Clinical Value of Vestibular Evoked Myogenic Potential in Assessing the Stage and Predicting the Hearing Results in Ménière's Disease

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Objectives. Our goal was to find the clinical value of cervical vestibular evoked myogenic potential (VEMP) in Ménière's disease (MD) and to evaluate whether the VEMP results can be useful in assessing the stage of MD. Furthermore, we tried to evaluate the clinical effectiveness of VEMP in predicting hearing outcomes.

Methods. The amplitude, peak latency and interaural amplitude difference (IAD) ratio were obtained using cervical VEMP. The VEMP results of MD were compared with those of normal subjects, and the MD stages were compared with the IAD ratio. Finally, the hearing changes were analyzed according to their VEMP results.

Results. In clinically definite unilateral MD (n=41), the prevalence of cervical VEMP abnormality in the IAD ratio was 34.1%. When compared with normal subjects (n=33), the VEMP profile of MD patients showed a low amplitude and a similar latency. The mean IAD ratio in MD was 23%, which was significantly different from that of normal subjects (P=0.01). As the stage increased, the IAD ratio significantly increased (P=0.09). After stratification by initial hearing level, stage I and II subjects (hearing threshold, 0-40 dB) with an abnormal IAD ratio showed a decrease in hearing over time compared to those with a normal IAD ratio (P=0.08).

Conclusion. VEMP parameters have an important clinical role in MD. Especially, the IAD ratio can be used to assess the stage of MD. An abnormal IAD ratio may be used as a predictor of poor hearing outcomes in subjects with early stage MD.

Keywords. Vestibular evoked myogenic potential, Ménière’s disease, Stage, Hearing loss, Vertigo
by pure tone threshold at 0.5, 1.0, 2.0, and 3.0 kHz [6]. Using the worst results during the 6-month period before treatment, stage I-IV have a four-tone average of <26 dB, 26-40 dB, 41-70 dB, and >70 dB.

Patients with MD present fluctuating hearing and vertigo. Therefore, it is important to identify irreversible damage among the fluctuating symptoms. Currently, irreversible damage from MD is measured solely on the basis of hearing impairment. But in the conventional staging system, intact vestibular function is usually evident in late stage MD [7]. One possible hypothesis is the differing susceptibility of patients to hydrops; vestibular sensory cells are relatively resistant to pressure compared with cochlear hair cells. Another possible hypothesis is that the caloric test does not reflect vestibular loss in MD [8]. A vestibular function test that reflects functional loss in MD is clearly required. Because the saccule is anatomically close to the cochlea, there is a possibility that its functional loss may occur just after the cochlear functional loss. Alternately, saccular function may be closely related with cochlear function.

We can assume the clinical importance of saccular function in MD because of its anatomical proximity to the cochlea. Okuno et al. [2] reported on the incidence of endolymphatic hydrops in each department of the labyrinth. Twenty-two temporal bones from deceased patients with MD were examined. The authors reported cochlear hydrops in all temporal bones; 86.5% had saccular hydrops, 50% had utricular hydrops and 36.4% had hydrops in the semicircular canal [9].

Based on this pathological background, we hypothesized that patients with MD will initially undergo cochlear hydrops. Next, the endolymphatic hydrops will serially proceed into the otolithic organ, saccule and utricle. Finally, hydrops will affect the membranous labyrinth of the semicircular canals. If this hypothesis holds, then clinical test tools reflecting these sequential processes could be developed. This would be a pivotally important discovery in MD diagnosis and treatment.

Candidate tests that could correlate well with pathologic changes are electrocochleography (ECoG), cervical or ocular vestibular evoked myogenic potential (VEMP) and the caloric test. Our previous study supported the value of ECoG as a predictor of poor hearing outcomes in subjects with MD [10]. The present study continued this line of investigation by assessing the saccular function test for a similar role as ECoG in MD.

VEMP can be used as a test of the otolithic organ and peripheral vestibular function [11]. Several studies have investigated the correlation of VEMP with hearing impairment in MD. Young et al. [12] defined the interaural amplitude difference (IAD) ratio in 40 patients, and reported a correlation of the IAD ratio of VEMPs with the conventional stage of MD. De Waele et al. [8] reported that saccular impairment correlates with low-frequency hearing loss. However, other studies did not report a significant difference in VEMPs from MD patients compared to normal subjects [13,14]. Thus, the clinical role of VEMP in MD remains debatable.

The aim of the present study was to determine the diagnostic value of VEMP in MD. The characteristic of each parameter was evaluated in MD patients and compared to that of normal subjects. Through this analysis, we tried to confirm the role of VEMP as a new staging system and as a predictor of future hearing aggravation.

