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### RESEARCH ARTICLE

#### VIDEO HEAD IMPULSE TEST AND CERVICAL VESTIBULAR EVOKED MYOGENIC POTENTIALS IN PATIENTS WITH MENIÈRE'S DISEASE

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#### Abstract

Meniere's disease is a labyrinthine disease that usually presents with episodes of vertigo associated with sensorineural hearing loss, tinnitus and aural fullness. There is no specific Vestibular function test objectively used for diagnosis of the disease.

**Objective:** Here, we compare findings of caloric test, cervical vestibular evoked myogenic potentials (cVEMP) and video-head-impulse test (vHIT) in patients with Meniere's disease to assess which one is more sensitive test for diagnosis of Meniere's disease.

**Methods:** This study was carried out on two groups of subjects including 20 adult subjects with Meniere's disease and 20 normal subjects free from any vestibular symptoms. Results: the most sensitive test was cVEMP (84.6%) followed by vHIT (75%) and then the caloric test (50%). Conclusion: The cVEMP test is the most sensitive test for diagnosing Meniere's disease, We also found that the presence of catch-up saccades due to abnormal VOR reflex is an important sign that greatly aids the diagnosis.

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#### Introduction:-

Meniere's disease (MD) is a labyrinthine disorder that is characterized by episodes of vertigo, ear fullness, tinnitus, and fluctuating sensorineural hearing loss. Endolymphatic hydrops (EH) is the accepted pathophysiological mechanism of MD<sup>(1)</sup>.

EH is a disorder characterized by endolymph accumulation in the cochlea and vestibular organs<sup>(2)</sup> and is revealed to be a frequent finding in histopathological and imaging studies of the inner ear of MD patients<sup>(3)</sup>.

Bárány Society classified MD into definite or probable. definite MD characterized by two or more spontaneous attacks of vertigo, each lasting from 20 min to 12 h; mild to moderate sensorineural hearing loss is proved; aural symptoms (hearing, tinnitus, and fullness) in the affected ear; and exclusion of other vestibular disorders that explain the sy had two or more episodes of vertigo or loss of balance, each lasting from 20 min to 24 h; floating aural symptoms (hearing, tinnitus, or fullness) in that ear; and exclusion of other vestibular disorders that explain the symptoms<sup>(4)</sup>.

As MD occurs in attacks it comprises two phases, either ictal (during MD attack) or outside the ictal. It is documented that the ictal phase could be subcategorized into three phases: (1) irritative, (2) parietic, and (3)

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recovery. The irritative and recovery phases are characterized by spontaneous nystagmus that beats toward the affected ear as opposed to the parietic phase that is characterized by a nystagmus beating toward the unaffected ear<sup>(5)</sup>.

As the vestibulo-ocular reflex (VOR) is affected by MD so examination of VOR is a main issue in diagnosis of MD. VOR can be examined using different methods, such as vHIT and caloric test. vHIT is known to evaluate VOR at frequencies between 5 and 7Hz<sup>(6&7)</sup> and caloric between 0.003 and 0.008Hz<sup>(8)</sup>. Many studies tried to understand how MD influences vHIT results. However, studies are sometimes contradictory as some found reduced VOR results, whereas others found enhanced VOR results. Also, findings between vHIT and caloric test were contradictory to each other in spite of both assessing horizontal canal function.

An interaction between duration of the disease and moment of the evaluation (ictal phase or outside the ictal phase) suggested by previous literature. Indeed, Maire and Van Melle<sup>(9)</sup> opposite results during the ictal phase. While early MD revealed enhanced VOR, late MD showed reduced VOR gain. This may explain differences with van Esch et al.'s<sup>(10)</sup> study that assessed participants between MD attacks (outside the ictal phase).the cervical Vestibular Evoked Myogenic Potential (cVEMP) is one of the more frequently used tests in diagnosis of MD because of the presence of hydrops in the saccular region.cVEMPrepresents an inhibitory biphasic response in the ipsilateral sternocleidomastoid muscle after loud sound stimulation of the sacculae, which can be recorded by surface electrodes.<sup>(11&12)</sup>

The diagnosis of MD can be difficult, especially in cases where vestibular symptoms are present in isolation (vestibular MD)<sup>(13)</sup>

**Objective:-**

In our study, we compare findings of the caloric test, the c VEMP and the video-head-impulse test in patients with Meniere's disease to assess which test is the most sensitive for diagnosis.

**Methodology: -**

This is a case- control study that was conducted in the Audio-vestibular medicine department of the Hearing and Speech Institute in Egypt. The study included 20 adult patients (12 males and 8 females) who have been diagnosed with definite MD (cases) and 20 comparable adults (9 males and 11females) asymptomatic of any vestibular symptoms (controls).

