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Vestibular-Evoked Myogenic Potential Findings in Patients with Unilateral Idiopathic Sudden Sensorineural Hearing Loss

Tek Taraflı Ani İşitme Kayıplı Hastalarda Vestibüler Uyarılmış Miyojenik Potansiyel Bulguları

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ABSTRACT Objective: We investigated vestibular function in patients with unilateral idiopathic sudden sensorineural hearing loss (ISSNHL) and vertigo, and assessed the relationship between hearing loss grade and cervical vestibular-evoked myogenic potentials (cVEMPs) and ocular VEMP (oVEMPs) findings. **Material and Methods:** The study included 31 patients diagnosed with unilateral ISSNHL and vertigo, and 26 healthy individuals (control group) with VEMP. In all participants, pure tone audiometry was used to assess the hearing threshold, and cVEMP and oVEMP tests were used to assess vestibular system function. The P1/N1 latency, P1-N1 interval and amplitude asymmetry ratio (AAR) were measured in the VEMP test. Additionally, the relationship between the VEMP findings and the degree of hearing loss was assessed. **Results:** We found no significant differences in VEMP parameters (N1 latency, P1-N1 interval, and amplitude) between the affected and control group ears (p>0.05). In contrast, the cVEMP P1 latency and AARs were significantly different between the patient and control groups (p=0.019 and 0.015, respectively). No significant differences were found in VEMP parameters (P1 latency, N1 latency, P1-N1 interval, and amplitude) or AAR in the patients with profound and nonprofound hearing loss in the cVEMP and oVEMP tests (p>0.05). **Conclusions:** Vestibular otolithic dysfunction can be detected using cVEMP and oVEMP in patients with ISSHL and vertigo. The VEMP amplitude asymmetry and VEMP responses have high diagnostic value in patients with ISSNHL with vestibular symptoms. Abnormal cVEMP responses provide more information than oVEMP responses about vestibular otolithic damage in patients with ISSHL. Although the saccule and utricle were affected in ISSNHL, the extent of saccular and utricular damage did not correspond to the amount of hearing loss.

Keywords: VEMP (Vestibular-evoked myogenic potentials); sudden hearing loss; inner ear

ÖZET Amaç: Tek taraflı idiyopatik ani sensorinöral işitme kaybı (ISSNHL) ve vertigo hastalarında vestibüler fonksiyonu araştırdık ve işitme kaybı derecesi ile servikal vestibüler uyarılmış miyojenik potansiyel (cVEMP) ve oküler VEMP (oVEMP) bulguları arasındaki ilişkiyi değerlendirdik. **Gereç ve Yöntemler:** Çalışmaya tek taraflı ISSNHL ve vertigo tanısı konmuş 31 hasta ve VEMP'li 26 sağlıklı birey (kontrol grubu) dahil edildi. Tüm katılımcılarda işitme eşiğini değerlendirmek için saf ses odyometrisi, vestibuler sistem fonksiyonunu değerlendirmek için cVEMP ve oVEMP testleri kullanıldı. VEMP testinde P1/N1 latansı, P1-N1 aralığı, ve Amplitüd asimetrisi oranı (AAR) ölçüldü. Ayrıca VEMP bulguları ile işitme kaybı derecesi arasındaki ilişki değerlendirildi. **Bulgular:** Etkilenen ve kontrol grubu kulakları arasında VEMP parametrelerinde (N1 latans, P1-N1 aralığı ve amplitüd) önemli bir fark bulamadık (p> 0,05). Buna karşılık, cVEMP P1 latansı ve AAR hasta ve kontrol grupları arasında anlamlı olarak farklıydı (sırasıyla p = 0,019 ve 0,015). cVEMP ve oVEMP testlerinde derin ve kanıtlanmamış işitme kaybı olan hastalarda VEMP parametreleri (P1 latansı, N1 latansı, P1-N1 aralığı ve amplütüd) veya AAR'da anlamlı fark bulunmadı (p> 0,05). **Sonuç:** Vestibüler otolitik disfonksiyon ISSHL ve vertigo hastalarında cVEMP ve oVEMP kullanılarak tespit edilebilir. Vestibüler semptomları olan ISSNHL hastalarında VEMP amplitüd asimetrisi ve VEMP yanıtları yüksek tanı değerine sahiptir. Anormal cVEMP yanıtları ISSHL hastalarında vestibüler otolitik hasarla ilgili oVEMP yanıtlarından daha fazla bilgi sağlar. Her ne kadar sakkülve utrikul ISSNHL'de etkilenmiş olsa da, sakküler ve utriküler hasarın derecesi işitme kaybı derece ile korele değildir.

