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Is There Any Effect of Subjective Tinnitus on Vestibular Evoked Myogenic Potentials

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ABSTRACT

Idiopathic subjective tinnitus has a complex pathophysiology in which not only cochlear and central classical auditory pathways but also nonclassical auditory pathways of different parts of the brain are involved. Vestibuloocular and vestibulocollic pathways are the central projections of utricle and saccule used in the vestibular evoked myogenic potential (VEMP) test. Aim of this study was to investigate the effects of idiopathic subjective tinnitus on vestibuloocular and vestibulocollic pathways via VEMP. We prospectively analyzed 30 unilateral idiopathic subjective tinnitus patient's cervical, ocular VEMP tests, tinnitus handicap index scores, symptom duration and compared with contralateral ear and 35 healthy volunteers. The latencies and amplitudes of P1 and N1 waves were recorded and pathologic wave criteria was calculated according to healthy volunteer's data. In cervical VEMP there were significant longer latencies of P1 and N1 waves with respect to contralateral ear and control group. In ocular VEMP test, N1 and P1 latencies and amplitudes were not significantly different. The percentages of pathologic wave of the tinnitus side were not significantly higher in both cervical VEMP and ocular VEMP tests with respect to contralateral side. Tinnitus handicap index scores and symptom duration had no relationship with latency and amplitude of VEMP tests. Although cervical VEMP P1 and N1 latencies were significantly longer, subjective tinnitus did not result in pathological alterations in the VEMP test. Presence of subjective tinnitus is not an influencing factor in the VEMP interpretation.

Keywords: Subjective tinnitus, vestibular evoked myogenic potential, cVEMP, oVEMP

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INTRODUCTION

Tinnitus is a kind of phantom phenomenon of the auditory system which is defined as perception of nonmeaningful sound without any external stimulus [1-3]. It is mainly classified as objective if the sound is detected by any observer and subjective if the sound is only heard by the patient [4-7]. Even though objective tinnitus mostly has an underlying etiology such as vascular, muscular or eustachian tube pathologies, subjective type is much more common and the vast majority is idiopathic due to unknown underlying neural mechanism of the central nervous system (CNS) [8-10]. It can be intermittent or continuous also defined as chronic if it lasts longer than 6 months[11]. Tinnitus is a very frequent auditory symptom in adult population with a prevalence rate of 4%-25% [12,13]. The differential diagnosis should be done to rule out the neurootologic diseases such as Menier's disease, otosclerosis, and vestibular schwannoma in which vertigo generally accompanies with tinnitus[14]. Detailed medical history, physical examination, audiovestibular and radiologic evaluations are the essentials for the differential diagnosis Vestibular evoked myogenic potentials (VEMP) have become an important noninvasive test battery for the vestibular system disorders[15]. It can separately investigate the superior vestibular nerve (vestibuloocular reflex pathway) and the inferior vestibular nerve (vestibulocollic reflex pathway) via ocular VEMP (oVEMP) and cervical VEMP (cVEMP) respectively[16,17]. For the evaluation; the latency and the amplitude of P1 and N1 wave are used and compared with the contralateral side and the vestibular laboratory's own normative value[18]. The absence of wave and the waveform morphology disorders according to normative value are defined as the pathology of the VEMP[19]. This test is used in the diagnosis not only for the peripheral vestibular system diseases such as vestibular neuronitis, Meniere's disease, superior semicircular canal dehiscence syndrome, but also for the CNS diseases involving vestibular system such as vestibular schwannoma, migraine, neurodegenerative, cerebrovascular and demyelinating diseases[20]

Although tinnitus is a significant symptom of the vestibular diseases accompanying to vertigo, subjective idiopathic tinnitus (SIT) is a distinct entity in which cochlear, central classical and nonclassical auditory pathways are involved[21]. The etiopathogenesis of SIT is still very complex and starts mostly after a triggering damage in the cochlea which results in neural plasticity, neuromodulation and spontaneous neural activity in different regions of the central auditory pathway and non-auditory centers[21]. This trigger is usually an acoustic trauma which can sometimes not result in symptomatic hearing loss. Vestibular end organs and the cochlea which have the same embryological origin, have harmonious intercommunications[22]. Moreover, vestibuloocular and vestibulocollic pathways are also acoustically sensitive to the sound via irregular otolithic neurons located in the saccule and the utricle as cochlear hair cells[16]. Up to date, there is no study investigating the effect of SIT on vestibuloocular and vestibulocollic pathway. Thus, the aim of this prospective study was to evaluate the VEMP findings in SIT.

