Value of VEMP in Detecting Saccular Affection in the Asymptomatic Ear in Patients with Ménière’s Disease

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Abstract

Aim: To assess the value of vestibular evoked myogenic potentials (VEMP) in detecting abnormalities in the affected ear and in the asymptomatic ear in patients with diagnosed unilateral Ménière’s disease.

Study Design: Case-control.

Material and Methods: Twenty two patients with unilateral Ménière’s disease and twenty two age and sex matched normal controls were subjected to audiological evalution and VEMP. The selection of individuals was based on the history and/or clinical evaluation suggestive of unilaterally defined Ménière’s disease. VEMP’s were evaluated in both ears of all cases and controls through absolute latencies of p13 and n23.

Results: VEMP’s were absent in 50% of the affected ears and in 27.3% of the asymptomatic ears of Meniere patients, whereas all normal subjects had preserved VEMP’s. Prolongation of both p13 and n23 latency was noted in in both ear of unilateral Meniere patients compared to normal group (p=<0.001 and 0.007 respectively).

Conclusion: The vestibular evoked myogenic potentials can detect abnormalities in the affected and asymptomatic ears in patients with diagnosis of unilaterally defined Ménière’s disease.


Introduction

MÉNIÈRE’S disease (MD) was described by Prosper Ménière in 1861 and it was defined as a membranous labyrinth disease, characterized by recurrent spontaneous episodes of vertigo, hearing loss, ear fullness and tinnitus on the affected side owing to endolymphatic hydrops [1]. Endolymphatic hydrops is most frequently found in the cochlea and saccule is the second most prevalent site of affection. Severe hydrops is more common in the saccule. Saccular hydrops may occur in 50% of the cases of MD. The definition of saccular hydrops may represent an important breakthrough in the diagnosis of MD.

Endolymphatic hydrops is a typical finding of MD in histopathologic examination of temporal bones. Endolymphatic hydrops has been thought to precede Ménière symptoms and be the cause of symptoms such as episodic vertigo and sensorineural hearing loss, but there are still controversies on this issue.

The presence of in vivo hydrops has never been confirmed, but it has been suggested by the results of glycerol or furosemide tests and by electrocochleography. However, these tests are not appropriate to assess otolithic organs or descending neural pathways (lateral vestibular-spinal tract). New clinical instruments are necessary to identify saccular hydrops. Vestibular Evoked Myogenic Potentials (VEMP) have been studied since the 60’s, but many different centers started to use it to assess the sacculocollic reflex after 1992. They are middle-latency evoked potentials generated by vestibular-spinal muscle reflex that depend on functional integrity of saccule macula, inferior vestibular nerve, vestibular nuclei, vestibular-spinal pathways and neuromuscular plates. Damage to any of these structures results in affection of potentials [2].

The recording of the first complex of biphasic wave p13-n23 presents a positive peak (p) with middle latency of 13ms, followed by a negative peak (n) with middle latency of 23ms. Amplitude of p 13-n23 expresses the magnitude of muscle reflex generated by sound stimulation of saccule macula. In unilateral MD, absence of vestibular myogenic potentials was observed in 54.2% of the
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cases; reduced amplitude of potentials was identified in 58.8% of the patients. Asymptomatic ears in patients with unilateral MD disease may evidence similar abnormalities to the affected ears, but at lower levels of intensity. This finding may be resultant from occult saccular hydrops in the asymptomatic ear or from binaural interactions in otolithic-cervical reflex arch of VEMP’s [2].

The purpose of the present study was to check whether VEMP’s could present abnormalities in the affected ear and in the asymptomatic ear in patients with diagnosed unilateral MD.

Material and Methods

We collected 22 patients with unilateral definite MD, according to clinical criteria set forth by the American Academy [1] from the Audiology Outpatient Clinic of Cairo University Hospital (Kasr El-Eini), from June 2010 till December 2010. There were 12 female and 10 male subjects. We compared them to 22 age and sex matched normal subjects not complaining of any audiological or vestibular disorders. They were 13 female and 9 male.

