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Ocular vestibular evoked myogenic potentials in patients with migraine

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Abstract

Background: Subclinical cerebello-vestibular impairment has been described in migraine patients.

Objectives: Our aim was to investigate the presence of subclinical vestibulopathy in migraine patients using ocular vestibular evoked myogenic potentials (oVEMP).

Patients and methods: Forty-three patients suffering from migraine without aura who had no vestibular complaints and 29 healthy controls were included in the study. The responses were recorded from contralateral lower eyelid just above of the inferior oblique muscle during 120 dB click stimulation.

Results: Eight migraine patients (18.6%) disclosed no response. Bilateral or unilateral response rates in the migraine group were 46.5% (n = 20) and 34.9% (n = 15) respectively. In controls, bilateral or unilateral responses could be obtained from 25 (86.7%), and 4 (13.2%) cases, respectively. In migraineurs group mean latencies of N1 and P1 were significantly longer, while N1-P1 amplitudes were found meaningfully lower.

Conclusion: These data demonstrate that using oVEMP subclinical vestibular dysfunction can be elicited in migraine patients without vestibular complaints.

Key words: Vestibular evoked myogenic potentials; migraine.

Introduction

Migraine is a pain syndrome characterized by severe headache and accompanying neurological and gastrointestinal disorders affecting patient's activities of daily living adversely (1). Neurootological symptoms are common in migraine. Sensitivity against motion is seen in two thirds of migraine patients. Nausea, dizziness and vertigo are frequently encountered symptoms in migraine. Abnormalities can be detected in vestibular tests like electronystagmography, caloric tests, and posturography. Neurootological tests can be abnormal during intertictal period where vestibular symptoms do not exist (2). Vestibular evoked myogenic potentials (VEMP) is a new technique based on residual acoustic sensitivity of sacculus which functions as an auditory organ during early stages of evolution, and it is still used as an hearing organelle in primitive vertebrates. Vestibular system can be easily and non-invasively evaluated using cervical VEMP (cVEMP) which measures vestibulocolic reflex recorded from electrodes placed on sternocleidomastoid (SCM) muscle, and ocular VEMP (oVEMP) which assesses vestibuloocular reflex elicited from extraocular muscles (3, 4, 5, 6). The aim of this study was to investigate subclinical vestibular dysfunction using oVEMP test in cases with migraine who have not vestibular complaints during interictal period.

Materials and methods

Forty-three patients without a systemic disease who were diagnosed as migraine without aura according to 2004 International Headache Classification (ICHD-II) were included in the study. The patients who received prophylactic treatment in last 3 months did not enroll in the study. The test was performed in migraine patients between attacks (at least 3 days after the last attack). For a better evaluation of the sensitivity of oVEMP test, patients who had auras or vestibular symptoms were excluded.

None of the subjects had a history of hearing loss, recurrent vertigo or vestibular disease. As a control group 29 healthy drug-naive subjects without complaints of headache were used. Ocular VEMP tests of migraine patients and healthy controls were made. The study was made using Medelec Synergy 2000 EP/EMG device with the patients in the sitting position on the examining table at room temperature. After cleansing the skin, surface silver electrodes were filled with a conductive paste, and active, reference, and ground electrodes were attached on

the lower eyelid, 1 cm below and on the forehead, respectively. The cases were requested to look towards superolateral direction so as to activate inferior oblique muscle. Meanwhile using an earphone 120 dB acoustic stimulation was delivered to the contralateral ear at 100 ms intervals (10/s) for duration of 150 seconds, and 1500 responses obtained were averaged. Monitor analyzing time, sensitivity, and filter settings were 100ms, 1 μV, 200 Hz-1Kz respectively. To prevent blinking of the patients during staring time, 3 second-intervals were allowed for every 10 seconds. The study was repeated for both sides twice, and mean (± SD) values were calculated. The first negative and positive responses were designated as a N1 and a P1 wave, respectively. Latencies of N1 and P1 and amplitudes of N1-P1 were measured.