MATERIALS AND METHODS

This prospective, clinical study was conducted with unilateral, non-pulsatile SIT patients.

Patient group inclusion criteria.

• Patients between 18- 65 years of age with the permanent symptom of at least 6 months duration of unilateral SIT

• No treatment for tinnitus at least 3 months before the study

• No history of ototoxic drug intake, vertigo related neurotologic or CNS disease, head and neck or significant acoustic trauma

• No history of significant vision and neck musculature, temporomandibular joint problems

• No otologic, cervical and ophthalmologic surgery history

• Normal tympanic membrane with pure tone thresholds < 26 decibels (dB) at frequencies between 500-4000 Hz with no air-bone gap and normal tympanogram (type A)

• No history of hearing loss

• No pathology in temporal and brain magnetic resonance imaging, vertebrocarotid system doppler ultrasonography and blood tests (hemoglobin, thyroid function test and lipid profile)

Control group inclusion criteria

• Healthy volunteers between 18- 65 years of age

• No history of vestibular suppressants, sedative or ototoxic drug intake

• No history of vertigo related neurotologic or CNS disease, head or acoustic trauma

• No otologic, cervical and ophthalmologic surgery history

• No history of significant vision or neck problems

• Normal tympanic membrane with pure tone thresholds < 26 dB at frequencies between 500-4000 Hz with no air-bone gap and normal tympanogram (type A

The tinnitus side and the contralateral side of the patient group and the healthy volunteers were evaluated with VEMP device (Neuro-Audio.NET; Neurosoft, Ivanovo, Russia) and ER-3A insert earphone. Self- adhesive electrodes (Neuroline 720; Ambu, Denmark) were used in both cVEMP and oVEMP tests. For the standardization, monoaural, short, tone-burst, (Blackman window, rise/fall time: 2 msec and plate time: 0 msec) air conducted stimulus with 105 dB nHL (rarefaction polarity, 1-1000 Hz band-pass filtered) was applied. The analysis time was 50 msec and the stimulation rate was 5 Hz with a maximum of 120 stimuli count. Two consecutive clear waves were

averaged for the analysis. The latency of N1, P1 (msec), interpeak amplitude of P1N1(uV) were compared with the control group and contralateral ear. Control group consisted of normative data of 70 ear's VEMP parameters of the 35 healthy subjects. Vestibular evoked myogenic potential pathologic wave criteria were designed as the number of patients with absence of the wave or latency and amplitude values which were out of mean +/- 2SD according to the normative value. The patients were also divided into subgroups according to tinnitus handicap index (THI) scores (THI≥38 and <38) and tinnitus symptom duration (TSD) (≥12 and <12 months). The latencies and the amplitudes of the waves were further evaluated according to these parameters.

Statistical Analysis: Statistical analyses were performed with the IBM SPSS for Windows Version 22.0. Numerical variables were summarized as mean ± standard deviation or median [minimum-maximum]. Categorical variables were given as frequencies and percentages. Categorical variables were compared by chi square test. Normality of the continuous variables was evaluated by the Kolmogorov Smirnov test. Homogeneity of variances was tested by the Levene test. Differences between the groups according to continuous variables were determined by independent samples t test. One way ANOVA was used to compare more than two independent groups. Related samples were compared by McNemar test. A p value less than 0.05 was considered as significant.

