THE EUROPEAN SOCIETY OF MEDICINE
Medical Research Archives, Volume 14 Issue 5

RESEARCH ARTICLE

Evaluation of Cervical and Ocular Vestibular Evoked Myogenic Potentials Results in Acoustic Neuroma Cases

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OPEN ACCESS

PUBLISHED
31 May 2026

CITATION
Özdemir, E., et al., 2026. Evaluation of Cervical and Ocular Vestibular Evoked Myogenic Potentials Results in Acoustic Neuroma Cases. Medical Research Archives, [online] 14(5).

ISSN
2375-1924

ABSTRACT

Vestibular evoked myogenic potentials are tests used to evaluate the integrity of the vestibular system. In this study, we aimed to assess cervical and ocular vestibular-evoked myogenic potentials in patients who underwent CyberKnife treatment for vestibular schwannoma.

The study included 23 patients who received Cyberknife treatment for VS and 26 healthy patients without complaints. The patients were given a 97 dB, 500 Hz tone-burst stimulus using monaural air conduction with the ICS-CHARTER EP 200 audiometry device, and cervical and ocular vestibular-evoked myogenic potential tests were applied. In analyzing the results, we assessed the failure rates in obtaining vestibular-evoked myogenic potential responses and the mean and standard deviation values of P1 latency, N1 latency, P1-N1 interval, and P1-N1 interpeak amplitude, and calculated the amplitude asymmetry ratio.

When comparing sick and healthy ears within the patient group, a statistically significant difference in non-response rates was found for both cervical and ocular vestibular-evoked myogenic potential tests. Comparing the patient group to the control group based on the vestibular-evoked myogenic potentials asymmetry rate revealed significant differences in both cervical and ocular vestibular-evoked myogenic potentials. Upon examining the ocular vestibular evoked myogenic potential responses, only a significant difference was noted in P1 latency. When analyzing the patient group by hearing level, ocular vestibular-evoked myogenic potential responses were statistically significantly reduced among patients with hearing levels greater than 60 dB. Conversely, no significant difference was observed as tumor size increased, and abnormalities in cervical vestibular-evoked myogenic potentials and ocular vestibular-evoked myogenic potentials responses also increased in patients with a medial tumor location.

The vestibular-evoked myogenic potential test is a noninvasive, easy-to-perform test method for evaluating vestibular functions in VS patients.

Keywords: asymmetry, Cyberknife, VEMP, vestibular schwannoma, vestibular system

Introduction

In addition to history and physical examination, specific vestibular tests are used to assess symptoms of dizziness and imbalance arising from vestibular system dysfunction. For this reason, the vestibular evoked myogenic potentials (VEMP) test also plays a significant role in evaluating the vestibular system. Vestibular-evoked myogenic potential is an electrophysiological test method in which the reflex arc terminating in the muscles, as a response to stimulation of peripheral vestibular organs, is measured.[1] Cervical is based on the principle of recording the contractions occurring in the saccule, inferior vestibular nerve (IVS), vestibulocollic reflex arc, and ipsilateral sternocleidomastoid (SCM) muscle due to a stimulus administered to them.[2] On the other hand, oVEMP is founded on the principle of recording extraocular muscle activity induced by the superior vestibular nerve (CVS) and vestibulo-ocular reflex (VOR) activity.[2] This comprehensive approach, integrating acoustic, vibratory, and galvanic stimuli, enhances lesion site identification and, when combined with audiometry and caloric testing, significantly improves the precise localization of affected areas and the evaluation of residual function in audiovestibular disorders.[3] Many studies have reported reduced or absent VEMPs in patients with cochleovestibular schwannoma, with a strong correlation to tumor size and abnormal cVEMPs [4.] Specifically, VEMPs have demonstrated clinical utility in identifying superior and/or inferior vestibular nerve dysfunction in patients with vestibular schwannoma, even when auditory nerve and horizontal canal functions remain normal.[1] VS is the most common tumor in the cerebellopontine angle and originates from the vestibular nerves. Although it is benign, it can enlarge and compress the surrounding neural and vascular structures.[5] Follow-up, microsurgery, and stereotactic radiosurgery are among the methods available for treating VS. CyberKnife is one of the newest technologies in stereotactic radiosurgery, serving as an alternative to microsurgery.[6] This study retrospectively evaluated the results of VEMP tests performed on patients diagnosed with VS who underwent CyberKnife treatment. VEMP abnormalities caused by VS were examined and compared with the contralateral intact ear and the control group. The clinical usability of the VEMP test in VS patients, its role in determining tumor origin, hearing profiles, tumor localization, and differences in results according to tumor size were investigated. Considering that vestibular schwannomas typically originate from the Schwann cells of either the superior or inferior vestibular nerve within the internal auditory canal[7], comprehensive vestibular function testing, including VEMPs, offers a non-invasive means to potentially differentiate between superior and inferior vestibular nerve involvement.[8]