**MATERIALS AND METHODS**

**Subjects**

A retrospective analysis of patients who had been diagnosed with MD between January, 2008 and February, 2011 at our tertiary care hospital was carried out. This study’s protocol was approved by the institutional review board. The study sample comprised 18 men and 23 women with a mean age of 48.8 years (range, 18 to 67 years). Only subjects who had been definitively diagnosed with MD and followed up for more than 6 months were included in this study. The patients had been diagnosed with MD according to the criteria for definite MD recommended in 1995 by the AAO-HNS Committee on Hearing and Equilibrium. Patients who underwent endolymphatic sac surgery or who were treated with an intratympanic injection of gentamicin during the follow-up period were excluded from the analysis. In addition, patients with a history of a brain tumor or vestibular schwannoma, or any neurological, psychiatric, or significant medical disease were excluded. Patients who had received a hearing test and simultaneous VEMP were included. A follow-up hearing test was performed at least 6 months after the previous test.

**Vestibular evoked myogenic potential**

VEMP was performed using Navigator Pro (Bio-logic Systems, Mundelein, IL, USA). Each subject was tested while supine and holding their head away from the floor to contract the sternocleidomastoid muscle (SCM). The active electrode was placed on the upper third of the SCM and a reference electrode was placed on the upper border of the sternum. The ground electrode was placed on the glabella. Acoustic stimuli were presented through inserted earphones. Acoustic stimuli were 500 Hz short-tone bursts presented five times/second. The rise-plateau-fall time was 1-2-1. VEMP threshold and response amplitude were measured at a stimulus of 95 dB HL. The EMG from each side was amplified and bandpass filtered (10 Hz to 1.5 kHz). Results from 200 repetitions in each ear were averaged. The mean peak latency (ms) of the P13 and N23 wave of the VEMP was measured. The peak to peak amplitude (μV) was measured for P13-N23 potentials. To estimate the relative response in both ears, we used the IAD ratio, calculated as: (right ear amplitude - left ear amplitude) ÷ (right ear amplitude + left ear amplitude) × 100. We modified this as follows to measure the relative response of the lesion side ear in MD patients. The modified for-
mula is \((\text{contralateral side ear amplitude} - \text{lesion side ear amplitude}) \div (\text{contralateral side ear amplitude} + \text{lesion side ear amplitude})\). In our laboratory, we interpreted the VEMP results based on the absolute value of the IAD ratio from 33 normal subjects. The results revealed a mean ±SD IAD ratio of 12.72% ± 7.94%. A mean IAD ratio exceeding 28.6% indicated abnormal VEMP. For clinical interpretation of the interaural difference, however, we used the real value of the IAD ratio. The negative value of the IAD ratios indicates the hyperactive response in the lesion side.

Categorization of hearing loss and VEMP findings
In this study, we compared each parameter of VEMP in MD patients to that of normal subjects. The level of hearing loss was calculated by averaging the thresholds obtained in the 500 Hz, 1 kHz, 2 kHz, and 3 kHz pure tone tests. Hearing tests were performed at least two times, and the results of the initial and last hearing test were included in the analysis. Then, the stage of the disease was compared with the IAD ratio of VEMP. Furthermore, we analyzed hearing aggravation according to the VEMP results.

Statistical analyses
Statistical significance was set at \(P<0.05\). All statistical analyses were performed using SPSS ver. 18.0 (SPSS Inc., Chicago, IL, USA). The independent \(t\)-test, Mann-Whitney test and Kruskal-Wallis test were used.

RESULTS

Demographics and hearing results
At the initial visit, the chief complaint among the patients was dizziness (\(n=14, 34.15\%\)), tinnitus (\(n=14, 34.15\%\)), hearing loss (\(n=7, 17.07\%\)) and ear fullness (\(n=6, 14.63\%\)). The mean period for these symptoms was 23.95±28.48 months. Fifteen patients (36.59%) were referred from another hospital. The study population had a mean hearing loss of 39.26±15.84 dB and 86.1%±20.49% of speech discrimination at the initial visit. A flat type audiogram was observed in 22 patients (53.7%), ascending in 14 patients (34.15%), descending in four patients (9.8%), and peaking in one patient (2.4%). The initial stage according to AAO-HNS criteria was stage I (\(n=8, 19.5\%\)), stage II (\(n=16, 39.0\%\)), stage III (\(n=16, 39.0\%\)), and stage IV (\(n=1, 2.4\%\)). The mean follow-up period was 26.83±28.27 months, during which the subjects had a hearing loss of 5.18±16.99 dB. Among 41 patients, 34 had an ECoG result (mean summing potential [SP]/action potential [AP] ratio, 0.42±0.17) and 24 patients were assessed using the caloric test (mean canal paresis was 30.69%±23.84%).

