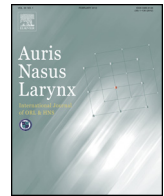




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Ocular vestibular evoked myogenic potential in patients with myasthenia gravis

A prospective clinical study

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ARTICLE INFO

Article history:

Received 5 April 2017

Accepted 6 June 2017

Available online xxx

Keywords:

Myasthenia gravis

Ocular vestibular evoked myogenic potential

Otolith

Utricular function

ABSTRACT

Objective: Myasthenia gravis (MG) is an archetypic disorder of neuromuscular junctions (NMJs) and autoantibody-mediated disease causing fatigable weakness of skeletal muscles with an ocular onset in up to 85%. The aim of this study was to detect extra ocular muscles (EOMs) abnormalities in MG patients using ocular vestibular evoked myogenic potential (oVEMP) n10 response.

Methods: The oVEMP was performed on 40 myasthenia gravis patients that were divided into three groups: newly diagnosed (10 patients), uncontrolled on treatment (15 patients) and controlled on treatment (15 patients) groups in addition to a control group of 10 subjects. Also a comparison of oVEMP response was held between patients with generalized and ocular MG.

Results: The oVEMP n10 showed significant difference between the 3 study groups and the control. The n10 showed no significant difference between the newly diagnosed group and the other 2 groups. There was also significant difference between uncontrolled and controlled on treatment group and between generalized and ocular types of myasthenic patients.

Conclusion: The oVEMP can be usefully used in diagnosis of new MG patients as regard n10 amplitude, threshold and AR except n10 latency with no therapeutic or monitoring value of oVEMP in MG.

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1. Introduction

Myasthenia gravis (MG) is an autoimmune disorder characterized by painless, fluctuating, fatigable muscle weakness caused by the failure of neuromuscular transmission, which results from antibodies (Abs) against the postsynaptic

acetylcholine (ACh) receptor or against muscle specific tyrosine kinase (MuSK) [1].

The incidence ranges from 0.04 to 5/100,000/year and prevalence estimates of 0.5–12.5/100,000/year [2]. Eye dysfunction (asymmetric ptosis and diplopia) is the first manifestation of the disease in over 50% of MG patients [3]; 50–80% of these patients go on to develop generalized disease [4].

It is clear that the chronic state of the disease is associated with permanent changes – in the form of permanent destruction of the basal membrane and OHCs by the prolonged exposure to

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<http://dx.doi.org/10.1016/j.anl.2017.06.001>

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the destructive Abs and secondary ACh neurotransmitter deficiency – that can't be corrected with pharmacological and interventional modalities of therapy [5].

The oVEMP is a negative potential with a short latency at 10 ms, composed of extraocular myogenic responses activated by loud sound stimulation and registered by surface electromyography (EMG) via ipsilateral otolith and contralateral EOM activation [6].

OVEMP abnormalities (reduction or absence of contralateral n10 response) may result from lesions along its pathway of starting from the receptor ending to the effector organ [7].

Early intervention in MG can slow or even stop the progress of the disease, however, diagnosis can be challenging as the disease usually starts at the eye muscles that are hard to access for testing, antibody tests produce false negative results in half of patients and finally other tests for MG are technically difficult [8].

Accordingly, the aim of the present study was to evaluate the usefulness of oVEMP response in patients with MG as tool for diagnosis of the disease.

2. Methods

2.1. Subjects

Study groups: forty MG patients classified into 3 groups:

Group 1: (newly diagnosed group) consisted of ten MG patients (20 ears) newly diagnosed prior to any medication with age range between 19 to 57 years. The diagnosis of MG was based mainly on clinical symptoms and signs (ptosis, diplopia, dysarthria, dysphagia or limb weakness that worsens during in the day).

Group 2: (uncontrolled on treatment group) consisted of fifteen old MG patients (30 ears) with age range between 9 to 57 years receiving treatment for MG and uncontrolled according to clinical symptoms and signs mentioned above.

Group 3: (controlled on treatment group) consisted of fifteen old MG patients (30 ears) with age range between 19 to 57 years receiving treatment and controlled (no ptosis, diplopia, dysarthria, and dysphagia or limb weakness).

Control group: ten normal subjects (20 ears) with age range between 30 to 38 years having normal hearing sensitivity and no neurologic disorder or history of ototoxic drug intake serving as controls. Age and sex matched to the study groups.

In the present study, a comparison between patients with generalized and ocular MG from the study groups was done.

All of subjects including study and control groups had no history of another neurological disorders, otological problems, ototoxic drug intake, diabetes mellitus or hypertension.

The local ethics committee approved this study and a written informed consent was obtained from all patients.

2.2. Methods

All subjects were submitted to: history taking, neurological examination, otological examination, basic audiological evaluation in the form of pure tone, speech audiometry, tympanometry and acoustic reflex threshold measurements and

vestibular evoked potentials testing using Navigator pro (biologic two channel evoked potential recording system) for recording oVEMP using tone burst of 500 Hz with a two cycle rise/fall time and plateau were used. They were presented at a rate of 5 cycles per seconds (through a TDH 39 headphone) at 95 dB nHL and down to threshold.

Measurements made on the oVEMP response n10 threshold, n10 latency, and the n10 base to peak amplitude using 500 Hz tone burst. The left–right difference in the n10 amplitude was evaluated using the n10 asymmetry ratio (AR) defined as $[(\text{larger n10} - \text{smaller n10}) / (\text{larger n10} + \text{smaller n10})] \times 100$. The absence/presence parameters were evaluated for each group. In all study results, latencies and amplitudes were obtained at 95 dBspl 500 Hz tone burst.

3. Results

All subjects in the control group have clear oVEMP responses in the 20 ears using AC 500 Hz tone burst at maximum acoustic stimulation down to threshold. The oVEMP response at 500 Hz is more reliable than those other frequencies [9]. It also had lower thresholds compared to those at other frequencies and seems to be clinically most appropriate [10].

In newly diagnosed group, 8 out of 20 ears (40%) did not give oVEMP response which showed significant difference in oVEMP response between control and newly diagnosed groups ($P = 0.002$), with approximately equal result [23 out of 60 ears (38.3%)] in old patients (uncontrolled and controlled on treatment groups) did not give response which showed significant difference in oVEMP response between control group and old patients ($P = 0.001$). So, the comparison between newly diagnosed group and old patients showed no significant difference in oVEMP responses ($P = 0.895$).

There was no significant difference in oVEMP response between uncontrolled on treatment (absence in 43.3%) and controlled on treatment (absence in 33.3%) groups ($P = 0.426$). And the same between generalized (absence in 40.0%) and ocular (absence in 38.3%) MG patients ($P = 0.895$).

4. Discussion

MG is an archetypic disorder of both NMJ and autoantibody-mediated disease [11] that causes fatigable weakness of skeletal muscles with an ocular onset in up to 85% [12].

NMJ properties vary among muscles and may influence muscle susceptibility to MG [13]. This is well illustrated by the NMJ of the EOMs, which are especially susceptible to developing myasthenic weakness. The NMJs of EOMs differ from those of skeletal muscle in several ways. They have less prominent synaptic folds, and therefore fewer postsynaptic Ach receptors and Na^+ channels, and a reduced safety factor. They are liable to very high neuronal firing frequency, making them prone to fatigue [14].

The oVEMP is considered a negative excitatory myogenic potential that measures utricular or superior vestibular nerve function as well as EOMs function [15].

In Table 1: the oVEMP test generated no sex-based difference in this study. The latency, threshold and amplitude

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