Klinik Araştırma

Ocular Vestibular Evoked Myogenic Potentials in Patients with Multiple Sclerosis

Multipl Skleroz Olgularında Oküler Vestibüler Uyarılmış Potansiyeller

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ABSTRACT

Introduction: *Vestibular evoked myogenic potential (VEMP) test is a technique based on activation of vestibular apparatus by acoustic stimulation. In this study we aimed to investigate the presence of vestibulopathy in patients with relapsing remitting multiple sclerosis (RRMS) who have not vestibular complaints using ocular VEMP (oVEMP) test.*

Materials and Methods: *Forty patients diagnosed as RRMS according to revised McDonald criteria and 30 healthy controls were enrolled in the study. oVEMP tests were performed through contralateral inferior oblique muscles. Active electrode was placed on the lower eyelid, and the reference electrode was attached 1cm below. The patients were requested to stare towards a superolateral direction so as to activate inferior oblique muscle. Meanwhile 120 dB click stimulation was delivered to the contralateral ear at 10/sec for 150 sec, and 1500 responses were averaged. The test was repeated twice for each side and the latencies and amplitudes of the initial negative (N1) and positive (P1) waves were measured. Availability of any response, their latencies and amplitudes were compared.*

Results: *Nine cases of RRMS (22.5 %) could not yield any response in both sides, while in the control group no bilateral response was obtained in 4 cases (13.3%). Also in RRMS group no unilateral response was obtained in 5 (12.5%) cases. In the RRMS group mean latencies of N1 and P1 were significantly longer, while N1-P1 amplitudes were found to be meaningfully lower.*

Conclusion: *These findings demonstrate that using oVEMP test subclinical vestibulopathy can be elicited in RRMS patients without vestibular complaints.*

Keywords: *ocular vestibular evoked myogenic potential; multiple sclerosis; vestibulopathy*

ÖZET

Amaç: *Relapsing-remitting Multipl Skleroz (RRMS) olgularında oküler vestibüler uyarılmış myojenik potensiyel (oVEMP) incelemesi ile subklinik vestibülopati varlığının araştırılması amaçlandı.*

Materyal ve Metod: *Revize McDonald tanı kriterlerine göre RRMS tanısı konan, atak dışı dönemde ve vestibüler yakınması olmayan 40 (23 kadın, 17 erkek) olgu ile 30 (21 kadın, 9 erkek) sağlıklı birey incelendi. Alt göz kapağı üzerine konan yüzeyel elektodlarla yapılan kayıt sırasında kontrlateral kulağa 120 dB klik uyarı verildi ve bu sırada inferior oblik kası aktive etmek için hastanın üst laterale bakması istenerek elde edilen 1500 yanıt averajlandı. İlk negatif dalga N1, ilk pozitif dalga P1 olarak adlandırıldı. Çalışma iki taraf için iki kez tekrarladı ve ortalamaları alındı.*

Bulgular: *RRMS olgularından 9'unda (%22.5) kontrol grubunun 4'ünde (%13.3) bilateral cevap elde edilemedi. Ayrıca RRMS grubunda 5 (%12.5) olguda tek taraflı cevap elde edilmedi. RRMS grubunda N1 ve P1 ortalama latansları anlamlı uzun, N1-P1 amplitüdleri anlamlı düşük bulundu.*

Sonuç: *Bu bulgular oVEMP incelemesinin RRMS olgularında subklinik vestibülopatiyi değerlendirmede yararlı olduğunu ortaya koymaktadır.*

Anahtar Kelimeler: *oküler vestibüler uyarılmış myojenik potensiyel; multipl skleroz; vestibülopati*

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INTRODUCTION

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 noninvasively 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 (1-8).

The aim of this study was to investigate subclinical vestibular dysfunction using oVEMP test in cases with relapsing remitting multiple sclerosis (RRMS) who have not vestibular complaints during non attack period.

MATERIALS AND METHODS

Forty patients diagnosed as RRMS according to revised McDonald criteria and 30 healthy controls were enrolled in the study. None of the cases had a history of hearing loss, recurrent vertigo or vestibular disease. Ocular VEMP tests of RRMS patients and healthy controls were made. The tests of RRMS patients were performed during non attack period. 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, 1cm 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 click 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 to assess the results. 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.

