

Peripheral and central vestibular system findings in Meniere's disease

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ABSTRACT

Aim: Meniere's Disease (MD) is a chronic disease that is characterized by intermittent episodes of tinnitus, vertigo, and progressive-fluctuating sensorineural hearing loss together with aural fullness. The aim of this study is to evaluate Meniere's disease patients with vestibular test battery as Videonystagmography (VNG), Vestibular Evoked Myogenic Potentials (VEMPs) and Video Head Impulse Test (V-HIT) to assess peripheral and central vestibular systems.

Methods: 16 bilateral, 17 unilateral patients suffering from MD (mean age, 40.90 years, range, 23 to 66 years; 20 women and 13 men) comprised the study group, and 39 healthy (mean age, 38.10 years, range from 21 to 60 years; 22 women and 17 men) volunteers formed control group. Evaluation of peripheral and central vestibular systems changes with oculomotor tests, caloric test, C-VEMPs, O-VEMPs, and the evaluation of the vestibular ocular reflex (VOR) using the V-HIT.

Result: Twenty-six ears out of the forty-nine ears that were affected by Meniere's disease were diagnosed as otolith or ampullary dysfunction. As to O-VEMPs testing, N1 and P1 waves could not be obtained from thirty of the forty-nine ears affected by Meniere's disease. As for obtained N1 and P1 waves, prolonged N1 and P1 wave latencies, and reduced amplitude was observed in Meniere's group. P1 and N1 waves were not observed in 5 bilateral and 2 unilateral Meniere's patients (12 ears out of 49 affected ears) in C-VEMPs recordings (23.9%). In Meniere's patients' group, 44.9% of the velocity gain values were obtained in the pathologic borders of v-HIT. In addition to lower velocity gain, higher ratios of asymmetry were obtained from the ears affected with Meniere's disease.

Conclusion: According to these results, it can be concluded that Meniere's disease significantly affects the peripheral vestibular system but the functions of the central vestibular system were not affected.

Keywords: Meniere's disease, VEMPs, V-HIT, central, vestibular.

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INTRODUCTION

Prosper Meniere first described Meniere's disease¹ (MD) in 1861. Meniere's disease is a chronic disease characterized by intermittent episodes of tinnitus, vertigo, and progressive-fluctuating sensorineural hearing loss together with an aural fullness^{2,3}. The diagnosis of MD is primarily clinical and can be based on criteria published by the American Academy of Otolaryngology and Head and Neck Surgery (AAO-HNS)⁴. Patients are graded as definite, probable, or possible, based on the number of clinical criteria they fulfill, with the diagnosis of "certain" Meniere's disease reserved only for cases with histopathological confirmation. Endolymphatic hydrops is the primary pathological entity seen in MD⁵. Ocular vestibular evoked myogenic potentials (O-VEMPs) are short-latency myogenic potentials which can be elicited in response to vestibular stimulation, e.g. by Air Conducted Sound (ACS) or Bone-Conducted Vibration (BCV)⁶. Otolithic afferent neurons trigger reflexive electromyography activity of the extra ocular muscles which can be recorded beneath the eye contralateral to the stimulated ear by use of surface electrodes. The pathway from the human otolith organs to the extra ocular muscles reflects the Vestibulo-Ocular Reflex (VOR)^{7,8}. The loud acoustic stimulation of the vestibular apparatus provokes short latency reflexes in the anterior neck muscles. As it is a Vestibular Evoked Myogenic Potentials (VEMPs) that are recorded from the tonically contracted cervical muscles, it gains its name: Cervical Vestibular Evoked Myogenic Potentials (C-VEMPs)^{9,10}. The C-VEMPs is thought to be assessing the descending vestibular pathway as an ipsilateral sacculo-collic reflex. This reflex is responsible for keeping right stance by information gained from saccular monitoring of head positions and movements¹¹. The video head impulse test (v-HIT) was proposed to indicate the status of the VOR at high frequencies (5-7 Hz). It relies on direct observation of the eyes whilst rapid short duration impulses are applied to the subject's head. The presence of overt saccades is an indirect indication of peripheral abnormality in the canal being stimulated. The v-HIT tests the VOR at higher frequencies than the caloric test¹². Caloric testing is the most widely used objective test for peripheral vestibular disorder in clinic. However, it is known that the caloric test is limited in how much of the vestibular system it tests: the stimulation primarily tests only the lateral semicircular canal at very low frequencies (around 0.002–0.004 Hz)¹³. The advent of the C-VEMPs, of the O-VEMPs and of the v-HIT has provided new diagnostic tools to assess an impairment of the otolith organs and semicircular canals. Their combined use may allow a more precise differentiation of the vestibular receptor involvement in different vestibular dysfunctions¹⁴. Presence of horizontal or rotatory nystagmus on Dix-Hallpike test is evaluated as posterior canal BPPV¹⁵. Down Beat (DB) rotatory nystagmus is evaluated as the BPPV of the anterior canal