Diagnostic criteria for MD:

MD is defined as recurrent, spontaneous episodic vertigo, hearing loss, aural fullness and tinnitus. Recurrent endolymphatic hypertension (hydrops) is believed to cause the episodes.

According to the guidelines from AAO-HNS Committee of Hearing and Equilibrium (1995) the three major symptoms are described as follows:

Vertigo:
- Recurrent, well-defined episodes of spinning or rotation.
- Duration ranging from 20 min to 24h.
- Nystagmus associated with attacks.
- Nausea and vomiting during vertigo spells common.
- No neurologic symptoms with vertigo.

Deafness:
- Hearing deficits fluctuate.
- Sensorineural hearing loss.
- Hearing loss progressive, usually unilateral.

Tinnitus:
- Variable, often low pitched and louder during attacks.
- Usually unilateral on the affected side.
- Subjective.

Diagnosis of MD:

Possible MD:
- Episodic vertigo of the Meniere’s type without documented hearing loss, or
- Sensorineural hearing loss, fluctuating or fixed, with dysequilibrium but without definitive episodes.
- Other causes excluded.

Probable MD:
- One definitive episode of vertigo.
- Audiometrically documented hearing loss on at least one occasion.
- Tinnitus or aural fullness in the treated ear.
- Other causes excluded.

Definite MD:
- Two or more definitive spontaneous episodes of vertigo 20 minutes or longer.
- Audiometrically documented hearing loss on at least one occasion.
- Tinnitus or aural fullness in the treated ear.
- Other cases excluded.

Certain MD:
- Definite MD, plus histopathologic confirmation [1].

Inclusion criteria: Patients having unilateral MD, (as suggested from their clinical evaluation, hearing thresholds, results of auditory evoked potentials, vestibular tests done) with variable duration and completely normal hearing thresholds in the other ear.

Exclusion criteria: 1) deviation from normal range hearing threshold, speech discrimination, and immittance data of asymptomatic ear; 2) inability to turn the head; and 3) any deformity in the ear.

The selection of subjects was based on clinical history and assessment suggestive of unilaterally defined MD. The studied subjects were submitted to evaluation, including pure tone audiometry, post glycerol dehydration test, speech audiometry, immittance and acoustic reflexes, auditory brainstem response (ABR) (to ensure cochlear affection), sensory organization test (SOT), videonystagmography (VNG) and VEMP.

Basic audiological evaluation:
- Pure tone audiometry (air conduction and bone conduction). Test for assessment of hearing threshold by pure tone stimulation using Two-
channel computerized Audiometer (Orbiter 922) including:

- Air conduction in the frequency range of 250-8000 Hz octave interval.
- Bone conduction in the frequency range of 500 – 4000 Hz Octave interval.

- Speech audiometry:
  - Speech reception threshold (SRT), using Arabic spondaic words [4].
  - Word discrimination score (WDS %), using Arabic Phonetically balanced (PB) word [5].

- Immittance (GSI 33 version II):

**Glycerol dehydration test:**

The glycerol test was conducted by the following modified procedure: Audiometry was carried out before administration. A total amount of 200ml of 10% glycerol was injected intravenously. Audiometry was also performed immediately after and 1 hour after the injection. According to the diagnostic criteria established by the Ménière’s Disease Research Committee of the Japanese Ministry of Welfare, endolymphatic hydrops was suggested if the hearing level improved by 10 dB or more at two frequencies at least [6].

**VEMP:**

VEMP’s were performed using Synapses Auris one channel auditory evoked potential and VEMP. The surface electrodes were placed as follows: Active electrode on the middle third of the sternocleidomastoid muscle with the reference electrode on the upper sternum and the ground electrode on the forehead.

For the recording of VEMP response click sound stimuli of 95 dB nHL and 250 Hz (duration, 8ms; rise/fall time, 1ms) were delivered via headphones. The repetition time of stimuli was 250ms. Due to limitation of our instrument, intensity below 90 dB nHL couldn’t be assessed, only p13-n23 latencies could be evaluated. We compared the p13-n23 latencies of affected ear and asymptomatic ear in Meniere patients, as well as with p13-n23 latencies in normal subjects.

