

Does Inferior Oblique Muscle Overaction Affect Ocular Vestibular Evoked Myogenic Potentials?

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ABSTRACT

Objectives: Inferior oblique muscle overaction (IOOA) is a common ocular motility disorder. Ocular Vestibular Evoked Myogenic Potentials (oVEMP) are tests that evaluate the reflex pathway between the utricular macula and the inferior oblique muscle to detect vestibular diseases. Our study is of great importance as it is the first study in the literature to evaluate the effect of inferior oblique muscle overaction on oVEMP parameters.

Methods: Thirty-five patients with unilateral inferior oblique muscle overaction (IOOA group) and 18 healthy volunteers without any neurological or vestibulocochlear disease were included in this study. All patients and healthy volunteers were evaluated with oVEMP.

Results: No statistically significant difference was found between the n1 latency, p1 latency, n1-p1 latency measurement values of the participants included in the study ($p>0.05$). A statistically significant difference was found between the n1-p1 amplitude measurement values of the participants in patient groups (non-squint eyes, squint eyes) and control groups (p -value was 0.038).

Conclusion: In IOOA patients, vestibulo-ocular reflex pathway may be affected, vestibular symptoms may develop thus o-VEMP responses may be affected. A careful anamnesis should be taken in IOOA patients, and it should be kept in mind that n1-p1 amplitudes and asymmetries may be significantly higher when o-VEMP is performed

Keywords: o-VEMP, Strabismus, Inferior oblique muscle overaction, Balance, Vertigo

INTRODUCTION

Inferior oblique muscle overaction (IOOA) is a common ocular motility disorder manifested by elevation of the affected eye during adduction and usually seen together with horizontal strabismus [1,2]. IOOA is divided into two types as primary and secondary in terms of aetiology [3]. In the primary type, the aetiology is unknown and it is not accompanied by other extraocular muscle paralysis. The secondary type occurs as a result of superior oblique muscle paralysis of the same eye or superior lateral rectus muscle paralysis of the opposite eye [4]. Clinically, in the primary type, excessive elevation of the eye in adduction and slight elevation in the opposite gaze is accompanied by a slight head tilt, however, the head-bending test is negative. In the secondary type, in the eye with muscle paralysis, elevation is observed at the adduction state, and hypertrophy is observed

at the overaction eye. The Bielschowsky test is positive with abnormal head position [5]. The treatment strategies of primary and secondary types -though differ from each other etiologically and clinically- is the same and these include surgeries such as desinsertion/tenotomy, myotomy/myectomy, regression and denervation-muscle extirpation [6].

Vestibular Evoked Myogenic Potentials (VEMP) are tests that evaluate the reflex pathway between peripheral vestibular organs and the muscles that respond to their stimulation to detect vestibular diseases. Cervical VEMP (c-VEMP) assesses the pathway between the saccular macula and the sternocleidomastoid muscle, the ocular VEMP (o-VEMP) assesses the pathway between the utricular macula and the inferior oblique muscle [7].

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The input signal for an oVEMP is either sound or vibration, and the output is the response triggered average of EMG from the ocular muscles, generally those just under the eye. While oVEMPs were developed using bone vibration, the most common method of eliciting oVEMPs is with sound, in a way similar to cVEMPs. The best sound frequency is identical to cVEMPs, about 500 Hz. For the bone stimulus, subjects are positioned lying supine and looking upward and undergo repeated applications of the stimulus through a source of vibration, commonly a "mini shaker". The electrodes are placed under the eye to record EMG activity from the inferior oblique muscle. Because the inferior oblique is located under the eyeball, it is activated by looking upward.

In the literature review, no study was found regarding o-VEMP responses in IOOA patients thus we think our study is important as the first study in the literature by evaluating the effect of inferior oblique muscle overfunction on o-VEMP parameters.

METHODS

Research Design

In this study, a descriptive cross-sectional study design was used to investigate the effect of inferior oblique muscle overfunction on o-VEMP responses.

Study Group

This is a single-center study conducted in a tertiary university hospital between January-March 2022 on 35 patients with unilateral inferior oblique muscle overaction (IOOA group) and 18 healthy volunteers without any neurological or vestibulocochlear disease.