on the same test¹⁶. BPPV of horizontal canal is evaluated as canalolithiasis or cupulolithiasis with the use of head roll test¹⁷. Thus the aim of this controlled cross sectional study was to evaluate changes of peripheral and central vestibular systems in the Meniere's disease patients using vestibular test battery such as VNG, VEMP and V-HIT.

MATERIALS AND METHODS

The study took place in the clinic of audiology and speech disorders of our tertiary academic medical center. After Ear, Nose and Throat Examination (ENT), Pure Tone Audiometry (PTA), immittance examination, Otoacoustic Emission (OAE), O-VEMPs, C-VEMPs, Videonystagmography (VNG), bitemal caloric test with air stimuli and v-HIT tests were performed on the patients. Ethics of this research have been approved by our institutional "Ethics committee for clinical research" with no 07 date of 28 May 2015. 33 patients clinically diagnosed with Meniere's disease (mean age, 40.90 years, range from 23 to 66 years; 20 women and 13 men) and 39 control group without any clinical entity of Meniere's disease or other vertiginous diseases (mean age, 38.10 years, range from 21 to 60 years; 22 women and 17 men) were included on study. Meniere's disease has been diagnosed as "certain Meniere" according to the criteria that were set by American Academy of Otolaryngology and Head and Neck Surgery (AAO-HNS) in 1995. Sixteen of the patients had bilateral, and 17 of the patients had unilateral Meniere's disease. In this study, we have selected participants according criteria that were set by AAO-HNS.

Recording of cervical and ocular VEMPs

All VEMP recordings were performed with subjects in supine position with the head rest elevated by 30 degrees; ("Eclipse" System, Interacoustics, Denmark), was performed by means of insert ear phone. Air-conducted sound (ACS) C-VEMPs were recorded at 500 Hz, 100 dBnHL, with a 7 msec tone burst stimuli. ACS O-VEMPs measurements were performed from the contralateral eye. The O-VEMPs were recorded with eyes open and a maximal gaze upward. For recording of ACS O-VEMPs, tone bursts (4/sec) at 500 Hz were applied with 100 dBnHL.

Video Nystagmography (VNG)

VNG tests include nystagmus with and without vision, saccade (velocity, accuracy, and latency), pursuit tracking (gain, asymmetry) and optokinetic (gain) oculomotor tests. In the saccade test, values of velocity 415 deg/sec, accuracy between 77-137%, and latency up to 260 msec have been considered normal.