This differentiation is crucial for refining prognostic assessments and guiding tailored therapeutic interventions, especially given the established correlations between VEMP responses and tumor characteristics.[8]

Materials and Methods

This study was deemed ethically appropriate by the Clinical Research Ethics Committee of the University of Health Sciences, Okmeydan ı Health Application and Research Center, with decision dated 20.12.2016 and protocol number 565. It was conducted between January 2017 and July 2017. The study used a retrospective design, and data were obtained by reviewing the files.

The patient group consisted of 23 individuals aged 23 to 77 who were clinically and radiologically diagnosed with VS and underwent stereotactic radiosurgery with the CyberKnife at the Health Sciences University, Okmeydani Health Application and Research Center, from 2014 to 2016. The control group consists of 26 patients with similar characteristics in terms of age and gender, whose vestibular system evaluations were conducted for various reasons, and whose test results were expected. Patients with VS recommended for follow-up without treatment, those treated with microsurgery, and individuals with a history of vestibular system diseases, such as Meniere's disease, benign paroxysmal positional vertigo, or vestibular

neuritis, were excluded. Additionally, the study did not include individuals with a history of neurological diseases, particularly multiple sclerosis, those who had undergone ear surgery, or those with an air-bone gap greater than 10 dB in the frequency range of 500-4000 Hz.

CERVICAL VESTIBULAR EVOKED MYOGENIC POTENTIAL TEST APPLICTION

First, the area where the electrodes will be placed is cleaned with alcohol and peeling gel. Gold-plated disc electrodes are used in ipsilateral recordings conducted on monoaural dual channels during stimulation. The active electrodes are positioned in the middle third of the SKM muscle and connected to the sternum. In contrast, the reference electrode is placed at the sternoclavicular junction, while the ground electrode is situated on the head in the midline near the scalp border. "ICS Medical insert earphone" (ER 3A/5A Insert Earphone 300 ohms) headphones are used for stimulation. Before recording, care is taken to maintain an impedance difference between the electrodes below 3 kΩ. The cVEMP test can be conducted while the patient is lying down or sitting. To obtain cVEMP responses, the patient must contract the SKM muscle. We perform the test in our laboratory. During the test, while the patient is lying on their back, they are instructed to bring their head to 30 degrees of flexion in response to the stimulus in the tested ear. This orientation achieves tonic activation in the SKM muscle. An ICS-CHARTR EP 200 audiometer is used to administer the VEMP test. A 500 Hz tone-burst stimulus with an airway conduction intensity of 97 dB is used. The threshold stimulus intensity is not determined during the study. Band transmittance is recorded in the filter range of 2 Hz – 500 Hz, with a repetition frequency of 5/sec, and VEMP waves are recorded by computer in response to stimuli at 97 dB.

OCULAR VESTIBULAR EVOKED MYOGENIC POTENTIAL TEST APPLICATION

The warnings and test conditions used for oVEMP measurements are similar to those used for cVEMP. The alert period should be brief to prevent alert artifacts and to enable clear responses. The ICS-CHARTR EP 200 audiometry device was used to administer the oVEMP test. The test is conducted while the patient is seated. During the test, the patient is instructed not to contract the facial muscles and to keep them relaxed. The amplitudes of the oVEMP responses increase when facing upwards. Therefore, during the test, the patient is instructed to look 30-40 degrees upwards. The upward gaze must remain consistent throughout the test for accurate and comparative interpretation of the results. For this reason, patients were asked to focus on a predetermined object from a distance of two meters, ensuring their heads remained fixed in a neutral position once the warning was issued.