RESULTS

Age distribution and mean (± SD) age of the control group were 19-47 years, and 31.1 ± 6.54 years respectively, while the corresponding values for the RRMS cases were 19-41 years, and 31.5 ± 5.67 years in that order. Control group consisted of 21 (70%) females, and 9 (30%) males. The numbers of females and males RRMS cases who enrolled to the study were 23 (57.5%) and 13 (42.5%) respectively. Any difference could not be found between groups as for mean ages and distribution of genders ($p>0.05$). The demographic data of cases and control group are shown Table 1. Nine cases of RRMS (22.5 %) could not yield any response in both sides, while in the control group no bilateral response was obtained in 4 cases (13.3%). Also in RRMS group no unilateral response was obtained in 5 (12.5%) cases (Table 2). In the RRMS group mean latencies of N1 and P1 were significantly longer, while N1-P1 amplitudes were found to be significantly lower (p=0,001; Table 3, Graphic 1, 2 and 3). Samples of oVEMP tracings are shown in Figure 1 and 2.

Table 1: The demographic data of RRMS and control group.

	Age (year)	Gender		Total
		Female	Male	
RRMS	31.52 ± 5.67	23 (57.5%)	17 (42.5%)	40
Control	31.13 ± 6.54	21 (70%)	9 (30%)	30
p	0.790	0.326		

Table 2: Comparison of rates of oVEMP responses obtained in RRMS and control groups.

	RRMS		Control	
	N	%	N	%
Bilateral lack of response	9	22.5	0	0
Unilateral lack of response	5	12.5	4	13.3
Bilateral obtainable responses	26	65	26	86.7

Table 3: Comparison of mean N1 latencies, P1 latencies and N1-P1 amplitudes detected in RRMS and control groups.

	RRMS	Control	p
N1 latency (ms) Mean ± SD	9,28 ± 1,10	7,96 ± 0,56	0,001
P1 latency (ms) Mean ± SD	13,78 ± 1,13	12,50 ± 0,75	0,001
N1-P1 amplitude (μV) Mean ± SD	0,42 ± 0,16	0,6 ± 0,26	0,001

DISCUSSION

Click evoked VEMP was used in the clinical practice for various peripheral and central vestibulopathies, however it has been scarcely studied in multiple sclerosis. VEMP responses are associated with oligosynaptic pathway encompassing saccular macula, inferior vestibular nerve, vestibular nucleus, vestibulospinal tract and SCM muscle (1). However in oVEMP, vestibuloocular tract and extraocular muscles are involved in the formation of responses instead of vestibulospinal tract and SCM, respectively (6, 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 dyssynaptic inhibition. A similar pattern was detected for vestibulomasseteric and trigeminoservical reflexes.

In recent years, it was discovered that short-termed latencies evoked by vestibular apparatus activated by acoustic stimulation can be detected with superficial electrodes placed around eyes. This response is accepted as analogous to the cVEMP response recovered from anterior neck muscles. These responses termed as 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 indicators of vestibuloocular reflex pathway (6).

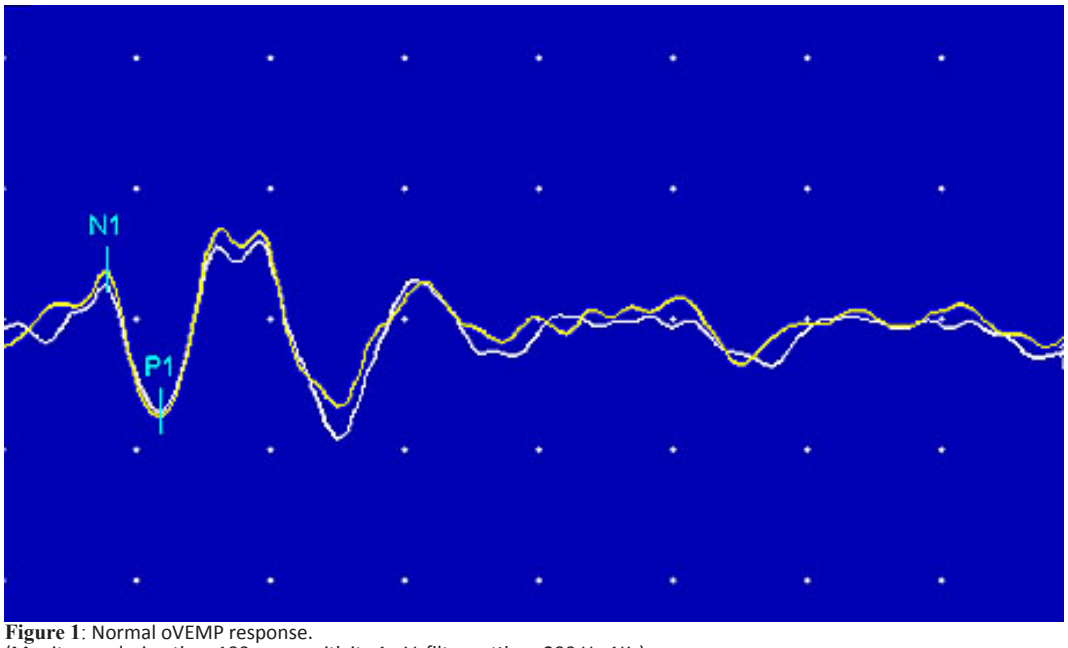

Figure 1: Normal oVEMP response.
(Monitor analyzing time 100ms; sensitivity 1 µV; filter settings 200 Hz-1Kz)