RESULTS

A total of 30 patients with unilateral SIT and 35 healthy volunteers were enrolled in this study. 14 of the patients had tinnitus on right side the remaining 16 had tinnitus on left side. Demographic results of the patient and control group were shown in Table 1. There was no statistically significant difference in age and sex between patient and control group (p: 0,27 and p: 0,325 respectively). There were statistically significant longer latencies of P1 on tinnitus side in cVEMP test with respect to the contralateral side and control group (p: 0,001 and p: 0,018 respectively). The latency of N1 on tinnitus side was statistically significantly longer than the N1 latencies of the contralateral side and control group (p: 0,001 and p: 0,047 respectively). The amplitude of P1N1 was lower on tinnitus side in cVEMP test when compared with control group but it was not statistically significant (p: 0,084). On the other hand, the latencies of P1 and N1 of contralateral ears were statistically significantly shorter than the control group and P1N1 amplitude was significantly lower than the control group (p: 0,01, p: 0,046 and p: 0,006 respectively).

Table 1: Demographic results of patient and control group.

	Age (year)	Sex (M/F)	Total
Patient Group	48,17+/-10,606	21/9	30
Control Group	46,2+/-10,528	20/15	35
***p* value**	0,27	0.325	

In oVEMP test, the latency of N1 on tinnitus side was longer than the control group and the contralateral side. Moreover, tinnitus side P1 latency was longer than the control group but shorter than the contralateral side. The amplitude of P1N1 on tinnitus side was lower than the control group and contralateral side. However, all these differences were not statistically significant which were shown in Table 2.

In both cVEMP and oVEMP test, the percentages of the pathologic wave of the tinnitus side were higher than the contralateral side according to pathologic wave criteria. (26,7% vs 13,3% in cVEMP, 50% vs 23,3% in oVEMP) However, these results were not statistically significant. (p: 0,344 in cVEMP, p: 0,07 in oVEMP) (Table 3).

According to THI score subgroup analysis, there were 14 patients with THI score ≥38 and 16 patients with THI score <38. In cVEMP test, the latencies of P1 and N1 of ≥38 THI score subgroup were longer than <38 THI score subgroup and the control group. The amplitude of P1N1 of ≥38 THI score subgroup was lower than the control group but higher than the <38 THI score subgroup. All the differences were not statistically significant which were listed in Table 4. In oVEMP test, the latencies of N1 and P1 of ≥38 THI score subgroup were shorter than <38 THI score subgroup but longer than the control group. The amplitude of P1N1 of ≥38 THI score subgroup was higher than the control group and the <38 THI score subgroup. All the differences were not statistically significant which were also shown in Table 4.

According to TSD subgroup analysis, there were 11 patients with duration ≥12 months and 19 patients with duration <12 months. In cVEMP test, the latencies of P1 and N1 of ≥ 12 months subgroup were shorter than <12 months subgroup but longer than the control group. The amplitude of P1N1 of ≥12 months subgroup

Table 2: Latency and amplitudes parameters of cVEMP and oVEMP in patient and control groups.

		Patient Group		Control Group	*p* value (tinnitus-contralateral)	*p* value (tinnitus-control)	*p* value (contralateral-control)
		Tinnitus Side	Contralateral Side				
cVEMP	**P1 Latency (msec)**	13,469+/-0,930	12,579+/-0,850	12,993+/-0,711	0,001	0,018	0,01
	N1 Latency (msec)	21,652+/-1,522	20,39+/-1,46	21,017+/-1,384	0,001	0,047	0,046
	P1N1 Amplitude (*μ*V)	105,721+/-23,338	98,872+/-23,103	116,959+/-39,670	0,169	0,084	0,006
oVEMP	**N1 Latency (msec)**	9,887+/-0,988	9,552+/-1,361	9,706+/-0,578	0,2	0,403	0,561
	P1 Latency (msec)	14,825+/-1,579	14,907+/-1,663	14,575+/-0,954	0,913	0,471	0,321
	P1N1 Amplitude (*μ*V)	6,708+/-2,103	6,941+/-1,955	6,904+/-4,518	0,941	0,78	0,956

Table 3: Comparison of the number of patients with pathologic wave on the tinnitus side with the contralateral side in cVEMP and oVEMP according to normative data.