Anahtar Kelimeler: VEMP (Vestibuler uyarılmış miyojenik potansiyel); ani işitme kaybı; iç kulak

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Idiopathic sudden sensorineural hearing loss (ISSNHL) is hearing loss exceeding 30 dB in at least three sequential frequencies in one or both ears within 3 days as assessed by pure-tone audiometry (PTA).[1,2] Of more than 100 etiologies that have been proposed for this disorder, the most prevalent are vascular and viral inflammatory etiologies.[3]

Tinnitus and vertigo are associated with ISSNHL.[4] Vertigo is more common in patients with profound hearing loss and the prognosis is worse in patients with vertigo than in those without vertigo at the onset.[5,6] The vestibular-evoked myogenic potential (VEMP) test is an electrophysiological procedure that measures the reflex arc activated by stimulation of the peripheral vestibular organs and muscles and is a valuable diagnostic tool for various otologic and vestibular diseases.[7,8] Cervical VEMPs (cVEMPs) are used to assess the function of the saccule, one of the two otolith organs and of the inferior vestibular nerve and central connections. The saccule which lies below the utricle, the other otolithic organ has slight sound sensitivity which can be measured. Sound stimulates the saccule and then impulses travel through the vestibular nerve and ganglion to the vestibular nucleus in the brainstem. From there, impulses are sent to the neck muscles via the medial vestibulospinal tract. The integrity of the vestibular system can be assessed by measuring reflex arcs from the extraocular and cervical muscles using ocular VEMP (oVEMP) and cVEMP tests, respectively. cVEMPs measure the vestibulocollic reflex pathway and oVEMPs measure the integrity of the vestibulo-ocular reflex pathway.[7,9] In contrast to cVEMPs which represent an uncrossed inhibitory vestibulospinal response, oVEMPs represent a crossed excitatory vestibulo-ocular reflex. These vestibular function tests are used to differentiate between peripheral vestibular dysfunctions.

Several studies have found otolithic involvement in the cochlear impairment of patients with ISSNHL.[10-12] Iwasaki et al. found that the pathology in patients with ISSNHL and vertigo involved the saccule more frequently than the semicircular canals.[10] Previous histopathological studies have shown that atrophic changes in the vestibular organs are most common in the macula of the saccule in patients with ISSNHL.[11,12] Although various neurophysiological tests have been used to evaluate labyrinthine function and predict the hearing results in patients with ISSNHL, no consensus has been reached. Thus, we investigated vestibular involvement in patients with ISSNHL using cVEMP and oVEMP testing. We investigated vestibular function in patients with unilateral idiopathic sudden sensorineural hearing loss (ISSNHL) and vertigo, and assessed the relationship between hearing loss grade and cVEMPs and oVEMPs findings.

MATERIAL AND METHODS

STUDY DESIGN

The study included the patients who were treated for sudden hearing loss and vertigo at our clinic between January and October of 2017. This retrospective study was approved by the Ethics Committee of our hospital (approval number: 48670771-514.10) (19.12.2017). Informed consent was obtained from each participant.

SUBJECTS

The study included 31 patients who were diagnosed with ISSNHL and complained of vertigo. The diagnoses were made within 3 days of sudden-onset sensorineural hearing loss >30 dB in three consecutive frequencies.[13] All patients received standard treatment with oral steroids and other medications. The exclusion criteria were retrocochlear pathology, a history of malignancy, multiple episodes of ISSNHL and vertigo and age less than 18 years. The findings in the affected ear were compared with those in the contralateral and healthy control group ears.

All patients underwent pre-treatment PTA and cVEMP and oVEMP tests on admission to our clinic. The pure-tone means were calculated by averaging the pure-tone hearing levels at 500, 1000, 2000 and 4000 Hz. The audiograms were classified as profound hearing loss (>90 dB) or nonprofound hearing loss (<90 dB). An ICS-CHARTR EP 200 audiometry device (Otometrics, Taastrup, Denmark) was used for the VEMP tests in which p13 and n23 latencies, the p13-n23 interpeak amplitude and the AAR were measured. The relationship between the hearing loss score and the cVEMP and oVEMP responses were

assessed and compared across all patients with ISSNHL. The upper limit of the AAR was defined as >34.2% for cVEMPs and >35.0% for oVEMPs, or as VEMP asymmetry if no response was obtained in the affected ear.