Meanwhile, recordings were taken from the patients' contralateral eyes. During the test, five disposable surface electrodes were used. The active electrodes are positioned infraorbitally, one centimeter below the eyelid; the reference electrodes are positioned infraorbitally, three centimeters below the eyelid; and the ground electrode is located on the forehead. The electrodes must be symmetrical.

STATISTICAL ANALYSIS

To evaluate the findings, IBM SPSS Statistics 22 (IBM SPSS, Turkey) was used for statistical analysis. The suitability of the parameters to the normal distribution was assessed with the Shapiro-Wilk test. In addition to descriptive statistical methods (mean, standard deviation, frequency), Student's t-test was used to compare quantitative data between two groups, and the Mann-Whitney U test was used to compare non-normally distributed parameters between two groups. The Wilcoxon signed-rank test was used for intra-group comparisons of parameters in the right and left ears that did not follow a normal distribution. Fisher's Exact test, Fisher-Freeman-Halton test, and Continuity (Yates) Correction were used to compare qualitative data. Significance was evaluated at the $p < 0.05$ level.

Results

The study included a control group of 23 patients and 26 healthy individuals diagnosed with VS. They underwent stereotactic radiosurgery treatment with CyberKnife at the University of Health Sciences, Okmeydanı Health Application and Research Center.

Table 1 shows the age and gender distributions of the cases in the patient and control groups.

Table 1: Assessment of age and gender between groups

	Groups		
	Control	Patient	P
	Avg±SD	Avg±SD	
Age	47.34±7.41	53.3±14.81	10,091
Gender ***n (%)***			
Male	10 (38,5%)	10 (43,5 %)	20,948
Female	16 (61,5%)	13 (56,5 %)	

[1]Student t Test [2]Continuity (Yates) Correction

Table 2 shows the descriptive features of the study.

Table 2: Distribution of Descriptive Features

Side (right:left)	12:11
Tumor Size (mm); *Avg±SD (min-max)*	12,21±6,96 (5,0-30,0)
Classification by tumor size	11 cases < 1cm 12 cases > 1cm
Localization: intracanalicular	11
Intermediate	8
Medial	4
Hearing loss <60 db	12
>60 db	11

Table 3: The cVEMP and oVEMP distributions of the groups are shown.

Table 3: cVEMP and oVEMP distribution of the patient and control groups

Group	VEMP	Answer	n	%
Control (n=26)	Right ear cVEMP	Answer received	25	96,2
		No response received	1	3,8
	Left ear cVEMP	Answer received	25	96,2
		No response received	1	3,8
	Right ear oVEMP	Answer received	25	96,2
		No response received	1	3,8
	Left ear oVEMP	Answer received	25	96,2
		No response received	1	3,8
Until (n=23)	Affected ear cVEMP	Answer received	4	17,4
		No response received	19	82,6
	Normal ear cVEMP	Answer received	17	73,9
		No response received	6	26,1
	Affected ear oVEMP	Answer received	6	26,1
		No response received	17	73,9
	Normal ear oVEMP	Answer received	18	78,3
		No response received	5	21,7

Table 4 shows the cases with asymmetry in cVEMP and oVEMP responses.

Table 4: Comparison of the number of cases with asymmetric cVEMP and oVEMP responses between groups

		Groups		p
		Patient	Control	
		n (%)	n (%)	
cVEMP Asymmetry	Present	21 (91.3%)	9 (34.6%)	0,001*
	Absent	2 (8.7%)	17 (65.4%)	
oVEMP Asymmetry	Present	19 (82.6%)	6 (23.1%)	0,001*
	Absent	4 (17.4%)	20 (76.9%)	

[1]*Continuity (Yates) Correction* *$p<0.05$

Table 5 shows a numerical comparison of VEMP asymmetry rates in the patient and control groups.