	Patient Group	Total	Number of pathologic wave (%)
cVEMP	**Tinnitus Side**	30	8 (26,7%)
	Contralateral Side	30	4 (13,3%)
	***p* value**		0,344
oVEMP	**Tinnitus Side**	30	15 (50%)
	Contralateral Side	30	7 (23,3%)
	***p* value**		0,077

Table 4: Comparison of the cVEMP and oVEMP parameters in patient group with control group according to THI score.

		THI Score	Number of patients	P1 Latency (msec)	N1 Latency (msec)	P1N1 Amplitude (μV)
cVEMP	**Tinnitus Side**	≥38	14	13,515+/-0,903	21,885+/-1,507	107,408+/-28,302
		<38	16	13,431+/-0,981	21,463+/-1,56	104,350+/-19,274
	Control Group		35	12,993+/-0,711	21,017+/-1,384	116,959+/-39,67
	***p* value**			0,956	0,709	0,972
			Number of patients	**N1 Latency (msec)**	**P1 Latency (msec)**	**P1N1 Amplitude (μV)**
oVEMP	**Tinnitus Side**	≥38	14	9,792+/-1,514	14,817+/-1,805	7,133+/-2,0799
		<38	16	9,983+/-1,326	14,833+/-1,398	6,283+/-2,127
	Control Group		35	9,706+/-0,578	14,575+/-0,954	6,904+/-4,518
	***p* value**			0,454	0,661	0,859

Table 5: Comparison of the cVEMP and oVEMP parameters in patient group with control group according to tinnitus symptom duration.

		Symptom Duration (month)	Number of patients	P1 Latency (msec)	N1 Latency (msec)	P1N1 Amplitude (μV)
cVEMP	**Tinnitus Side**	≥12	11	13,318+/-0,903	21,336+/-1,894	100+/-22,192
		<12	19	13,561+/-0,961	21,844+/-1,266	109,217+/-23,944
	Control Group		35	12,993+/-0,711	21,017+/-1,384	116,959+/-39,670
	***p* value**			0,697	0,622	0,780
		Symptom Duration (month)	**Number of patients**	**N1 Latency (msec)**	**P1 Latency (msec)**	**P1N1 Amplitude (μV)**
oVEMP	**Tinnitus Side**	≥12	11	9,706+/-0753	14,59+/-1,375	6,790+/-1,5645
		<12	19	10,021+/-1,136	14,993+/-1,741	6,650+/-2,474
	Control Group		35	9,706+/-0,578	14,575+/-0,954	6,904+/-4,518
	***p* value**			0,31	0,463	0,976

was lower than both the <12 months subgroup and the control group. All these differences were not statistically significant which were shown in Table 5. In oVEMP test, the latencies of N1 and P1 of <12 months subgroup were shorter than ≥ 12 months subgroup and the control group. The amplitude of P1N1 of <12 months subgroup was lower than the control group and the ≥12 months subgroup. All these differences were not statistically significant which were also shown in Table 5.

DISCUSSION

Tinnitus is a complex heterogeneous disorder of CNS which involves not only the auditory pathway but also non-auditory regions such as prefrontal cortex, cingulate cortex, parahippocampus, amygdala, insula and cerebellum. This functional connectivity and alteration of these regions are important especially in the maintenance of the tinnitus perception[4]. This neuronal activity alteration has been investigated with functional magnetic resonance imaging, positron emission tomography, electroencephalographic and magnetoencephalographic methods. There was an abnormal neural activity in various part of CNS regions related with auditory and non-auditory pathways in the tinnitus patients[6]. There are a few studies investigating the vestibular system involvement in tinnitus patients. Jozefowicz-Korczynska et al[7] evaluated the oculomotor tests electronystagmographically in 50 tinnitus patients and compared with 30 healthy individuals. They concluded that the persistence of the abnormal oculomotor findings may suggest a subclinical CNS impairment in tinnitus patients. Mezzalira et al.[23] studied the oculomotoricity in 25 tinnitus patients and compared with control group of 35 healthy adults. They concluded that abnormal oculomotor test findings may indicate functional compromise in CNS. However, in Jozefowicz-Korczynska's study, 82% of the patient group