CVEMP

Gold-plated disk electrodes were used for ipsilateral recording via dual channels from monaural stimulation. The active electrodes were connected by a connecter and placed just below the jugular notch of the sternum, the reference electrode was placed in the middle third of the sternocleidomastoid muscle and the ground electrode was placed on the nasion over the midline of the forehead near the hairline.

The stimuli were delivered via ICS Medical Charter insert earphones (ER 3A/5A, 300 ohms; Schaumburg, IL, USA). Before recording, we ensured that the impedance difference between the electrodes was below 3 kohm. Patients were placed in the supine position and asked to flex their neck 30 degrees by looking at their toes when they heard a sound in the test ear.

A 500 Hz (97 dB) tone-burst stimulus with rarefaction polarity was used to stimulate airway conduction. In tests with transmittance frequencies between 2 and 500 Hz, at a repletion rate of 5/s, the VEMP waves that occurred at 97 dB were recorded on a computer. Two recordings were made to verify the responses. As per the Hanning protocol, the duration of the stimulus was 2–0 loops/cycle with a 25 ms delay per frequency. The interpeak amplitude values of the VEMP responses were calculated from waves obtained with a 95 dB stimulus. The AAR (AAR=100 x [Ar-Al]/[Ar+Al], where Ar is the right ear amplitude and Al is the left ear amplitude), the latencies of the first positive wave (p13) and following a negative wave (n23), the interpeak interval, the amplitudes between the two peak points and the threshold stimulus intensity of the VEMP responses were assessed.

OVEMP

The oVEMP test was performed with the patients in the supine position. During the test, the patients were asked to relax their facial muscles and gaze upward 30-40 degrees. Participants were asked to keep their heads in a neutral position after the stimuli were administered. The active electrode was placed near the infra-orbital ridge, approximately 1 cm below the lower eyelid and the reference electrode was placed approximately 2 cm below the active electrode.

The ground electrode was placed on the nasion over the midline of the forehead near the hairline. The peak points of the first waveform following stimulation were designated as N1 and P1. Latencies, amplitudes, the interpeak intervaland the AAR of the waves were measured.

STATISTICAL ANALYSIS

All statistical tests were conducted using Statistical Package for Social Sciences (SPSS) version 22 (IBM Corp., Armonk, NY, USA). The Shapiro-Wilks test was used to determine whether the parameters were normally distributed. Student's *t*-tests were used for between-group comparisons of the normally distributed parameters, and Mann-Whitney *U* tests were used for between-group comparisons of the non-normally distributed parameters and descriptive statistics (i.e., mean, standard deviation, and frequency).

RESULTS

The study included 57 participants: 31 patients diagnosed with ISSNHL and vertigo at our clinic between January 2017 and October 2017 and 26 healthy control subjects. The participants ranged in age from 18 to 74 years; 24 participants (42.1%) were male and 33 (57.9%) were female. The mean age of the patients was 47.35±15.95 years; that of the control group was 44.65±8.56 years. (Two patients age was older than 60. We take response both of cVEMP and oVEMP). The mean age and sex distribution were not significantly different between the patient and control groups (p>0.05, Table 1).

In the cVEMP test, 83.9% of the responses were positive in the affected and contralateral healthy ears of the patients compared with 96.2% positive responses in the control group. In the oVEMP test, 71% of the responses were positive in the affected ear, 77.4% were positive in the contralateral healthy earand 96.2% of the responses were positive in the control group (Table 2).

TABLE 1: Comparison of age and sex distribution in the patient and control groups.

		Group		
		Patient Mean±SD	Control Mean±SD	p
Age		47.35±15.95	44.65±8.56	[1]**0.420**
Sex				
n (%)				
	Male	14 (45.2%)	10 (38.5%)	[2]0.810
	Female	17 (54.8%)	16 (61.5%)	

[1]Student's t-test, [2]Continuity (Yates) correction, SD, standard deviation.

TABLE 2: Percent of cVEMP and oVEMP responses in the patient and control group ears.

		Group		
	Response	Affected ear (n [%])	Contralateral healthy ear (n [%])	Control group (n [%])
cVEMP	+	26 (83.9%)	26 (83.9%)	50 (96.2%)
	-	5 (16.1%)	5 (16.1%)	2 (3.8%)oVEMP
	+	22 (71.0%)	24 (77.4%)	50 (96.2%)
	-	9 (29.0%)	7 (22.6%)	2 (3.8%)

cVEMP, cervical vestibular-evoked myogenic potential; oVEMP, ocular vestibular-evoked myogenic potential

TABLE 3: Comparison of cVEMP and oVEMP findings in the affected and control group ears.