Informed written consent was obtained from all the subjects prior to conducting the study.

All subjects enrolled in this study were subjected to the following:full history taking that confirmed definite MD in cases only who are of different stages and duration of MD attending to our vestibular clinic seeking for medical advice while control group were selected from relatives of the patients attending our outpatient vestibular clinic who are asymptomatic of any vestibular complaint, all of study groups underwent to full audiological evaluation in the form of pure tone audiometry in form of air conduction audiometry at frequency range (250Hz -8000 Hz) and bone conduction audiometry in frequency range( 500Hz -8000Hz),also speech audiometry was performed. Audiological evaluation was done by using Two Channel Audiometer (Interacoustics, model AC40) Denmark, Acoustic Immittancemetry using Middle ear analyzer (Interacoustics model Az26) Denmark.

Vestibular assessment performed using the caloric test, cVEMP, and, also, vHIT test using Eyeseecam video headimpulse testing (Interacoustics)

As regards to the caloric test, slow-phase eye movements were recorded using SYNAPSYS SA; VISIO USB, France. Digital video image technology Eye movements were recorded while external auditory canals were alternately irrigated with warm (approx. 43.5° C) water for 40 seconds, followed by a recovery period, then cool (approx. 30.5° C) water for 40 seconds, then canal paresis was calculated [Abnormal: unilateral weakness (UW) >22%]cVEMPwas performed using Evoked potential system GSI Eclipse, and was recorded from the sternocleido-mastoid muscle (SCM). The active electrode was placed on the upper third of each SCM with a reference on the lateral end of the upper sternum while the common electrode was placed on the forehead. During the test, subjects were instructed to turn their heads toward the contralateral side of the tested ear to activate SCM. Stimuli presented mono-aurally; 500 Hz tone burst, were presented at a rate of 5 pulses per second and an intensity of 95dBnHL.

The mean peak latency (ms) of the P<sub>13</sub> and N<sub>23</sub> wave of the VEMP was measured. The peak to peak amplitude (μV) was measured for P<sub>13</sub>-N<sub>23</sub> potentials.

The vHIT was performed in a seated position in room light. During this procedure, the subjects wore a pair of light-weight goggles integrated with a gaze-driven high-speed digital camera system (sampling rate of 220 Hz) that records real time eye movement. The calibration process was performed by integrated laser dots projected on a wall. After calibration the subjects were instructed to fixate on a target located on the wall approximately 1 meter straight ahead. At least 10 unpredictable head impulses (amplitude 15°-20°, duration 150-200 ms, target head velocity 100-200°/s) were administered along the planes of the horizontal SCC and in LARP and RALP planes for testing the vertical SCC, respectively. The software calculates the vestibulo-ocular reflex gain as the ratio of peak slow phase eye velocity to peak head velocity for each SCC. Corrective saccades were also analyzed and classified as a covert saccade if they occur during head movement or as an overt saccade if they occur after head movement.

#### **Statistical Analysis: -**

Statistical presentation and analysis For Windows using the statistical software package statistical package for the social sciences (SPSS), version 26, 2019 for (SPSS Inc., USA) and Graphpad (prism) version 14.

The results of the present study were conducted, using the mean, standard error and linear correlation coefficient. Testing the correlation between the two variables was done using Pearson's correlation coefficient test. A linear correlation coefficient was used for the detection of correlation between two quantitative variables in one group.

ROC curve was used to determine the Area under curve (AUC) and calculation of sensitivity and specificity of markers. ROC curve in logistic regression was used to determine the best cut off value for predicting new observation and calculation of sensitivity and specificity of markers.

Statistical results were analyzed using the mean, and standard error. ANOVA with Post Tukey Test and the categorical data were expressed as percentages, and differences between the groups were compared using the Chi-square test. All data were presented in the form of mean ± standard error (SE).

#### **Results:-**

The present study consisted of 2 groups, the study group (20 adults) with definite Meniere's disease and the control group (20 adults) with no vestibular symptoms. The mean age for the control group was 36 years ± 2.17 years with an age range from 20- 54 years. The mean age for the Meniere's disease group was 43 ± 2.74 years with an age range of 23 –60. There was a statistically significant difference between the groups with regards to age, with the patients from the control group being older than those from the study group. According to PTA results we found all patients in our study group had unilateral MD which showed mild to moderate SNHL in study group and within normal hearing in controls. As for the distribution of the unilateral MD, 11(55%) had MD in the right ear and 9(45%) in the left ear. Regarding caloric testing comparing was done between ears affected by MD (with canal weakness) and adjacent ears of controls. We found the mean of the canal weakness in controls was 12.7% while the mean of the canal weakness in DM group was 33%, the comparison between the study group and the control group showed a statistically significant difference (Table 1).