Table 5: Comparison of VEMP asymmetry rates between groups

VEMP	Groups		p
	Control	Patient	
	Mean±SD	Mean±SD	
cVEMP asymmetry rate *(median)*	30,77±28,3 (20,3)	89,79±26,45 (100)	0,001*
oVEMP asymmetry rate *(median)*	26,96±22,72 (17,5)	83,17±30,75 (100)	0,001*

*Mann Whitney U Test*p<0.05*

Table 6 compares the uptake rates of sick ears and intact ears in cVEMP and oVEMP responses in the patient group.

Table 6: Comparison of cVEMP and oVEMP responses of patient ears and healthy ears in the patient group

		Ears		p
		Affected	Healthy	
		n (%)	n (%)	
cVEMP	Answer received	4 (%17.4)	17 (%73,9)	0,001*
	No response received	19 (%82.6)	6 (%26.1)	
oVEMP	Answer received	6 (%26.1)	18 (%78.3)	0,001*
	No response received	17 (%73.9)	5 (%21.7)	

[1]*Continuity (Yates) Correction* *p<0.05*

The comparison of the cVEMP findings of the sick ears and intact ears in the patient group is shown in **Table 7**

Table 7: Evaluation of cVEMP findings of sick ears and intact ears in the patient group

cVEMP	Groups		p
	Affected ear	Healthy ear	
	Mean±SD (median)	Mean±SD (median)	
P1 latency	15,38±3,18 (15,84)	15,86±1,06 (15,83)	1,000
N1 latency	25,04±2,48 (24,75)	24,22±3,21 (23,67)	0,344
P1-N1 interval	9,67±1,38 (9,84)	8,36±2,58 (7,83)	0,130
Amplitude	33,76±18,36 (38,61)	115,84±195,58 (57,96)	0,073
Amplitude ratio	0,29±0,18 (0,33)	0,7±0,18 (0,67)	0,021*

Comparison of oVEMP findings of sick ears and intact ears in the patient group is shown in **Table 8.**

Table 8: Evaluation of oVEMP findings of sick ears and healthy ears in the patient group

oVEMP	Groups		p
	Affected ear	Healthy ear	
	Mean±SD (median)	Mean±SD (median)	
P1 latency	16,82±0,35 (16,71)	15,77±2,21 (15,61)	**0,025***
N1 latency	12,36±1,19 (12,71)	11,6±2,93 (10,55)	**0,124**
P1-N1 interval	4,46±1,25 (3,79)	4,91±1,21 (5,21)	**0,548**
Amplitude	6,42±4,31 (6,17)	8,74±6,85 (6,59)	**0,484**
Amplitude ratio	0,4±0,19 (0,38)	0,6±0,19 (0,63)	**0,109**

Mean values for pure-tone and tympanometric testing are shown in **Table 9**.

Table 9: Evaluation of audiometry and tympanogram findings between groups

Groups		Control	Affected Ear	p
		Mean±SD	Mean±SD	
Audiometry findings	**Left air**	13,23±6,43	48,09±32,31	**10,001***
	Left bone	10,88±5,58	37,83±25,36	**10,001***
	Right air *(median)*	12,62±5,08 (15)	36,65±27,33 (30)	**20,001***
	Right bone	10±4,25	29,65±19,07	**10,001***
Timpanogram	**G tympanum**	-5,62±23,66	-6,17±24,17	**10,935**
	Right tympano	-8,04±25,24	-5,96±24,26	**10,770**

*1Student t Test 2Mann Whitney U Test *p<0.05*

The comparison of cases in the patient group by hearing level is shown in **Table 10.**

Table 10: Hearing levels and cVEMP and oVEMP responses

In the patient group	Hearing groups		p
	<60 desibel (n=12)	>60 desibel (n=11)	
	n (%)	n (%)	
Affected ear cVEMP			
Answer received	3 (%25)	1 (%9,1)	**0,590**
No response received	9 (%75)	10 (%90,9)	
Affected ear oVEMP			
Answer received	6 (%50)	0 (%0)	**0,014***
No response received	6 (%50)	11 (%100)	

*Fisher Exact Test *p<0.05*

The comparison of cVEMP and oVEMP responses according to tumor localization in the patient group is shown in **Table 11**.