		Affected ear	Control ear	
		Mean±SD	Mean±SD	p
cVEMP	**P1 latency**	16.93±1.62	16.09±1.33	[1]**0.019***
	N1 latency	26.87±3.67	25.58±2.19	[1]**0.115**
	P1–N1 interval	10.27±2.86	9.49±1.51	[1]**0.212**
	Amplitude	172.38±139.16	151.67±123.38	[1]**0.513**
	AAR (median)	50.43±37.81 (40.1)	26.15±26.47 (20.3)	[2]**0.015***
oVEMP	**P1 latency**	15.92±1.26	15.46±1.14	[1]**0.128**
	N1 latency	10.74±1.47	10.5±1.1	[1]**0.452**
	P1–N1 interval	4.88±1.09	4.99±1	[1]**0.699**
	Amplitude	9.39±6.89	8.38±6.37	[1]**0.548**
	AAR (median)	44.49±40.47 (31.1)	23.50±20.28 (17.5)	[2]**0.216**

[1]Student's t-test, [2]Mann-Whitney U test, * p<0.05, AAR: amplitude asymmetry ratio; cVEMP: cervical vestibular-evoked myogenic potential; oVEMP: ocular vestibular-evoked myogenic potential.

The mean±standard deviation [SD] cVEMP latencies in the affected ear were 16.93±1.62 ms for P1 and 26.87±3.67 ms for N1. The P1 latency and AAR median were significantly different between the patient and control groups (p=0.019 and 0.015, respectively). The N1 latency, P1-N1 interval and amplitude values were not significantly different between the affected and control group ears (p>0.05, Table 3).

The oVEMP test showed no significant differences in VEMP parameters and AAR values between the affected and control group ears (p>0.05, Table 3).

We found no statistically significant differences in VEMP parameters, and AAR values between patients with profound and nonprofound hearing loss (p>0.05; Table 4).

TABLE 4: cVEMP and oVEMP parameters according to degree of hearing loss in the affected ear.

		Affected ear		
		Profound (n=15)	Nonprofound (n=16)	
		Mean±SD	Mean±SD	p
cVEMP	P1 latency	16.74±1.54	17.1±1.73	[1]0.584
	N1 latency	26.45±1.58	27.27±4.93	[1]0.576
	P1–N1 interval	9.71±1.71	10.79±3.62	[1]0.346
	P1–N1 amplitude	169.86±126.98	174.71±154.73	[1]0.933
	AAR (median)	49.8±40.95 (47.3)	51.02±35.97 (37.8)	[2]0.644
oVEMP	P1 latency	16.05±1.29	15.82±1.29	[1]0.682
	N1 latency	10.91±1.05	10.6±1.78	[1]0.632
	N1–P1 interval	5.14±0.84	4.67±1.26	[1]0.320
	N1–P1 amplitude	10.0±7.25	8.88±6.85	[1]0.714
	AAR (median)	48.11±39.67 (32.4)	41.09±42.2 (31.1)	[2]0.410

[1]Student's t-test, [2]Mann-Whitney U test, SD: standard deviation; cVEMP: cervical vestibular-evoked myogenic potential; oVEMP: ocular vestibular-evoked myogenic potential.

DISCUSSION

Vestibular symptoms were reported in 28–57% of the patients with ISSNH.[13] Given that vertigo is comorbid with ISSNHL and has prognostic value, several studies have investigated vestibular function in patients with sudden sensorineural hearing loss. Recent findings indicate that sudden sensorineural hearing loss can affect the vestibular otolith organs and that otolith dysfunction can be detected using the objective VEMP test.[14-16] We used cVEMP and oVEMP recordings to assess vestibular function in patients with ISSNHL who had vertigo and investigated the effect of hearing loss severity on vestibular function. Given that previous histopathological and clinical studies have shown that otolith organs are affected more than the semicircular canals, we used oVEMPs to assess utricular and superior nerve function and cVEMPs to assess saccular and inferior vestibular nerve function.[17,18]

