A Comparison of Vestibular Evoked Myogenic Potential (VEMP) between Definite Meniere’s Disease Patients and Normal Healthy Adults

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Objective: To compare the results of VEMP between unilateral definite Meniere’s disease patients and normal healthy adults.

Material and Method: Thirty-two patients with unilateral definite Meniere’s disease patients and 32 age-matched normal healthy adults (control) underwent VEMP tests with short tone burst of 500 Hz at 90 dBnHL. Student-t test was used for comparison of means of all parameters between two groups.

Results: Absent VEMP response was found in 14 MD patients and abnormal asymmetry ratio (AR) was found in five MD patients. Normal responses were found in all subjects of the control group. The mean P1 and N1 latencies, VEMP amplitude between unilateral MD, and control were not significantly different between two groups. However, the difference between the mean AR of both groups showed statistically significant (p-value <0.05). The upper limit of normal AR was calculated to be of 35.15%.

Conclusion: The absence of VEMP response and AR of VEMP were more dominant than other parameters such as P1 and N1 latencies or VEMP amplitude in the detection of saccular dysfunction in MD. The results suggested that AR should be used as a tool in interpretation of VEMP response for the diagnostic batteries in MD. The upper limit of normal AR of ≤35% should be recommended.

Keywords: Vestibular evoked myogenic potential (VEMP), Meniere’s disease, Asymmetry ratio

Clinically, endolymphatic hydrops in Meniere’s disease (MD) are found most often in the cochlear area(1-3). Besides cochlea, the second most frequent site for hydrop formation is the saccule(2). The study of 22 temporal bones with Meniere’s disease has revealed endolymphatic hydrops occurring more often in the cochlea (22/22), followed by the saccule (19/22) and utricle (11/22), and they are present less often in the semicircular canals(2). Changes induced by endolymphatic hydrops may damage hair cells in the cochlea and saccule(2,4).

Vestibular evoked myogenic potential (VEMP) is a biphasic wave form that exhibits electromyographic responses to loud sound stimuli and can be recorded from the sternocleidomastoid (SCM) muscle(8). The VEMP pathway consists of the saccule, inferior vestibular nerve, vestibular nucleus, vestibulospinal tract, and SCM muscle(7,8).

A variety of studies investigating VEMP in Meniere’s patients has shown various results. Most studies found that VEMPs were absent with clicks or tone burst stimuli but the absence of VEMP responses ranged from 10.5 to 100%(4,9,14). Some studies showed P1 latency prolongation in these cases(9,12,14). Decreased VEMP amplitude was found in a few papers(12,14). In addition, abnormal asymmetry ratio was found in these patients(9,14,15). The aim of the present study was to investigate dominant VEMP parameters in Meniere’s disease for selection in assessing the Meniere’s disease.

Material and Method
All subjects received detailed information about the present study and the testing. Informed
consent was obtained from each individual, and the present study was approved by the Ramathibodi Hospital Ethics Committee. The study involved 32 patients with unilateral Meniere’s disease and 32 normal healthy subjects as a control group.

All subjects with MD were consecutive patients who presented to the Otolaryngology Department of Ramathibodi Hospital. There were 24 females and eight males having mean age 49±8.3 years (range 27 to 61 years). All patients were diagnosed using the criteria established by the 1995 American Academy of Otolaryngology Head and Neck Surgery, Balance and Hearing Committee. The control normal healthy subjects were volunteers who had no history of vertigo and tinnitus. This group was composed of 19 females and 13 males with mean age of 45.5±9.5 years (range 27 to 61 years), age matched with the Meniere’s group.

All subjects received a detailed history taking and local checkup of ear, nose, and throat fields, followed by audiologic test battery including pure tone audiometry, tympanometry, and VEMP test. Subjects with external and middle ear problem, cervical spine problem or inability to turn their head were excluded.

**VEMP test**

VEMP testing was performed using an auditory evoked response apparatus (Smart EP Multi Channel, Intelligent Hearing Systems, Miami, Florida, USA). VEMPs were recorded from the sternocleidomastoid (SCM) muscle. Surface electromyography (sEMG) activity was recorded from the subject in an upright position, with active electrodes placed on both sides of the middle part of the SCM muscle. The reference electrode was placed on sternoclavicular joint and the ground electrode was at the midline of the forehead. During recording, the subject was instructed to turn the head to the opposite side of testing ear and maintained in this position throughout the entire test. The EMG signals were amplified, with bandpass filtered between 30 and 1,500 Hz. The EMG levels were maintained at least 50 μV. Short tone burst of 500 Hz at 95 dB nHL was delivered through an earphone. Monaural acoustic stimulation with monaural recordings was employed. The stimulation rate was 5 Hz, analysis time was 50 ms, and 256 responses were averaged for each run.

The positive and negative peaks of biphasic waveforms were termed as waves P1 and N1. Consecutive runs were performed to confirm reproducibility of peaks P1 and N1, which represented VEMP responses. In contrast, VEMP responses were absent when reproducibility of the biphasic P1-N1 waveform was missing. Finally, the latencies of P1 and N1, VEMP amplitude, and asymmetry ratio (AR) were measured.