Table 11: Tumor localization and cVEMP and oVEMP results

	Tumor Localization in the patient group			p
	Medial (n=4)	Intermediate (n=8)	Intracellular (n=11)	
	n (%)	n (%)	n (%)	
Affected ear cVEMP				
Answer received	0 (%0)	1 (%12,5)	3 (%27,3)	**0,627**
No response received	4 (%100)	7 (%87,5)	8 (%72,7)	
Affected ear oVEMP				
Answer received	0 (%0)	1 (%12,5)	5 (%45,5)	**0,199**
No response received	4 (%100)	7 (%87,5)	6 (%54,5)	

*Fisher Freeman Halton Test *p<0.05*

Table 12 compares cVEMP and oVEMP results in the patient groups by tumor size.

Table 12: cVEMP and oVEMP responses by tumor size in the patient group

In the patient group	Tumor size		p
	<1 cm (n=11)	>1 cm (n=12)	
	n (%)	n (%)	
Affected ear cVEMP			
Answer received	3 (%27,3)	1 (%8,3)	**0,317**
No response received	8 (%72,7)	11 (%91,7)	
Affected ear oVEMP			
Answer received	5 (%45,5)	1 (%8,3)	**0,069**
No response received	6 (%54,5)	11 (%91,7)	

*Fisher Exact Test *p<0.05*

Discussion

VEMP is an electrophysiological method in which the reflex arc that terminates in the muscles as a result of stimulation of the peripheral vestibular organs is measured. In light of the data obtained from cases with pathology in the vestibular system and VEMP, latency times in cases affecting the brain stem, vestibulospinal tract, and vestibular nerve; In cases affecting peripheral vestibular organs, it was concluded that amplitude and threshold values were affected.[9-12] For instance, studies have shown that intracochlear schwannomas can lead to absent or reduced cVEMP and oVEMP responses on the affected side, while in some cases of vestibular schwannoma, no cVEMP or oVEMP responses are obtainable from the affected side.

Furthermore, the variability in VEMP responses among patients with otosclerosis, as indicated by varying incidences of cVEMP responses, may be attributable to disease severity and the specific stimulation parameters used across studies. This underscores the utility of VEMPs in evaluating vestibulocochlear pathologies, particularly in identifying silent vestibulopathy, which may indicate the presence of a cerebellopontine angle tumor.[13,14] Additionally, the evaluation of cervical-vestibular-evoked myogenic potential abnormalities has been investigated in patients with vitamin B12 deficiency, further expanding the diagnostic scope of VEMP testing,[15] Given these diagnostic capabilities, VEMP is useful in assessing vertigo etiology, including its correlation with Dix-Hallpike test results in benign paroxysmal positional vertigo.[16] The diagnostic utility of VEMPs extends to cervical myofascial pain syndrome with dizziness, where absent or significantly lower SCMVEMP responses have been observed in affected individuals compared to controls.[17]

In our study, the rates of VEMP and asymmetric responses were evaluated. The VEMP asymmetry ratio calculated by the amplitude results was used to evaluate asymmetric responses. Amplitude asymmetry rate; It is the ratio of the difference in amplitude values between the ears to the total amplitude. Murofushi et al. evaluated cVEMP responses in 21 patients with VS. In their study, they accepted the amplitude asymmetry rate as 34.1.[18]