The VEMP test is useful for assessing the integrity of the sacculo-collic reflex pathway.[19,20] cVEMP and oVEMP amplitudes are quantitative measures of otolith function. In general, the clinical interpretation of a VEMP test includes p13 and n23 latencies, the peak-to-peak p13–n23 amplitude and the AAR.[21] We used the VEMP asymmetry ratio which was calculated from the amplitude to evaluate asymmetric responses. We used the AAR to compare vestibular function in the right and left ears of patients. Murofushi et al. defined an AAR >34.1% in the cVEMP test as abnormal, while Taylor et al. defined an AAR >38.9% in the oVEMP test as abnormal.[22,23] We designated the upper limits of AAR as 34.2% for cVEMPs and 35.0% for oVEMPs using data obtained from our patients. We found that in the affected ear, the cVEMP AAR was 50.43±37.81 and the oVEMP AAR was 44.49±40.47. Moreover, the cVEMP and oVEMP AARs were significantly higher in the affected ear group than in the normal ear control group.

The findings of the few studies that have investigated the diagnostic usefulness of VEMP for ISSNHL are inconsistent. The percentage of positive (decreased or increased) and absent VEMPs differs widely among previous studies.[6,10,14-16,24] Hong et al. found an abnormal cVEMP response in patients with ISSNHL without vertigo, and they found subclinical involvement, particularly in the vestibular saccule.[24] Iwasaki et al. reported that click-VEMPs were absent on the affected side in 77% of the patients with ISSNHL and vertigo.[10] Fujimoto et al. reported that more cVEMP than oVEMP responses were abnormal.[14] You et al. reported abnormality rates of 47% in the cVEMP test and 48% in the oVEMP test.[16] Zhang et al. found that oVEMP and cVEMP responses were observed in 40.0% and 62.5% of ears, respectively.[15] From a total of 31 affected ears, we obtained cVEMP responses in 5 (16.1%) ears and oVEMP responses in 9 (29.0%) ears. Therefore, the

abnormal VEMP response rates were 54.8% in the cVEMP test and 41.9% in the oVEMP, consistent with previous findings. Similarly to the findings of Fujimoto et al., we detected more abnormal cVEMP responses than abnormal oVEMP responses.[14]

The additional VEMP parameters examined were threshold, P1 latency, N1 latency, P1–N1 interval and amplitude. Zhang et al. measured cVEMP and oVEMP parameters in patients with ISSNHL and controls and found no statistically significant differences among the affected ear, contralateral ear and control ears in either cVEMP or oVEMP parameters.[15] Similarly, we found no differences among VEMP parameters with the exception of the prolonged P1 latency in the cVEMP test.

Previous investigations of the relationship between hearing impairment grade and VEMP have yielded inconsistent results. Hong et al. reported that patients with a hearing impairment >90 dB had an abnormal VEMP rate of 47.1% and that saccular damage was more frequent in patients with severe hearing impairment (≥90 dB).[24] Wu et al. detected normal biphasic VEMP responses in the affected ears of patients with ISSHL but found no correlation between hearing level and VEMPs.[25] Ogawa et al. investigated the correlation between cVEMP and grade of hearing and found no significant correlation between the initial hearing level and cVEMPs in 57 patients with sudden sensorineural hearing loss.[26] Similarly, Niu et al. found no association between hearing levels and abnormal or normal cVEMP and oVEMP responses.[27] We found no significant differences in cVEMP and oVEMP responses or parameters between patients with profound and nonprofound hearing loss ($p>0.05$). No relationship was found between degree of hearing loss and VEMP parameters. Our findings indicate that hearing loss is not related to saccular or utricular function.

The missing points of our study are the low number of patients and absence of the relationship between VEMP responses and prognosis.

CONCLUSION

cVEMPs and oVEMPs can detect vestibular otolith dysfunction in patients with ISSNHL and vertigo. Abnormal cVEMP responses provide more information about vestibular otolithic damage in patients with ISSNHL than do oVEMP responses. Although the saccule and utricle were affected in the patients, the extent of saccular and utricular damage did not correspond to the degree of hearing loss.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Güler Berkiten;* ***Design:*** *Belgin Tutar, Muhammed Enis Ekincioğlu;* ***Control/Supervision:*** *Ziya Saltürk;* ***Data Collection and/or Processing:*** *Tolgar Lütfi Kumral;* ***Analysis and/or Interpretation:*** *Yavuz Uyar;* ***Literature Review:*** *Ömür Biltekin Tuna;* ***Writing the Article:*** *Güler Berkiten;* ***Critical Review:*** *Yavuz Uyar.*

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