**Data analysis**

A statistical package SPSS for Windows was used for data analysis. Means and standard deviations (SD) were calculated for presenting the absolute latencies of P1 and N1, the VEMP amplitudes, and the AR. An independent t-test was used for comparing differences in the means of absolute latency of P1, N1, VEMP amplitudes, and AR between both groups.

**Results**

Fig. 1 showed the VEMP waveforms from MD patient. There was no significant difference in age between control and MD groups. In Table 1, the mean P1 and N1 latencies, VEMP amplitude and AR of both groups are shown. In control group, the mean P1 and N1 latencies were 13.88 and 20.72 ms, respectively, whereas the mean VEMP amplitude was 54.65 μV and the mean AR was 15.53%.

From Table 1, the upper limit of AR was then calculated from the mean and SD of AR in the control group which were 15.53 and 9.81, respectively. The upper limit (mean + two standard deviations) of AR was equal to 35.15%.

**Fig. 1** The VEMP waveforms form MD patient showing tracing A: normal response in unaffected ear and B: absent response in Meniere’s ear. Tracing A also showed P1, N1 wave with interpeak amplitude measurement.
In Meniere’s group, testing of VEMP in this group revealed 14 cases with absent VEMP response. Of the 18 responding ears, five showed abnormal AR and 13 exhibited normal responses. From Table 1, the mean P1, N1 latencies and VEMP amplitude obtained from 18 ears were not significantly different from those in the control group. There was a significant difference only in the mean AR between both groups (p<0.05). In the study, no abnormal latency and VEMP amplitude were found in any group of the present study.

Discussion

Comparisons of mean P1 and N1 latencies, VEMP amplitude and asymmetry ratio were investigated by independent t-test. The mean absolute latencies of P1 and N1 and the mean VEMP amplitude in affected ears of unilateral MD were not significantly different from those in control subjects. The finding of the absolute latencies of P1 and N1 were similar to the study of De Waele et al and Murofushi et al. In the present study of 54 unilateral Meniere’s disease patients, De Waele et al suggested that sacculocollic pathways, including the inferior vestibular nerve, retained normal velocity conduction. Murofushi et al clarified the diagnostic value of VEMP latencies. They reviewed VEMP recordings from 43 Meniere’s disease patients and compared their results with those of 18 healthy subjects. They concluded that prolonged VEMP latencies seemed not to be a sign of inner ear lesions.

In the present study, the reason for no significant difference in the mean VEMP latencies between unilateral MD patients and control subjects might be due to the pathology of MD involved into the inner ear, especially cochlea and saccule. The pathology of MD may not affect the conduction pathway of VEMP, including the vestibular nerve and brainstem pathway, which supported the study of De Waele et al and Murofushi et al.

The mean VEMP amplitude between unilateral Meniere’s disease patients and control subjects showed no significant difference in the present study, and was similar to the study of De Waele et al. They reported that the VEMP amplitude in their study varied substantially among subjects. In their reason, the change of VEMP amplitude was related to the EMG activity. The relationship was not significant because of the high standard deviation (SD) of the VEMP amplitude. In addition, other researchers also found high SD of the VEMP amplitude. In the present study, the VEMP amplitude exhibited large SD in both control and MD groups. The VEMP amplitude scales in direction proportion to the level of SCM muscle activity and to stimulus level. These factors did have influence on VEMP amplitude. Moreover, the recording surface EMG levels have been affected by motor units and thickness of skin, subcutaneous fat and muscle underneath. These may be the reason that why SD in VEMP amplitude was variable in the present study and in other studies. In the present study, the VEMP amplitude seemed to be a non-specific value for VEMP in detecting abnormal VEMP response in unilateral MD patients or other vestibular disorders involving the saccule.

Ribeiro et al suggested that VEMP amplitude should not be used for interpersonal comparison of vestibular-spinal muscle reflex but rather as AR. Some factors could not be controllable such as individual differences in level of SCM contraction, thickness in the fat layer of muscle, the number of motor units in SCM muscle reflecting variations of VEMP amplitude. The mean AR in MD patients and control subjects were 25.52 and 15.53 respectively. The mean

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control (n = 32)</th>
<th>MD (n = 32)</th>
<th>p-value</th>
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<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>P1 latency (ms)</td>
<td>13.88</td>
<td>1.01</td>
<td>14.33</td>
</tr>
<tr>
<td>N1 latency (ms)</td>
<td>20.72</td>
<td>1.72</td>
<td>21.30</td>
</tr>
<tr>
<td>VEMP amplitude (μV)</td>
<td>54.65</td>
<td>32.37</td>
<td>58.95</td>
</tr>
<tr>
<td>AR (%)</td>
<td>15.53</td>
<td>9.81</td>
<td>25.52</td>
</tr>
<tr>
<td>Upper limit of AR</td>
<td>35.15</td>
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* p<0.05
AR between both groups were significantly different at p<0.05. There has been no report comparing the mean AR of unilateral MD patients.