Concerning the cVEMP, it was present only in 16 right ears and 17 left ears in study group, there was a statistically significant difference of both tested groups in the inter- amplitude p<sub>13</sub>, N<sub>23</sub> in both the right and left ears (Table 2).

Analysis of the gain value of the lateral canal, RALP, and LARP between the two studied groups showed a statistically significant difference as well. (Table 3)

When comparing the groups in relation to the occurrence of catch up saccades in the lateral canal, RALP, and LARP Saccades (covert and overt) it was found to be absent in the control group while it was somewhat present, in varying percentages, in the study group (Table 4). A statistically significant difference was present.

When measuring the sensitivity and specificity of each test using the ROC curve, we concluded that the most sensitive test was cVEMP and the most specific test was the caloric test for the diagnosis of Meniere's disease.

**Table 1:-** comparison between control and studygroups in caloric test.

Caloric	Control group		Study group		t-test	p-value
	Mean	SD	Mean	SD		
weakness	12.7%	3	33%	25.2	-1.96	0.05*

\*Statistically significant difference.

**Table 2: -**Comparison between control and study groups in cVEMPtest using t- test.

VEMP	Control group		study group		t-test	p-value
	Mean	SD	Mean	SD		
P <sub>13</sub> - Rt	14.07	1.1	15.02	1.8	1.859	0.191
N <sub>23</sub> -Rt	23.5	0.72	24.60	2.9	1.568	0.003*
AMP-Rt	117.9	58.9	46.69	16.8	-4.670	0.000*
P <sub>13</sub> -Lt	14.10	1.15	14.48	2.4	0.662	0.011
N <sub>23</sub> -Lt	23.58	0.765	23.97	2.9	.633	0.001*
AMP-Lt	148.37	60.03	101.22	80.6	-.709	0.042*

\*Statistically significant difference

**Table 3:-** Comparison between control and study groups in regards to the gain of vHIT for each group.

vHIT		Control group		study group		T	p-value
		Mean	SD	Mean	SD		
Gain	Lat	0.76	0.013	0.69	0.032	0.036	0.007*
	RALP	0.77	0.012	0.66	0.032	0.003	0.000*
	LARP	0.75	0.015	0.67	0.031	0.028	0.010*

\*Statistically significant difference.

**Table 4:-** Comparison between control and study groups as regards the presence of overtsacc and covertsof vHIT for control and study groups.

vHIT		Study group		control group		f-test	p-value
		Valid Percent		Valid Percent			
		yes	No	Yes	no		
Overtsacc.	Lat	30%	70%	0%	100%	7.05	0.020*
	RALP	35%	65%	0%	100 %	8.48	0.008*
	LARP	35%	65. %	0%	100%	9.12	0.002*
Covertsacc.	Lat	30%	70%	0%	100%	5.71	0.047*
	RALP	35%	65%	0%	100%	7.05	0.020*
	LARP	30%	70%	0%	100%	7.05	0.020*

**Table 5:-** Sensitivity and specificity of caloric test, cVEMPtest, andvHIT.

	Area under curve (AUC)	Std. Error <sup>a</sup>	Cut off value	Asymptotic 95% Confidence Interval		specificity	Sensitivity
				Lower Bound	Upper Bound		
Caloric Test	0.686	0.089	>16	0.512	0.861	95%	50%
cVEMPTest	0.919	0.047	>0.41	0.828	1.000	90%	84.6%
vHIT	0.755	0.079	> 0.37009	0.601	0.909	70%	75%

**Discussion:-**

The diagnosis of Menière’s disease is mostly subjective, made through the symptoms reported by patients, namely attacks of vertigo, tinnitus and hearing loss, with objective investigation still having a minor role. In our study, we attempt to find an objective test that is more sensitive in diagnosing Meniere’s disease and thereby facilitating the process of diagnosis. This was done by comparing patients with definite Meniere’s disease to normal subjects using the values of the caloric test, cVEMP test and vHIT test.

The patients selected for our study were found to all have unilateral MD, 11(55%) had MD in the right ear and 9(45%) in the left ear. This is in concordance with a study by Grigoletal.,<sup>(14)</sup> where most of the patients enrolled for the study had unilateral disease (75.90%), more on the right side; the right ear was affected in 12 subjects (54.50%). Similarly, most of the studies conducted included patients with unilateral MD<sup>(15, 16, 17, and 18)</sup>

When comparing the results of the caloric test between the study and the control group, we found that there was a significant difference between them (Table 1).