In the statistical analysis independent samples *t* test, Levene test, matched samples t test, and *chi*-square test were performed with the aid of SPSS (Statistical Package for Social Sciences for Windows 15.0). The significance was evaluated at $p < 0,05$ level.

Table 1

Prevalence of oVEMPs in migraine and control groups

	Migraine	Control
Bilateral response	20 (46,5%)	25 (86%)
Unilateral response	15 (34,9%)	4 (13%)
No response	8 (18,6%)	0 (0%)
Total	43 (100%)	29 (100%)

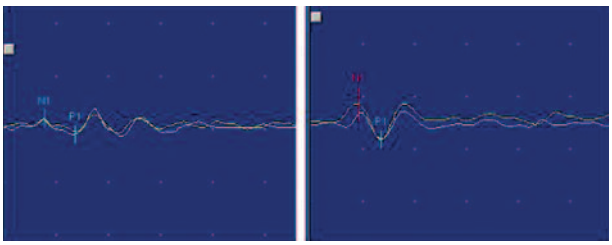

FIG. 1. — Samples of oVEMP tracings (left: migraine, right: control).

Results

Age distribution and mean (± SD) age of the control group were 19-47 years, and 31.34 ± 6.55 years respectively, while the corresponding values for the migraine cases were 18-48 years, and 31.6 ± 7.67 years in that order. The control group consisted of 20 (69%) females, and 9 (31%) males. Thirty (69.8%) female and 13 male (30.2%) migraine patients were enrolled in the study. There was no statistical difference between groups as for mean age or gender distribution ($p > 0.05$).

Twenty-five bilateral (86.7%) and 4 unilateral (13.2%) responses could be elicited in the control group, while 20 bilateral (46.5%) and 15 (34.9) unilateral responses could be obtained in the migraine group. Bilateral responses could not be elicited from 8 (18.6%) migraine cases (Table 1). Illustrative samples of oVEMP tracings are shown in Figure 1.

In the controls and migraine patients where responses could be obtained, there was no difference between the right and the left sides as for N1 latency, P1 latency, and N1-P1 amplitudes ($p > 0.05$). Therefore in further analyses, means (± SD) of right and the left recordings were used for each individual case.

In migraineurs, mean N1 and P1 latencies were significantly prolonged when compared with those of the control group ($p < 0.001$). In addition, mean N1-P1 amplitude was significantly lower when compared with the control group ($p < 0,001$). Comparisons of mean N1 and P1 latencies and N1-P1 amplitudes of the control and patient groups are shown in Table 2.

Discussion

Click evoked vestibulaor evoked myogenic potentials (cVEMP) have been used in clinical practice for various peripheral and central vestibulopathies, but it has been scarcely studied in migraine. VEMPs are mediated by an oligosynaptic pathway encompassing saccular macula, inferior vestibular nerve, vestibular nucleus, vestibulospinal tract and sternocleido-mastoid (SCM) muscle. However in ocular VEMP (oVEMP), vestibulo-ocular tract and extraocular muscles are involved in the responses. This rapid three-neuron circuit between vestibular receptors and neck muscles has been investigated in cats in detail (7). Electrical stimulation of the saccular nerve evokes mainly excitatory postsynaptic potentials in the vestibular nucleus, and inhibitory postsynaptic potentials in the ipsilateral SCM motor neurons, while it exerts almost no effect on contralateral SCM motor neurons. This phenomenon has been interpreted as an indication of a correlation between saccular-SCM reflex pathway and basically ipsilateral disynaptic inhibition (8). A similar pattern was detected for vestibulo-masseteric and trigeminocervical reflexes (9, 10).