Caloric testing

Air caloric test was used. Eye movements were recorded by means of a video-based system (CHARTR VNG, ICS

Medical, Schaumburg, IL, USA). Each ear was irrigated alternately with a constant flow of air at temperatures of 50°C and 24°C, and for a constant period of time (60 sec). In addition, air pressure has been fixated to 8 bar. The maximum Slow Phase Velocity (SPV) of nystagmus was calculated following each irrigation and Jongkees's formula was used to determine Canal Paresis (CP). It was considered abnormal if CP was $\geq 25\%$. A positive value means that CP is on the Meniere's side. Total eye speed of >20 deg/sec. or over have been evaluated as normal. Binocular goggles were checked for light 90 sec. after signaling for suppression with fixation. Results were evaluated as normal if they contained suppression that is 50% or over or a fixation index of 0.3 or better¹⁸.

Video Head Impulse Testing (v-HIT)

All subjects underwent v-HIT testing using the ICS Impulse system (GN Otometrics, Denmark). The goggles have a built-in video camera which records real time eye movements, a motion sensor that measures head movement, and a laser light for calibration. Calibration is performed first to ensure accurate recording. The patient sits straight upright one meter away from a fixed target. The patient is instructed to stare at the fixed target regardless of head movements in any direction. 20 head thrusts are administered in the horizontal, LARP (left anterior, right posterior), and RALP (right anterior, left posterior) planes. Tracings of head and eye velocity are displayed simultaneously on the screen for each direction in each canal plane, resulting in tracings for each of the 6 individual semicircular canals. Corrective saccades are identified on the tracing as a delayed eye movement occurring during (covert saccade) or after (overt saccade) the head movement. The software calculates the VOR gain for each semicircular canal as the ratio of peak slow phase eye velocity to peak head velocity.

Positional tests

All 33 patients underwent the Dix-Hallpike maneuver and supine head-roll test. The Dix-Hallpike maneuver was considered positive for posterior and anterior SCC BPPV when vertigo was provoked. The supine roll test was considered positive for horizontal SCC BPPV when intense vertigo was provoked.

Statistical analysis

SPSS (Statistical package for Social Science) for Windows 20.0 software was used for statistical analysis. For the evaluation of the continuous variables, we used Student's t-test for parametric data and the Mann-Whitney U test for nonparametric data; the categorical variables were analyzed with the chi-square test. Pearson correlation coefficient was used for comparing groups with normal range of distribution. Data were expressed as mean \pm standard deviation. A value of $p < 0.05$ was accepted as significant.

RESULTS

In this study v-HIT, O-VEMPs, C-VEMPs, VNG and air caloric tests were done to compare the results of 49 ears with MD, 78 ears from healthy individuals. Of the Meniere's patients; 16 were affected bilaterally, 10 of them were affected on the right ear and 7 of them got affected from their left ear. Spontaneous nystagmus was present in 5 of the patients. As a result of Dix-Hallpike test, BPPV was present on 23 ears that were affected by Meniere's disease (2 anterior, 21 posterior). As for the head roll test, geotropic nystagmus was present on 3 ears (3 horizontal BPPV). Oculomotor tests (saccade, pursuit tracking, optokinetic) and suppression of fixation in air caloric tests were used for evaluating functions of central vestibular system. No significant statistical differences in oculomotor and suppression with fixation values were found between patients with Meniere's disease and healthy individuals ($p > 0.05$). Suppression with fixation on the Meniere's group was achieved over 50%. No meaningful statistical difference was found between the average values of velocity 415 deg/sec, accuracy between 77-137 and latency 260 msec obtained from the saccade test on healthy individuals as well as patients with Meniere's disease ($p > 0.05$). Results obtained from the pursuit tracking test for 0.1 and 0.2 Hz groups velocity gain values were in normal range, but abnormal results were obtained for 0.4 Hz group. No statistically significant results were obtained from optokinetic test as the results obtained were in the normal range ($p > 0.05$). Velocity gain values obtained from patients with MD and healthy groups for anterior, lateral and posterior SSC were shown in Table 1. In Meniere's patients' group, 44.9% of the velocity gain values were obtained on the pathologic border. The comparison of the results was made on anterior, lateral, and posterior canals in the velocity gain values obtained from v-HIT test ($p < 0.05$) (Table 2). Statistically significant higher asymmetric ratios were obtained from the ear affected by Meniere's disease (Table 3). P1 and N1 waves were not observed in 5 bilateral and 2 unilateral Meniere's patients totaling up to 12 effected ears in C-VEMPs test evaluation (24%). Prolonged P1 and N1 wave latencies, as well as increase in amplitude were observed in Meniere's disease group (Table 4). In O-VEMPs test evaluation, N1 and P1 waves were not observed in 30 affected ears of which 10 bilateral and 10 unilateral Meniere's patients. Prolonged N1 and P1 wave latencies and reduced amplitudes were observed in Meniere's group (Table 5). In 17 of the ears affected by Meniere's disease, the N1 and P1 wave values were obtained by C-VEMPs test as they could not be obtained via O-VEMPs test. However, in one of the patients, N1 and P1 waves were observed in O-VEMPs test but not in C-VEMPs test.