Anamnesis of the participants was taken carefully, their medical records were reviewed, and ear, nose and throat, neurological and vestibular examinations were performed. Exclusion criteria for this study were; patients with vestibular cochlear and neurologic disease, who used ototoxic or vestibule-suppressant drugs, who had conductive hearing loss, who had an ocular disease other than IOOA or who had a history of ocular surgery. They were evaluated with o-VEMP tests.

o-VEMP test was performed with Neurosoft brand Neuro-Audio model device. Electrodes were placed in the middle of the

forehead, 15-20 mm below the orbits, and on the cheeks, not too far or too close with these electrodes. Electromyographic signals were amplified and filtered between 1 and 1000 Hz. The patients were asked to look up and measurements were made by sending a 500 Hz tone-burst stimulus at a sound intensity of 105 dB nHL. N1 and P1 absolute latencies, N1-P1 interlatency, N1-P1 amplitude and percent of asymmetry of the obtained waves were evaluated.

Statistical Analysis

The analysis of the data was carried out with the SPSS (Statistical Program in Social Sciences) 25 program. The conformity of the data to the normal distribution was tested with the Shapiro Wilk test. The differences between the two groups for the variables providing the assumption of normal distribution were examined with the independent sample t test.

On the other hand, the difference between the two groups was examined with the Mann Whitney u test for the variables that did not provide the assumption. The difference between more than two groups was examined with the Kruskal Wallis test for the variable that does not assume a normal distribution. The gender and right and left ear variables in the patient group presented in Table 1 are categorical variables, and the chi-square (χ^2) analysis was performed to investigate the relationship between the groups. At the same time, the age variable is continuous, and the independent sample t test was used to examine the difference between groups.

Ethical Principles of Research

Ethical approval was obtained from the University Health Sciences Institute Non-Interventional Clinical Research Ethics Committee (decision number: 2021/2754, date: 30.11.2021), and written and verbal informed consent was obtained from the parents of all children participating in the study.

RESULTS

The participants included in the study showed any difference between and within the groups according to demographic variables, and the results are shown in Table 1.

There was no statistically significant difference between the case and control groups according to age and gender ($p>0.05$), and the groups showed a homogeneous distribution. There was no statistically significant difference between the case groups in the study, with a squint in the right eye and a squint in the left eye according to gender ($p>0.05$, Table 1).

It was tested whether the participants included in the study showed a difference between squinted and non-squinted eyes in terms of n1 latency, p1 latency, n1-p1 latency, n1-p1 amplitude measurements in the right-eyed and left-eyed squint groups, and the results are shown in Table 2.

No statistically significant difference was found between the squinted and non-squinted sides according to the n1 latency, p1 latency, and n1-p1 latency measurement values in both the right-eye and the left-eye group ($p>0.05$). A statistically significant difference was found between the squinted and non-squinted

Main Points:

- Inferior oblique muscle overaction (IOOA) is a common ocular motility disorder manifested by elevation of the affected eye during adduction and is usually seen together with horizontal strabismus.
- Vestibular Evoked Myogenic Potentials (VEMP) are tests that evaluate the reflex pathway between peripheral vestibular organs and the muscles that respond to their stimulation to detect vestibular diseases. The ocular VEMP (o-VEMP) assesses the path between the utricular macula and the inferior oblique muscle.
- In IOOA patients, the vestibular-ocular reflex pathway may be affected, therefore, o-VEMP responses may be complicated.

sides in terms of n1-p1 amplitude measurement values in both the right-eye group and the left-eye group of the participants (p values were 0.032, 0.034, respectively). A statistically significant difference was found between the groups (right eye, left eye, and control groups) according to the asymmetry measurements (p-value was 0.042, Table 2).

It was tested whether a difference exists between the groups in terms of the presence of o-VEMP wave between the squint eyes and controls, and the results are shown in Table 3.

There was no statistically significant difference between the groups regarding o-VEMP wave presence between the right and

left eyes with or without squint (p>0.05).

It was tested whether there was a difference between the groups (right squint, left squint, and control) according to both right and left n1 latency, p1 latency, n1-p1 latency, n1-p1 amplitude, and asymmetry measurements, and the results are shown in Table 4.

According to the n1 latency, p1 latency, and n1-p1 latency measurement values, no statistically significant difference was found between the eyes without squint, eyes with squint and control groups (p>0.05). A statistically significant difference was found between the n1-p1 amplitude measurement values between the eyes without squint, eyes with squint, and control groups (p-value was 0.038, Table 4).