In the present study, abnormal AR was found in 15.6%, which was less than that in Young et al (22.5%)\textsuperscript{(13)}. They hypothesized that the abnormal AR in MD cases may correlate to the severity of saccular hydrops in the late stage of disease. They suggested that absent VEMPs or abnormal AR in MD cases may be reflected from the pathologic findings in the saccule\textsuperscript{(13)}.

The AR was calculated using a formula according to Welgampola et al\textsuperscript{(28)}. In control subjects, the AR of the group showed small variation (SD = 9.81%) (Table 1). The reason to explain in this result may be due to the saccular function on both sides of an individual, which could be at the same level function or a small interaural difference in anatomical variation between both sides. In contrast, the AR in unilateral MD patients varied more (SD = 21.06%), because in the affected ear, the VEMP amplitude was certainly smaller than that in the unaffected side.

Young et al\textsuperscript{(13)} found that the percentage of abnormal AR in the late stage of disease in their study was 43.5%, which was more than that in the early stage (41%). The present study showed that the percentage of abnormal AR was 40% in late stage, which was more than in the early stage of disease (27.27%), and this seemed to be similar to Young et al\textsuperscript{(13)}. The explanation of this result may be due to the fact that the endolymphatic hydrops are more extensive in the late stage of disease damage to saccular structure\textsuperscript{(31)} and the inferior vestibular nerve, which might be a cause in reduction of VEMP response especially, the VEMP amplitude. Additionally, in the early stage, MD might be present with only cochlear symptoms such as hearing loss and pressure or fullness in the ear without true vertigo or even ringing in the ears. Moreover, the fluctuating or reversible of symptom in the early stage of disease brought the amplitude closer to normal condition that might cause difficulty to distinguish abnormal AR. The abnormal AR in the present study may be a type of hypo-function in saccule on the affected side, which led to depressed VEMP responses when compared to the unaffected side.

The AR seemed to have advantage in the comparison of unilateral vestibular disorder, because this method inspected inter-side difference, which might have small effect from anatomical variation. This reason makes the asymmetry ratio be used in comparison between individual cases or groups, and the present study found obvious differences in the mean AR between both groups (Table 1).

Conclusion
The VEMP testing is a new way of assessing the saccular function in MD. The results suggested that AR should be used in interpretation of VEMP response for diagnosis in MD and upper limit of normal AR of ≤35% should be recommended. Further experimentation should be focused on the results in patients with bilateral MD.

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Potential conflicts of interest
None.

References
การศึกษาเปรียบเทียบ vestibular evoked myogenic potentials (VEMP) ระหว่างผู้ป่วยโรคมีเนียร์กับผู้ใหญ่สุขภาพดี

วัตถุประสงค์: เพื่อศึกษาเปรียบเทียบผลการตอบสนอง VEMP ระหว่างผู้ป่วยโรคมีเนียร์กับผู้ใหญ่สุขภาพดี

วัสดุและวิธีการ: กลุ่มโรคมีเนียร์ประกอบด้วยผู้ป่วยมีเนียร์ข้างเดียว และกลุ่มควบคุมประกอบด้วยผู้ใหญ่สุขภาพดี จำนวนกลุ่มละ 32 ราย ทุกรายได้รับการทดสอบ VEMP โดยกระตุ้นด้วยเสียงโทนสั้น 500 เฮิรทซ์ ความดัง 95 เดซิเบล ใช้สถิติ student-t เปรียบเทียบค่าเฉลี่ยต่างระหว่างสองกลุ่ม

ผลการศึกษา: พบว่ากลุ่มมีเนียร์ตรวจไม่พบการตอบสนอง VEMP จำนวน 14 ราย และความผิดปกติของ asymmetry ratio (AR) จำนวน 5 ราย พบการตอบสนอง VEMP ในกลุ่มควบคุมทุกคน จากการเปรียบเทียบทางสถิติ ค่าเฉลี่ยของ P1 และ N1 latencies และ VEMP amplitude ไม่แตกต่างกันระหว่างกลุ่มมีเนียร์และกลุ่มควบคุม อย่างไรก็ตามพบว่าค่า AR ระหว่างสองกลุ่มมีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ (p-value <0.05) และค่า AR สูงสุดในกลุ่มมีเนียร์ปกติ ได้จากการค่าเฉลี่ยเท่ากับ 35.15%

สรุป: ผลการศึกษาพบว่าการตรวจไม่พบการตอบสนองของ VEMP และความผิดปกติของ AR เป็นตัวแปรที่สามารถนำมาใช้ในการแปลผลการผลิตเกิดจากภาวะที่เสื่อมหรือ VEMP ได้ดีกว่าการใช้ P1 และ N1 latencies และ VEMP amplitude ซึ่งอาจช่วยในการตรวจสอบทหารอัลตราไวไฟส่วนของอวัยวะทรงตัวในหูที่มี saccule การศึกษานี้แนะนำว่าควรน้าค่า AR มาใช้ในประเมินผลการทดสอบ VEMP ในผู้ป่วยโรคมีเนียร์ข้างเดียว และแนะนำให้ใช้ค่า AR สูงสุดในผู้ใหญ่ปกติควร ≤35%