**Statistical analysis:**

Analysis of data was performed using SPSS 18 (Statistical Package for Scientific Studies) for Windows. Description of variables was presented as follows:
- Description of quantitative variables was in the form of mean, standard deviation (SD).
- Description of qualitative variables was in the form of numbers (No.) and percents (%).

Data were explored for normality using Kolmogorov-Smirnov test of normality. The results of Kolmogorov-Smirnov test indicated that data were normally distributed (parametric data) so parametric tests were used for the comparisons.

- Comparison between quantitative variables was carried out by student \(t\)-test of two independent variables. \(t\)-paired test was applied to check whether there was difference between the means of values of two paired groups with numeric measurement. Repeated measures Analysis of Variance (ANOVA) test was used instead of \(t\)-test when comparing between more than two groups of independent variables. Results were expressed in the form of \(p\)-values.
- Comparison between qualitative variables was carried out by Chi-Square test (\(X^2\)). Fisher exact test was used instead of Chi-square test when one expected cell or more were 5.

The significance of the results was assessed in the form of \(p\)-value that was differentiated into:
- Non-significant when \(p\)-value >0.05.
- Significant when \(p\)-value < 0.05.
- Highly significant when \(p\)-value < 0.01.

**Results**

VEMP was tested in 22 patients with unilateral MD, according to clinical criteria set forth by the American Academy [1]. There were 12 female and 10 male subjects, mean age of 35.45±11.37 years. We also compared VEMP results to results of VEMP in 22 normal subjects not complaining of any audiological or vestibular disorders. Their ages mean was 34.5±11.58 years. They were 13 females and 9 males. The control group was age and sex matched with Meniere patients (\(p=0.12 & 0.761\) respectively).

Meniere patients had different grades of hearing thresholds, 7 had mild sensorineural hearing loss (SNHL), 10 had moderate SNHL, 4 had moderately severe SNHL, and only one patient had severe SNHL, as shown in Fig. (1). Improvement in hearing thresholds occurred in only 5 cases post glycerol, while 17 had no improvement.
Fig. (1): Severity of hearing loss among Ménière patients.

We divided all subjects according to ear status into three groups, Group 1 included ears with MD (22 ears), Group 2 included asymptomatic ears of Meniere patients (22 ears), and Group 3 included 44 ears of normal controls. Comparing hearing threshold results of Groups 2 and 3 revealed no statistically significant difference ($p>0.05$ at all frequencies).

Table (1) shows VNG and SOT results in Meniere patients and controls, showing statistically significant differences in both groups, showing worse results in Meniere patients. Among Meniere patients 2 had falls on conditions 5 & 6 of SOT. None of the patients had spontaneous nystagmus, abnormal oculography, nor positional test. Among Meniere patients 21.36% had unilateral canal weakness.

<table>
<thead>
<tr>
<th>VEMP</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>$p$ value</th>
<th>$p$ value (1&amp;2)</th>
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<tbody>
<tr>
<td>P13:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>11/50.0</td>
<td>6/27.3</td>
<td>0/0</td>
<td>&lt;.001</td>
<td>.122</td>
<td>.001</td>
</tr>
<tr>
<td>Present</td>
<td>11/50.0</td>
<td>16/72.7</td>
<td>22/100</td>
<td></td>
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<tr>
<td>N23:</td>
<td></td>
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Table (2): Comparison between VEMP results among 3 groups; Comparison between p13-n23 complex of symptomatic (group 1) versus asymptomatic ears (group 2) of Meniere cases and normal subjects (group 3).