Table 1: v-HIT velocity gain values of the healthy and Meniere's groups (Results include unaffected ears of the patients with Meniere's disease Healthy Group's n=95 ears; Meniere Group's n=49 ears).

	Anterior				Lateral				Posterior			
	Min.	Max.	Mean	SD	Min.	Max.	Mean	SD	Min.	Max.	Mean	SD
Healthy Group	0.7	1.32	1.06	0.09	0.64	1.26	1	0.11	0.63	1.43	1.03	0.15
Meniere Group	0.4	1.49	0.92	0.21	0.19	1.27	0.92	0.18	0.45	1.22	0.91	0.19
p			p<0.05			p<0.05					p<0.05	

Table 2: Average v-HIT velocity gain values of the healthy individuals and Meniere's patients (Evaluation of the unaffected ears from the Meniere's group in the same group).

	Anterior (mean-SD)	Lateral (mean-SD)	Posterior (mean-SD)
Healthy Individuals (n=78 ears)	1,01 ± 0,11	1,02 ± 0,10	1,03 ± 0,07
Meniere's Patients (n=66 ears)	0,93 ± 0,09	0,92 ± 0,07	0,93 ± 1,02
p	p<0,05	p<0,05	p<0,05

Table 3: v-HIT asymmetry comparison of healthy individuals and the Meniere's disease group.

	Anterior	Lateral	Posterior
Asymmetry Ratios of Meniere's Patients	17.04 ± 15.21	13.25 ± 18.24	25.60 ± 11.06
Asymmetry Ratios of Healthy Individuals	10.13 ± 8.23	9.70 ± 11.56	9.13 ± 11.76
p	p<0,05	p<0,05	p<0,05

Table 4: Evaluation of C-VEMPs using 500 Hz tone burst stimuli.

	Meniere's Group (Mean ± SD) (n=37)	Healthy Individuals (Mean ± SD) (n=78)	p
P1 Latency Values (msec)	16.78 ± 3.22	13.40 ± 2.70	p<0.05
N1 Latency Values (msec)	25.25 ± 3.72	22.10 ± 2.90	p<0.05
P1 Amplitude Values (µV)	35.61 ± 12.11	31.20 ± 11.80	p<0.05
N1 Amplitude Values (µV)	44.73 ± 10.26	38.00 ± 22.40	p<0.05

Table 5 : O-VEMPs evaluation using 500 Hz tone burst stimuli.

