to the treatment of MG, including human immunodeficiency virus (HIV) infection, or a family history of congenital or hereditary immunodeficiency.
6. History or evidence of administration of immunoglobulins within 3 months prior to the tetanus revaccination.
7. History or evidence of plasmapheresis within 3 months prior to the tetanus revaccination.
8. At high risk for aspiration.
9. Pulmonary: forced vital capacity reduced to less than 70% of predicted capacity.
10. History of allergic disease or reactions likely to be exacerbated by any component of the vaccine.
11. History of relevant chronic degenerative, psychiatric, or neurological disorder other than MG.
12. Severe hepatic, renal or cardiac insufficiency.
13. Major congenital defects or serious chronic illness other than MG.
14. Pregnancy or desire to become pregnant during the study.
15. Use of vitamin-K antagonist or new anti-coagulants (NOACS)
16. The patient is unable to fill out the study questionnaires or be interviewed in Dutch, or is unable to undergo the tests needed for the study, or is unable to give informed consent for participation in the study.
17. The investigator can exclude patients for this trial which are deemed not suitable for any reason.

Study design

Design

Study phase: 4

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	18-10-2016
Enrollment:	96
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Influenza vaccine

Ethics review

Approved WMO

Date:	08-08-2016
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	04-10-2016
Application type:	First submission
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
EudraCT	EUCTR2016-003138-26-NL
CCMO	NL58746.058.16

Study results

Date completed: 24-02-2017

Results posted: 28-10-2020

First publication
04-01-2019