<table>
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<tr>
<th>VEMP</th>
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<td>P13</td>
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Regarding VEMP results, the p13-n23 complex was present in all subjects of the control group (group 3) in both ears. For Meniere patients, the p13-n23 complex was detected in 11 out of 22 symptomatic ears (50%) (group1), and 16 out of 22 asymptomatic ears (72.7%) (group 3). Comparing these results using ANOVA test revealed statistically significant difference ($p<0.001$). This difference was not statistically significant between groups 1 & 2 (symptomatic versus asymptomatic ears of Meniere patients), and highly significant between groups 2 & 3 (asymptomatic ears of Meniere patients and normal subjects) as shown in Table (2).

Latencies of P13 and N23 among 3 groups are shown in Table (3) showing statistically significant differences between groups 1, 2 and 3 ($p<0.001$), while comparison between normal ears in Meniere patients and affected ears revealed no statistically significant difference as regards latencies of p13 and n23 ($p=0.548$ and 0.349 respectively). Biphasic p13-n23 complex wave revealed significant prolonged latencies in Meniere patients in both ears, where waves were preserved, compared to ears in normal subjects ($p<0.001$ & 0.007).

Table (3): Comparison between P13 & N23 latencies among 3 groups.

We divided all subjects according to ear status into three groups, Group 1 included ears with MD (22 ears), Group 2 included asymptomatic ears of Meniere patients (22 ears), and Group 3 included 44 ears of normal controls. Comparing hearing threshold results of Groups 2 and 3 revealed no statistically significant difference ($p>0.05$ at all frequencies).

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Discussion

VEMP is a relatively noninvasive method to assess patients with vestibular disorders. VEMPs are believed to be a good indicator of saccular and inferior vestibular nerve function in clinical evaluations. The VEMP pathway has been speculated to include the saccule, inferior vestibular nerve, vestibular nucleus, and medial and lateral vestibulospinal tract to the ipsilateral sternocleidomastoid muscle (SCM). Thus, VEMPs indirectly measure vestibular function through a vestibulocollic reflex [7].

Schuknecht & Richter [8] showed that the most frequently involved sites by endolymphatic hydrops are the cochlea, followed by the saccule and the utricle, respectively. Since the saccule is considered the site of origin of VEMPs, it is expected to find VEMPs altered even in early stages of the MD.

Results of the current study denote that even unaffected ears of unilateral MD patients have significant saccular affection, which may eventually result in development of MD in the unaffected side. Prolongation of latency suggests retrolabyrinthine damage, especially of the vestibular-spinal tract. In dysfunctions of saccular macula or inferior vestibular nerve, the affection described is asymmetry of amplitude or absence of response in the affected side, showing reflex blockage, but due to limitation in the instrument used we could not assess the alteration in amplitude, as well as we couldn’t assess the thresholds in asymptomatic ears which had preserved VEMP’s. Probably if we could assessed those thresholds compared to normal subjects, we could have found threshold affection as well in the asymptomatic ears. Our results as other previous authors results suggested that MD is a bilateral disease in most cases which usually present with one ear first, followed by the other ear. The affection usually starts with vestibular affection as noticed from alteration in VEMP response whether prolongation of latencies, absent or reduced amplitude of P13-N23 waves. These results contradict the fact of, the vestibular system being more robust than cochlear part, which is more rapidly affected. In this study, we had 6 out of 22 (27.3%) of asymptomatic ears of Meniere patients had their waves lost, though their hearing thresholds remained in normal hearing range.

Many other recently published studies were also published in the international literature recently about VEMPs in patients with MD [9,10] have reported abnormal findings in vestibular testing of the asymptomatic ear in MD. Endolymphatic hydrops may be evidenced in electrocochleography of asymptomatic ears in 15 to 35% of patients with unilateral MD. Murofushi, et al. [11] reported that 51% of the patients with MD had no response to the VEMP test, while [12] doing the same study, observed an index of 54% of response absence in the VEMP test in patients with MD. Abnormal responses were detected in 53.3% of affected ears and in 6.6% of asymptomatic ears of patients with unilateral MD [2].