had at least unilateral sensorineural hearing loss and 42% of the patients had episodic vertigo or dizziness history. In our study, the patient group was selected from the patients without any history of hearing loss and vertigo in order to make a more homogenous subjective tinnitus group. In Mezzalira's study the laterality of tinnitus was not mentioned. We only included the unilateral SIT patients to compare the results with the contralateral side and with the control group. Both studies mentioned above examined the vestibulocular pathway electronystagmographically. Thus, we aimed to evaluate the vestibuloocular pathway and vestibulocollic pathway seperately via VEMP in SIT which has been not investigated in literature up to date. Cervical VEMP test shows the pathologies of not only the saccular macula peripherally but also inferior vestibular nerve, vestibular nucleus and medial vestibulospinal tract (vestibulocollic projections) in lower brainstem centrally. Our findings showed that there were a significant delay in latencies of P1 and N1 waves with respect to contralateral side and control group. In pathologic wave analysis of cVEMP, there was a higher percentage on tinnitus side with respect to contralateral side (26,7% vs 13,3%) which was not statistically significant. In general, delay in latency is an important finding of retrolabyrinthine and central vestibular disorders. On the other hand, latency and amplitude values of the contralateral side without tinnitus symptom were significantly shorter and lower with respect to control group in an interesting manner. Thus, subjective tinnitus may have a relationship in the alteration of the neural activity in vestibulocollic reflex arc. Ocular VEMP uses the same reflex arc as in oculomotor tests. Utricular macular projection travels within superior vestibular nerve to vestibular nucleus then projects upwards and crosses to the contralateral side in medial longitidunal fasciculus in midbrain and finally ends in the nuclei of the extraocular muscles[17]. We didn't find any significant difference in latencies and amplitude of the oVEMP wave. However, the percentage of the pathologic wave in oVEMP in tinnitus side was interestingly higher than the contralateral side (50% vs 23,3%). This study has some limitations. In order to make a homogenous study group, we only took the patients with unilateral, chronic, continuous, SIT with normal hearing thresholds. We have no data of bilateral SIT patients with sensorineural hearing loss which is the most common type of SIT. We examined tinnitus which is a subjective symptom with an objective VEMP test. Because there is no objective evaluation method for the SIT. Moreover we didn't find any significant difference between tinnitus subjective characteristics such as tinnitus handicap scores and tinnitus symptom duration with VEMP findings. Although tinnitus group included patients with normal hearing, auditory brain response wave morphology changes may be compared with VEMP morphology changes whether tinnitus has an impact on lower brainstem auditory pathway or not. Finally, vestibular system evaluation of the patients in the study group was done according to detailed history. We didn't perform any other vestibular test to evaluate the vestibular system integrity.

CONCLUSION

Tinnitus is an unknown disorder of the CNS in which classification can be only done by the patient's subjective complaints. There are some factors that influences the results of the VEMP such as age, recording parameters and middle ear pathologies which result in conductive hearing loss Although cVEMP wave latencies were significantly altered, we concluded that subjective tinnitus did not result in pathological alterations in the VEMP test. Presence of subjective tinnitus is not an influencing factor in the VEMP interpretation. The VEMP changes in SIT with larger groups should be studied to demonstrate whether subjective tinnitus affects the VEMP pathway or not.

STATEMENT OF ETHICS

All participants signed the informed consent and the local institutional ethics committee approved the protocol before starting the study (No:42/02/06.11.2017)

CONFLICT OF INTEREST

The authors declare no potential conflict of interest on publishing this paper.

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