As regards to the cVEMP test our results were concerned with the latency of P<sub>13</sub> and N<sub>23</sub> and the inter-amplitude P<sub>13</sub>-N<sub>23</sub>. The results showed that the mean latency of P<sub>13</sub> in the study group was 15.02±1.8 and 14.48 ± 2.4 in the right and left ear respectively. The mean latency of N<sub>23</sub> was 24.60 ± 2.9 and 23.97 ± 2.9 in the right and left ear respectively. We also found that the inter-amplitude of P<sub>13</sub>-N<sub>23</sub> in the study group was smaller than that of the control group (Table 2).

A study by Kim., etal<sup>(19)</sup> displays similar patterns, where the VEMP profile of MD patients showed a low amplitude compared to that of the control group. Also, Kingma et al.<sup>(20)</sup> measured cVEMP in 22 patients affected by MD. On average, significantly lower VEMP amplitudes were measured at the side of the affected ear for both stimulus frequencies (250 and 500 Hz). On the Contrary, research by Angeli and Goncalves<sup>(21)</sup> showed that when using a stimulus at the 1,000 Hz, the mean amplitude was higher in the MD group. This difference in the results may be due different parameters used in each study and also the stage of (MD).

Concerning the gain of the vHIT test in all semicircular canals, the average gain in control group was while a statistically significant difference was present when comparing both groups, with decreased gain in all tested semi circulars in the study group (<0.7) more than that of the control group [0.76 in lateral canal and 0.75 and 0.77 in LARP and RALP respectively] (Table 3). Our abnormal values of the average gain agree with McCaslin et al.,<sup>(22)</sup> who considered Abnormal: VOR gain < 0.7.

Moreover, when we assessed the presence of catch –up saccades (either overt or covert) we found that a significant difference between the study group and control group existed; with presence of catch –up saccades in about 30-35% of total subjects from the study group which is considered a sign of diagnosis for abnormal VOR reflex.

This is contradictory to results from a study by Rubin et al.,<sup>(16)</sup> Who evaluated vHIT in definite MD subjects and found the vHIT gain to be the same as in the enrolled non-diseased group with the established standard of normality being 0.78 for the lateral canals and 0.64 for the vertical canals. However; the sample from that study included only advanced MD, and so, the difference in results may be attributed to that our results were found to be similar to studies that have also used the previous AAO-HNS criteria.<sup>(23)</sup>

The discrepancies in results between different studies may be due to the varying methods and diagnostic criteria used, the period that was evaluated (crisis or inter-crisis) or the standard of normality for VOR gain.

In addition, our results are in line with those reported by Jerin et al.<sup>(24)</sup> They studied 54 subjects with certain MD and found that about (74%) showed normal VOR gain with catch-up saccades. These saccades were present in <50% of the trials, and they concluded that the abnormality of vHIT includes reduced gain or the presence of corrective saccades (covert or overt).

Furthermore, as regards the assessment of the sensitivity and specificity of each test; using the ROC curve we found that the most sensitive test was cVEMP (95%) followed by vHIT (75%) and then the caloric test (50%). While the most specific test was the caloric test (97%) followed by cVEMP (80%) then vHIT (70%).

A valuable study by Angeli & Goncalves<sup>(21)</sup> evaluates the sensitivity and, specificity, and positive predictive values of the caloric test giving values of 41.9% (95% CI [24.5, 60.9]), 50% (95% CI [24.6, 75.3]), and 61.9% (95% CI [46.1, 75.5]), respectively. On assessment of cVEMP 1,000/500 Hz amplitude ratio in that study, they found a value of 1.048 or greater, denoting that this test had greater sensitivity, specificity, and positive predictive value than the caloric test.

**Conclusion:-**

The cVEMP test is the most sensitive test for diagnosing Meniere's disease and the presence of catch –up saccades is an important sign that greatly aids the diagnosis.

**Limitation of the study:**

The main limitation of the present study is the selection of Definite MD with different stages and phases. This is attributed to difficulty to collect sufficient sample size with documented hearing loss. For the same reason, it was not possible to compare patients with the same disease duration.

**Recommendations:-**

Further studies needed to investigate cVEMP test, and vHIT in both early and late phases of MD in addition a correlation with the MD phase (during or between MD episodes), to understand the pathophysiology of MD and how it affects the results.

**Institutional Review Board Statement:**

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board of General organization of teaching hospitals and institutes (GOTHI)

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