Murofushi, et al. [11] reviewed the results of VEMPs in patients with MD, vestibular neuronitis, acoustic neuromas, and multiple sclerosis. In patients with MD or vestibular neuronitis, the latency of the waveform was not affected; however, the amplitude of the waveform was greatly affected, which could be considered an abnormal response. Patients with MD have exhibited increased VEMP thresholds and altered frequency tuning of the VEMP response.

Lin, et al. [13] questioned if this change in VEMP response was also seen in unaffected ears of patients with unilateral MD. Through postmortem histopathologic evaluation of the temporal bone in patients with unilateral MD and 82 current patients with unilateral MD, the authors concluded that endolymphatic hydrops appears to precede symptoms of MD. They reported that six of 17 (35%) temporal bone cases with unilateral MD (11 definite, three probable, and three possible) have saccular hydrops in the asymptomatic ear, and 27% of 82 patients with unilateral MD have “Ménière-like” VEMP changes of both threshold and tuning in the asymptomatic ears. It was concluded that saccular hydrops precedes clinical symptoms in MD, and VEMP may detect asymptomatic or presymptomatic saccular hydrops [13]. However, the presence of endolymphatic hydrops in asymptomatic contralateral ears is questionable in that study, as saccular hydrops was not clinically visualized using diagnostic imaging in the patients who showed VEMP changes in the asymptomatic ear. In a previous study, the contralateral ear in patients with unilateral MD showed significantly more damage in the inner ear structures compared with the age-matched normal control temporal bones, which may be a reason for minor changes in the VEMP test observed in the asymptomatic ear of unilateral MD [3].

Rauch, et al. [14] published a study in which they showed VEMPs present in about 94% of the patients with MD in the affected side and the frequency thresholds between 250 Hz and 2,000
Hz were increased. Nonetheless, one of the most interesting data of this study was the fact that about 27% of the asymmetric ears from these patients with unilateral MD had alterations in this test. When they compared this result to data from temporal bone studies, they found about 38% of endolymphatic hydrops in asymptomatic ears of patients with MD and epidemiological studies that reported bilateral involvement of MD in 30% to 35% of the patients. They concluded that VEMPs may be a diagnostic method for endolymphatic hydrops in initial stages, and it can serve as a prognostic factor for bilateral involvement in MD.

In a related study [13], hypothesized that VEMP abnormalities would be greater in the ears of patients with MD with drop attacks than in patients with normal ears or those with Meniere’s ears without drop attacks. In a retrospective review, the authors performed VEMP testing on three groups of individuals: Patients with MD without a history of drop attacks, those diagnosed with MD and a history of drop attacks, and normal controls. The VEMP response was absent in 41% of ears affected by drop attacks and in 13% of ears affected by MD; VEMP response was always present in normal ears. The alterations of frequency tuning and increased threshold findings were present in the patients with MD as well as those with MD and drop attacks. Unaffected ears of patients with MD, however, also showed slight threshold and tuning changes [13,15], which denotes that VEMP measures may provide value when monitoring patients with MD [7].

A significant number of patients with MD eventually develop involvement of their second ear, a situation with a profound impact on patients’ symptoms, quality of life, and management options. It has been shown previously that ears affected by MD show elevated thresholds and altered frequency tuning of VEMPs. Similar changes in mean VEMP threshold and tuning are also seen in the unaffected ears of patients with unilateral MD, although to a lesser degree than in the affected ears. One possible explanation for this observation is that the group of unaffected ears is really two groups, a group of true normal ears and a group of ears with asymptomatic or presymptomatic endolymphatic hydrops. The Ménière literature suggests that progression from unilateral to bilateral disease is seen in approximately one third of cases [13].

**Conclusion:**

VEMP is a valuable tool in detecting initial saccular abnormalities in the affected and asymptomatic ears in patients with diagnosis of unilaterally defined MD. Also prolongation of P13-N23 latencies hints for a retrolabyrinthine affection in Meniere patients.

**Recommendations:**

Follow-up of unilateral MD patients with close observation could add to the predictive value of VEMP test as a tool for early diagnosis of bilateral MD.

**References**