Table 1. Comparison of Demographic Variables Between Groups

		Group			Total	Test	p
		Case n (%)		Control n (%)			
Gender	Female	20 (57.1)			10 (55.6)	0.012 ^a	0.912
	Male	15 (42.9)			8 (44.4)		
	Total	35 (100.0)			18 (100.0)		
		Squint eye				0.010 ^a	0.922
		Right n (%)	Left n (%)	Total n (%)			
	Male	9 (56.3)	11 (57.9)	20 (57.1)			
	Female	7 (43.8)	8 (42.1)	15 (42.9)			
	Total	16 (100.0)	19 (100.0)	35 (100.0)			
		Mean ± sd (Min-Max)			Mean ± sd (Min-Max)		
Age		8.77 ± 1.71 (7-13)			9.11 ± 1.68 (7-14)	-0.927 ^b	0.354

^a Chi-square Test value (χ²), ^b independent sample t test

Table 2. Comparison of o-VEMP Parameters According to Squint Eyes

Strabismus Condition	Measurement	Right eye mean ± sd (M) [Min-Max.]	Left eye mean ± sd (M) [Min-Max.]	p		
Right Eye Squint	n1 latency	9.63 ± 0.93 (9.4) [8.4 - 11.8]	9.94 ± 0.77 (9.8) [8.6 - 11.9]	0.154		
		p1 latency	15.05 ± 1.35 (14.5) [13.1 - 17.4]		15.26 ± 1.12 (15) [13.9 - 17.2]	0.552
			n1-p1 latency		5.48 ± 1 (5.5) [3.6 - 7.3]	
	n1-p1 amplitude			9.5 ± 5.79 (8.8) [1.9 - 20.9]	9.02 ± 6.52 (8.9) [1.1 - 23.9]	

Left Eye Squint	n1 latency	9.7 ± 0.96	9.83 ± 0.94	0.594
		(9.7)	(10)	
		[8.4 - 11.7]	[8.3 - 11.7]	
	p1 latency	15.22 ± 1.25	15.48 ± 1.42	0.510
		(15.1)	(15.8)	
		[13 - 17.6]	[12.4 - 18.7]	
	n1-p1 latency	5.46 ± 0.71	5.59 ± 0.91	0.707
		(5.5)	(5.5)	
		[4-7]	[4.1 - 7.2]	
	n1-p1 amplitude	6.5 ± 4.37	8.51 ± 4.67	0.032*
		(5.1)	(8.3)	
		[1.8 - 19.8]	[1.4 - 16.8]	
	Right Eye Squint	Left Eye Squint	Control	
Asymmetry	22.36 ± 11.24	20.97 ± 14.07	13.45 ± 8.64	0.042* Difference
	(21.3)	(23.8)	(14.0)	
	[8.8 - 48.4]	[50.3 - 0]	[0.4 - 28.2]	

^a; Mann Whitney U Test, ^b; Kruskal Wallis Test, *, p<0.05

Table 3. Comparison of o-VEMP Parameters Between Squint Eyes and Control Groups

o-VEMP Wave Presence		Right Eye Squint n (%)	Left Eye Squint n (%)	Control n (%)	Total	Test	p
Right o-VEMP Wave Presence	Yes	16 (100.0)	17 (89.5)	17 (94.4)	50 (94.3)	0.426	0.514
	No	0 (0.0)	2 (10.5)	1 (5.6)	3 (5.7)		
	Total						
Left o-VEMP Wave Presence	Yes	14 (87.5)	19 (100.0)	18 (100.0)	51 (96.2)	3.431	0.064
	No	2 (12.5)	0 (0.0)	0 0.0	2 (3.8)		
	Total	16 (100.0)	19 (100.0)	18 (100.0)	53 (100.0)		

Test value; Chi-square Test value (χ^2)

Table 4. Comparison of o-VEMP Parameters of Case Group's Squint Eyes, Healthy Eyes, and Control Group

Measurement	Squint Eyes	Healty Eyes of Squints	Control	Test	p
	mean ± sd (M)	mean ± sd (M)	mean ± sd (M)		
	[Min-Max.]	[Min-Max.]	[Min-Max.]		
n1 latency	9.74 ± 0.93 (9.5) [8.3 - 11.8]	9.81 ± 0.87 (9.8) [8.4 - 11.9]	9.66 ± 0.96 (9.5) [8.2 - 12.1]	0.825	0.662
p1 latency	15.28 ± 1.39 (15.2) [12.4 - 18.7]	15.24 ± 1.17 (15.0) [13 - 17.6]	14.87 ± 1.09 (14.9) [12.4 - 17.4]	2.058	0.357
n1-p1 latency	5.54 ± 0.94 (5.5) [3.6 - 7.3]	5.4 ± 0.86 (5.3) [3.9 - 7.1]	5.17 ± 0.84 (5.3) [3.9 - 7.1]	2.661	0.265
n1-p1 amplitude	8.96 ± 5.16 (8.5) [1.8 - 20.9]	7.64 ± 5.5 (6.7) [1.1 - 23.9]	7.73 ± 4.56 (7.5) [1.4 - 21.6]	3.995	0.038*