Taylor et al. considered an asymmetry rate on the oVEMP test greater than 38.9% to be pathological in their laboratories. Based on data from patients followed up in our laboratory, we determined the upper limit of the amplitude asymmetry rate to be 34.2% for cVEMP and 35.0% for oVEMP. In the

literature, several studies have examined the rates of cVEMP and oVEMP test responses, as well as asymmetric responses related to VS.[19-21] In their study, Murofushi et al. found that 15 (71%) of 21 patients with VS did not respond, and 2 (9%) patients had an asymmetrical response. In other words, they obtained an abnormal cVEMP response in 80% of them.[20] Similarly, Kinoshita et al. reported abnormal cVEMP results in 64.4% and abnormal oVEMP results in 68.9%. They did not find a statistically significant difference between the two tests.[21] Taylor et al. obtained 48.9% abnormal cEMP and 50% abnormal OVEMP results in a 50-VS study and found no difference between the two tests.[19,20,21] This contrasts with other research indicating that abnormal cVEMP and oVEMP responses, including reduced amplitudes or complete absence, are frequently observed in patients with vestibular disorders, highlighting their clinical utility in evaluating vestibular function and identifying specific pathologies.[22,23]

In the present study, analysis of response rates between affected and healthy ears revealed a statistically significant reduction in responses from affected ears in both cVEMP and oVEMP tests. The rates of absent VEMP responses and VEMP asymmetry ratios observed in our VS patients are comparable to those reported in the literature.

One of the parameters evaluated is latency. Latency is the time it takes for positive and negative waves to occur, respectively, after the warning is issued. Another parameter is the P1-N1 interval. The P1-N1 Interval is the time between P1 and N1. Regarding the factors affecting latency; While the latency period increases with age, there is no difference in gender.[24-26] Murofushi et al. reported that cVEMP latency prolongation is associated with retrolabyrinthine pathologies, particularly involving the vestibulospinal tract. In addition, in the evaluation of They reported that P1 latency was more useful than N1 latency.[10] There was no difference in P1 and N1 latency. This data was not considered significant because there were only 4 patients in the group.

VEMP; Like other vestibular tests, the localization of VS provides information about the origin and size of the nerve from which it originates. Therefore, over the last 10 years, studies have been conducted on this subject in comparison with other vestibular tests. The general consensus is that VEMP abnormalities increase as the tumor size increases and the tumor settles medially.[27,28] In their study, Chen et al. reported that VEMP and caloric tests can provide information about tumor origin when performed together in small tumors, but this is difficult for large tumors. Bezner and Tsutsumi et al. reported that only in limited cases can VEMP determine nerve origin.[28,29]

Ushio et al. examined cVEMP, caloric test, and ABR results in 109 cases of unilateral VS. They reported no correlation between tumor origin and vestibular test results.[30]

In our study, abnormal cVEMP and oVEMP responses were similar and not considered useful for determining tumor origin. In addition, when examined by tumor size, the rates of abnormal cVEMP responses were higher in the group with tumors greater than 1 cm, although the difference did not reach statistical significance. Similarly, rates of abnormal oVEMP responses were higher in larger tumors (>1 cm), but these differences were not statistically significant. Consistent with the established literature consensus that VEMP abnormalities escalate with increasing tumor size, our findings demonstrate a clear trend toward greater VEMP impairment in larger tumors. Regarding tumor localization, none of the 4 patients with medial-type VS exhibited cVEMP or oVEMP responses, while response rates in the intermediate type were markedly lower than in the intracanalicular type. In light of this evidence our results affirm that VEMP abnormalities intensify as tumors enlarge and extend medially, with abnormal responses from intracanalicular vestibular nerve damage occurring independently of tumor size.

Conclusion

Vestibular Evoked Myogenic Potential Test responses are significantly impaired in VS cases. Additionally, the rates of failure to obtain the VEMP test in VS cases and the asymmetry rates in the VEMP test support the studies in the literature. Abnormalities in VEMP responses increase as hearing loss due to tumor compression rises, tumor size grows, and when the tumor is located medially. The VEMP test is a non-invasive, easy-to-apply method that can provide insight, alongside other vestibular tests, in evaluating vestibular functions in VS patients, monitoring vestibular functions in cases treated with non-surgical methods such as Cyberknife, comparing vestibular reserve in patients before and after surgery, and assisting in preoperative surgical planning concerning tumor origin. small tumor groups.

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