Table 2

Comparison of mean N1 latencies, P1 latencies and N1-P1 amplitudes in migraine and control groups

	Migraine	Control	p
N1 (ms) Mean ± SD	9,01 ± 1,73	7,95 ± 0,57	< 0,001
P1 (ms) Mean ± SD	13,27 ± 1,66	12,47 ± 0,74	< 0,001
N1-P1 amplitude (μV) Mean ± SD	0,45 ± 0,24	0,56 ± 0,16	< 0,001

In recent years, it was discovered that short-latency responses evoked by acoustic stimuli activating the vestibular apparatus can be detected with superficial electrodes placed around the eyes. This response is considered to analogous to the cVEMP response recovered from anterior neck muscles. These responses termed oVEMP by Todd *et al*. have been reported to be associated with oligosynaptic linkage to the oculomotor nucleus, and thus they could be considered as exploring the vestibuloocular reflex pathway (11). The response consists of an initial negative wave (N1) and a successive positive wave (P1). Estimates of N1, and P1 latencies, and N1-P amplitudes are around 8 ms, 12 ms, and 0.5-2.0 μV, respectively. The responses elicited by the contraction of extraocular muscles are best identified when contralateral inferior oblique muscle is used for testing. These potentials cannot be confounded with eye-blink reflex and startle responses which a much longer latency of 30-40 ms. Studies in subjects with intact vestibular function in the presence of hearing loss, or vestibular dysfunction associated with an intact auditory function suggest a vestibular origin for these potentials. Cervical VEMPs recorded from SCM begin with a positive wave indicating an inhibitory vestibulospinal response. While extraocular potentials start with an initial negative wave which represents an excitatory vestibuloocular response. In the evaluation of vestibular function, in the elderly, and in patients unable to contract their neck muscles, oVEMP test can be used as an alternative to cVEMP (11-16).

In migraine patients complaining of vertigo or dizziness, vestibular tests can yield abnormal results. In a study performed by Kayan *et al*. neuorotological disorders were reported in 77% of migraine patients (17). Some tests such as vestibuloocular tests can also yield abnormal results in cases without vestibular symptoms. Examination of static posturograms of migraine patients without vertigo and dizziness demonstrated deterioration in equilibrium parameters favoring central vestibular involvement relative to the healthy controls (18). Since vestibular nuclei receive noradrenergic inputs from locus ceruleus, and serotonergic inputs from dorsal raphe nucleus, activation of these structures in migraine can affect central vestibular processing. Mutation of calcium channel gene in patients with familial hemiplegic migraine result in paroxysmal symptoms like headache and vertigo. Channelopathy seems to be a model which might be associated with central and peripheral vestibular dysfunction (19).

A significant decrease in P13-N23 amplitudes and habituation of cVEMPs was reported between attacks in migraine patients without vestibular symptoms (20-21). This pattern resembles that detected in evoked cortical responses during the interictal period in patients with migraine. Habituation deficit in migraine has been also reported for subcortical components of evoked potentials and nociceptive blink reflex which is also a brainstem reflex (22). Liao *et al*. found abnormal VEMPs in 10 out of 20 cases with basilar type migraine. In the above mentioned study, VEMP responses could not be recorded bilaterally in 7 cases, 2 cases showed delayed responses, and 1 patient had no response on one side, and from the other side a delayed response. After 3 months of prophylactic anti-migraine treatment, pre-treatment abnormal VEMP responses normalized in 9 cases which was speculatively attributed to reversible ischemia secondary to hypoperfusion in the territory of the basilar artery (23). Abnormal excitability of the cerebral cortex between migraine attacks might explain abnormalities in VEMPs. In a study done in cats, the presence of descending cortical projections on vestibular nuclei has been demonstrated (24). The habituation deficit in evoked cortical potentials might be associated with the hypofunction of subcortical serotonergic projections innervating the cortex, and subsequent decline in preactivation levels (25). On the other hand, reciprocal connections exist between vestibular nuclei and dorsal raphe nucleus (26). In the pathogenesis of migrainous vertigo, the serotonergic input to the vestibular nucleus has been implicated (27). Decreased activation in serotonergic afferents to the reflex circuitry of the VEMP might thus explain the abnormailities found inmigraine.

In our study, the number of migraine patients unresponsive to oVEMP testing was remarkably high, and a significant prolongation of latencies and decrease in amplitude were detected in responsive cases when compared with the control group. In the literature, we could not find any study of oVEMP test in migraine patients.

oVEMP is an easy to use and non-invasive technique which is able to demonstrate vestibular involvement in migraine patients, even in the absence of overt vestibular symptoms.

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