Mann Whitney U Test *, p<0.05

DISCUSSION

o-VEMP is an EMG recording of extra-ocular muscle activity resulting from the vestibulo-ocular reflex pathway. Fibers emerging from the utricle macula reach the 8th nerve nucleus and from there to the opposite side 3rd nerve nucleus via the medial longitudinal fasciculus (MLF) in the brain stem. The extraocular muscles, especially the inferior oblique muscle, are stimulated by the 3rd nerve [8]. In this study, it was aimed to investigate how o-VEMP responses are affected in the case of overfunction of the inferior oblique muscle, which is the last stop of the vestibulo-ocular reflex pathway.

There are various studies on vestibular diseases that may affect VEMP responses. VEMP responses were compared especially in benign paroxysmal positional vertigo (BPPV) [9], Meniere's Disease [10], vestibular neuritis [11], vestibular migraine [12], semicircular canal dehiscence syndrome (SCDS) [14], which are the most common vestibular system diseases. In addition, VEMP responses were also examined in diseases such as sudden hearing loss, inner ear diseases and otosclerosis that may affect the utricle and saccule, and significant differences were found [14,15].

Since VEMP reflects the functions of the peripheral as well as the central autolytic pathways, it can also be used for disorders of the central nervous system. VEMP studies have been reported in central nervous system disorders related to multiple sclerosis (MS) [16], spino-cerebellar degeneration [17], brain stem and cerebellar infarction [18], Parkinson's disease [19]. The difference between c-VEMP results and o-VEMP results is considered an important method for evaluating lesions in the brainstem [8]. There are also other factors that will affect o-VEMP responses such as, older patients have been shown to have a lower o-VEMP amplitude while younger patients are more likely to have higher o-VEMP amplitudes [20]. This appears to be the result of age-related vestibular loss rather than a change in static muscle tension with aging [21]. In this study, careful selection of the age distribution of the patient and control groups was made in order to reduce the effect of the aging factor.

Various studies have been conducted to investigate whether o-VEMP responses were affected in eye-related diseases. Monitoring of EMG responses in patients with eyeball enucleation but with preserved extraocular muscles [22] or in patients with eyes closed [23] for o-VEMP responses, the findings supported the view that these responses are potentials in the extraocular muscles independent of retina but due to vestibular stimulation. The finding of a study by Bayram et al. the fact that there was no significant difference between the o-VEMP responses between the healthy and blind eyes of patients with visual loss and the o-VEMP responses between the control group- also supports this theory [24]. As o-VEMP responses rely on activation of the contralateral inferior oblique muscle, control of muscle contraction is important for reproducible and reliable results [25,26].

Other variables to consider when performing o-VEMP testing include electrode positioning [27] and stimulus repetition rate [28]. In this study, all tests in terms of standardization were

performed by an experienced audiologist.

In our literature review, no study was found regarding o-VEMP responses in IOOA patients.

In our study, it was predicted that the overfunction of the inferior oblique muscle may affect the vestibular system, as it causes a change in the vestibulo-ocular reflex arc of the patient and a change in the eye-head position.

The finding of n1, p1 and n1-p1 latencies in IOOA patients are similar with the control group draws attention to that, muscle overfunction has no effect at the time of muscle contraction and reflex formation. However, the significant difference in n1-p1 amplitude and asymmetry rates in IOOA patients compared to the control group shows the effect of muscle overfunction on amplitudes and the effect of asymmetry rates due to amplitudes.

Limitations

Studies with larger sample groups are needed to say that IOOA disease may affect the o-VEMP responses and cause vestibular symptoms. In addition, following the clinical improvement of these patients after surgical treatment, control o-VEMP tests should be performed and compared with previous results. It is also important to monitor the process with quantitative data by evaluating it in combination with all vestibular test batteries in order to objectively reveal whether VEMP effects on these patients and vestibular system symptoms.

CONCLUSION

In IOOA patients, the vestibulo-ocular reflex pathway may be affected, vestibular symptoms may develop, and therefore, o-VEMP responses may be complicated.

A careful anamnesis should be taken in these patients, and it should be kept in mind that n1-p1 amplitudes and asymmetries may be significantly higher when o-VEMP is performed. In addition, it is essential to follow these patients regarding vestibular involvement and vestibular symptoms.

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