	Meniere's Group (Mean ± SD) (n=19)	Healthy Individuals (Mean ± SD) (n=78)	p
N1 Latency Values (msec)	12.84 ± 2.12	10.68 ± 1.49	p<0.05
P1 Latency Values (msec)	17.59 ± 2.56	15.51 ± 1.90	p<0.05
N1 Amplitude Values (µV)	3.13 ± 1.72	4.19 ± 0.97	p<0.05
P1 Amplitude Values (µV)	3.22 ± 7.26	4.10 ± 1.07	p<0.05

DISCUSSION

Pathological events take place in the ear that is affiliated with Meniere's disease. Central vestibular system is involved in Meniere's disease to suppress the symptoms; with that said, its situation, when the disease is inactive, deserves investigating. Amount of literature using vestibular test battery is low, as many of the existing studies have been done using O-VEMPs, C-VEMPs, V-HIT or caloric test. Our caloric test results have shown that the suppression with fixation values were 50% or over and values obtained from oculomotor tests (saccade, pursuit tracking and optokinetic tests) were normal, thus it is thought that a compensation system came into play and the central system was not affected in the ears that were affected by Meniere's disease. Meaningful differences were observed in V-HIT test velocity gain values of the ears that were affected by Meniere's disease when compared to healthy ears. In relation to high percentage of asymmetry, the semicircular canals are also affected

by Meniere's disease according to V-HIT test results. Acquired asymmetry percentages on healthy individuals are 10% in average. These results can also be used to evaluate Meniere or other vestibular pathologies. It have evaluated horizontal VOR (hVOR) on normal individuals and found out the mean gain to be 0.96 ± 0.08^{19} . However, in our study we found out the average to be 1.00 ± 0.11 . 54% of Meniere's patients obtained abnormal results, while in our study it was 44.9%. Resemblance of abnormal results obtained from Meniere's patients shows the similarity between these two studies. Acknowledged that 22 of the patients, fit AAO-HNS criteria, had V-HIT responses within the normal range²⁰. It was previously noted in existing literature v-HIT test results are between 27-55% in Meniere's patients^{21,22}. Similarly, abnormal values obtained from the study that was also done by 37% from v-HIT tests. It was observed that 11% of the ears affected by the Meniere's disease contained covert saccades. Covert saccades could arise from variety of

vestibular disorders. We have observed 10% covert saccades and approximately 1% overt saccades in our study reported a study where they show a decreased return from v-HIT test and VOR when their aim was to create an easier way for the brain to compensate by implementing intratympanic gentamicin that is used in Meniere's patients to create peripheral vestibular system hypofunction. Short term control of vertigo attacks were observed from changes in horizontal SSC one month after treatment. It is emphasized that changes in asymmetrical gains and decrease in amount of gains will aid in the treatment and clinical advances with the help of future research²³. Saccular function could be evaluated with C-VEMPs test. Abnormal results have been obtained in vestibular test from the ears that were affected by Meniere's. On the contrary, Waele and colleagues were not able to find significant differences between Meniere's and control group²⁴. Identified 3 cases with endolymphatic hydrops of increased C-VEMPs (high amplitude and asymmetry on the suspected ear ratio >0.36)²⁵. Our study was done on C-VEMPs records that were taken in between attacks. Despite precautions, C-VEMPs records were not obtained from 12 of the 49 affected ears (24%). Under these circumstances, it could be questioned that deep and permanent saccular damage could have been present in the 24% of the affected ears. Different studies have shown that it is not possible to obtain C-VEMPs from 34%-55% from the ears that are affected from Meniere's disease and emphasized that this could be in relation to low frequency hearing loss^{26,27} have stated that they were not able to obtain C-VEMPs from 13% of the ears that are affected with Meniere's disease in their one-sided study²⁸. We were not able to obtain a response from 24% of the ears that were affected in our study. Few studies have reported cases where if the bilateral C-VEMPs are received, the side with low amplitude does not need to be affected and that the amplitude can even be increased due to hydrops⁸ Welgampola ve Colebatch have stated that increase of saccule pressure in the early stages of Meniere's may increase responses; however, response may not be received in the late stages of Meniere's as a result of saccule dilation and sensorial epithelium damage²⁷. Although we have not done any tests in the attack stages, observation of changes in C-VEMPs amplitude and latency could be identified as late stage sensorial effects of hydrops²⁸ have done a study where they compared a group that they received VEMP response composed of 33 affected ears to a control group using P1 and N1 wave latency and stated that they have not found any significant differences²⁹ in Observations of states that prolongation of P1 and N1 wave latencies only occurs when the brainstem is motionless²⁷. Even if the brain stem remains motionless, the responses we have received after the attack show that prolongation of the latencies could be due to long term neurosensorial effects of hydrops. Normal results obtained from oculomotor tests show us