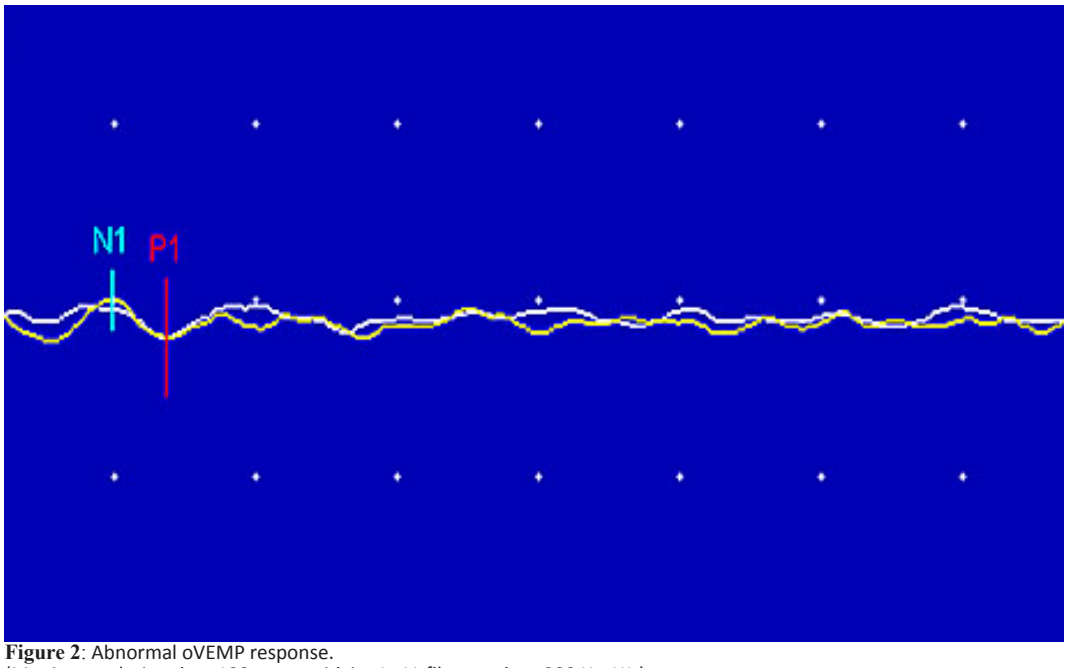

Figure 2: Abnormal oVEMP response.
(Monitor analyzing time 100ms; sensitivity 1 µV; filter settings 200 Hz-1Kz)

This 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 nearly 8ms, 12ms, and 0.5-2.0μV, respectively. The responses elicited with the contraction of extraocular muscles are best revealed when contralateral inferior oblique muscle is used for testing. These potentials cannot be associated with eye-blink reflex and startle response with a more delayed latency of 30-40ms. Intact vestibular function in the presence of hearing loss, and vestibular dysfunction associated with an intact auditory function suggest vestibular origin for these potentials.

Cervical VEMP recorded from SCM begins with a positive wave indicating an inhibitory vestibulospinal response. While extraocular potential starts with an initial negative wave which represents an excitatory vestibuloocular response. In the evaluation of vestibular function, in the elder, and in the patients unable to contract their neck muscles, oVEMP test can be used as an alternative to cVEMP test.

There are a lot of studies about abnormal results of cervical VEMPs in patients with multiple sclerosis (9-14). However the studies using oVEMP in patients with multiple sclerosis are relatively new and reveal abnormal results as cVEMP studies (15-17). Gazioglu et al. were found higher abnormality ratio of oVEMP according to cVEMP responses in patients with multiple sclerosis (45% and 18% respectively). They did not found any correlation between abnormal VEMP responses and brainstem clinical or magnetic resonance imaging lesions (16). Gabelić et al. reported 30% prolonged latencies and 40% conduction block in at least one ocular response using oVEMP in patients with multiple sclerosis (17).

In our study, the number of RRMS patients unresponsive to oVEMP test was found to be markedly higher, and a significant prolongation of latencies and meaningful decrease in amplitudes were detected in responsive cases when compared with the control group

CONCLUSION

Though VEMP is not the only diagnostic test for multiple sclerosis, it is a significant, easy to use, and non-invasive technique which demonstrates vestibular involvement. As a result, the data retrieved, reveal that subclinical vestibular dysfunction can be demonstrated using oVEMP test in RRMS patients without vestibular complaints.

KAYNAKLAR

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