that there are no chronic effects on the arc of VOR but there may be neurosensorial effects on the vestibulospinal arc due to changes in VEMP have stated that VEMP responses are effective in identifying Meniere's syndrome however latency measures are not useful as they change with age²⁶ have acknowledged that N1 latency is more trustable in VEMP test³⁰ have done a study on 134 patients and their results show clear prolongation of latencies in cases with Meniere's syndrome. They stated that P1 wave latencies give more meaningful results as prolongation was particularly noticed on P1 waves according to VEMP responses from lesions of brain stem³¹ stated that 30% of the patients with Meniere's disease have prolonged wave latencies and this prolongation is especially more pronounced at P1 latency wave³² Prolongation of latencies in Meniere's disease is beneficial for the retrocochlear pathologies, while decrease in amplitude is seen as a loss of function is peripheric vestibular system. Although our study shows meaningful differences between latency waves, results from oculomotor test show no evidence of retrocochlear pathology. In addition, fixation and suppression over 50% in caloric testing show no effect on functions of central vestibular system. Our results indicate that prolongation of wave latencies that were obtained from ears affected by Meniere's disease could be a result of peripheric vestibular pathologies and do not always need to show evidence of retrocochlear pathology or brain stem lesion. O-VEMPs are tests that evaluate utricular functions have done O-VEMPs test on 22 Meniere's patients where 2 of them received abnormal results and 20 of them received normal results according to their data found that the asymmetry percentages on O-VEMPs test is 19.0 ± 14.6 . 8 of the patients have received abnormal results from the C-VEMPs test. O-VEMPs responses indicate that out of 8 patients, 1 of them responded abnormal and the remaining 7 responded normal³³. Endolymphatic and saccular hydrops develop in early stages of Meniere's disease, and utricular hydrops develop in the late period³³ acknowledged that O-VEMPs get affected in late stage of Meniere's disease. We were not able to obtain O-VEMPs responses from 30 (61%) of the 49 affected ears. Utricular functions of the patients who have been identified with Meniere's disease have been affected according to the results. Observed changes in latency and amplitude support these results. Thus, the results show that Meniere's disease does affect the utricular and saccular functions of the peripheric system as well as unfavorably affecting the angular acceleration³⁴. Meniere's disease causes the otoconias found in otolith organs to be free which sets up all the SSCs required for BPPV formation. 26 ears out of the 49 ears that are affected with Meniere's disease have developed BPPV in our study. Out of the 26, the 2 are in anterior, 3 in horizontal and 21 is at the posterior canal. BPPV may not have been noticed in participating individuals due to chronic Meniere's disease made a retrospective study composed

of 345 patients who were identified with BPPV where 29 of them were identified with Meniere disease in which 22 of them are located in posterior and 7 of them are located in horizontal canals. In this study spontaneous nystagmus were seen in 4 patients along with Meniere's and BPPV³. In addition to this research, other studies have also shown Meniere's and BPPV synergy^{35,36}.

CONCLUSION

We have evaluated central vestibular and peripheral system on the patients who were identified with Meniere's according to AAO-HNS unilateral or bilateral criteria. We have analyzed how vestibular test battery with otolith organs, semicircular canals and central vestibular system function were affected. It is now proven that Meniere's disease significantly affects the function of the peripheral system and all the test results have proven this abnormality. It has also been concluded that this disease does not affect the central vestibular system in the passive stages. It is thought again that the compensation mechanism steps in for the central vestibular system in these stages. Effects on the central vestibular system could only be determined by doing these tests on the patient when the disease is active and after.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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