VEMP results in MD patients
The VEMP results of the 41 MD patients were compared with the results of the 33 normal subjects. The mean peak to peak amplitude was 100.16±73.15 μV, which was significantly decreased from the 153.03±89.91 μV obtained from normal subjects (\(P=0.01\), independent \(t\)-test) (Fig. 1). But, the peak latency of each wave was similar with the data from normal subjects (Fig. 2). To compare the two groups more objectively, the IAD ratio was calculated for each patient. In normal subjects, there was little asymmetry in the VEMP responses (-0.16%±15.17%). In the MD patients, VEMP was decreased in the lesion side and the IAD ratio was calculated as 23.55%±38.34%. This difference was statistically significant (\(P=0.01\), independent \(t\)-test) (Fig. 3). Next, we looked at whether the VEMP results reflected the AAO-HNS staging system. To this end, the 41 patients were classified into two groups. Group 1 (\(n=24\)) included stage I and stage II, and group 2 (\(n=17\)) included stage III and stage IV. One group 1 patient and five group 2 patients had no response on VEMP testing. Following stratification by initial hearing stage, the mean IAD ratio in group 1 was 12.62%±29.77%, which was similar to that of the normal subjects. The ratio was increased in group 2 (38.98%±44.37%) and the increase was statistically significant (\(P=0.03\), Mann-Whitney test) (Fig. 4A). Because there was only one stage IV patient in the study population, this patient was excluded from the statistical analysis. As shown in Fig. 4B, the IAD ratio was largest in stage III MD and smallest in stage I MD subjects. The mean IAD ratio of stage I, stage II, and stage III subjects was 7.94%±30.86%, 14.96%±29.95%, and 40.20%±45.53%, respectively (\(P=0.09\), Kruskal-Wallis test). As shown in Fig. 5, group 1 subjects with abnormal VEMP at the initial visit showed a decrease in hearing during the follow-up period compared to those with normal VEMP. In 17 patients with normal VEMP, the mean hearing decline was 5.44±16.1 dB during 32.76±27.43 months of follow-up. In seven patients with abnormal VEMP, hearing was lowered to 21.07±22.07 dB.

![Fig. 1. The peak to peak amplitude of vestibular evoked myogenic potential (VEMP): Ménière’s disease vs. normal subjects. The mean (±SD) peak to peak P13-N23 amplitude in Ménière’s disease was 100.16 (±73.15) μV, which was significantly lower than normal subjects (153.03±89.91 μV, \(P=0.01\)).](image-url)
after a mean 43.29 ± 47.53 months of follow-up, compared to the initial hearing level (P = 0.08, Mann-Whitney test). But, in group 2 patients, whose hearing was already deteriorated, the VEMP result did not affect hearing outcomes. The 10 patients with a normal VEMP result had a mean 12.9 ± 6.64 months of follow-up, and displayed hearing improvement of 1.25 ± 11.13 dB. Seven patients with abnormal VEMP had 15.86 ± 10.51 months of follow-up, during which their hearing threshold improved by 2.14 ± 11.59 dB (P = 0.76, Mann-Whitney test) (Fig. 6).

**DISCUSSION**

Among the 41 unilateral MD patients, 14 patients (34.1%) revealed abnormal VEMP results. Compared with normal subjects, the amplitude was lower and the latency was similar in early potentials of VEMP. The IAD ratio was significantly increased in the MD subjects. Echoing the previous result of Young et al. [12] in the present study, the IAD ratio of VEMPs correlated with the AAO-HNS stage of MD. This supports the value of VEMP in hearing prediction.

Endolymphatic hydrops is the main pathologic change in MD. Prevalence of endolymphatic hydrops is 100% in the cochlea, 86.3% in the sacculus, 50% in the utricle and 36.4% in the semicircular canals [3]. The previous results and the present findings support the view that endolymphatic hydrops in MD begins in the cochlea and sequentially proceeds through the sacculus, utricle, and finally, to the semicircular canals. Recently, we reported the predictive value of ECoG for hearing in MD, in which a high SP/AP ratio at the initial visit could be used as a predictor of poor hearing outcomes in subjects with MD [10]. Also, we conclude that although vertiginous symptoms may be controlled after treatment, the underlying endolymphatic hydrops may be unaffected.

In this same vein, we designed a similar study assessing saccular hydrops. The VEMP test, which is regarded as a reflection of saccular function, can be used as a predictor for hearing outcome in MD patients.

First, we evaluated the clinical role of VEMP in MD. Among the study population, 34.1% of patients had no/decreased response in VEMP. This is similar with previous studies; the small variations among the studies may result from different hearing levels of the patients [8,12,15,16]. Next, we compared VEMP with the MD staging system to evaluate the clinical usefulness of VEMP in predicting the disease stage. There was a tendency toward a decreasing response of VEMP, but this trend was not statistically significant. It is possible that such a decreased re-
response only reflected low hearing levels. To confirm the result, we also measured the patients’ VEMP threshold. In our study population, regardless of their hearing threshold, all patients had a constant VEMP threshold (83.0 ± 7.72 dB). Therefore, the decreased VEMP responses almost certainly came from saccular hypofunction, as found previously [12]. The data indicate that VEMP could be a new staging test tool in MD. Furthermore, since the amplitude of VEMP can be affected by subcutaneous thickness [17], the relative difference of amplitude is a more precise way to measure actual saccular function.

The most notable outcome of this study is the possibility that VEMP can be used to predict hearing outcome. To the best of our knowledge, there has been no report concerning hearing prediction on the basis of VEMP results. The patients classified as low stage in the conventional AAO-HNS staging system but who had saccular hydrops or dysfunction will experience more hearing aggravation than patients with normal saccular function. In other words, patient with minimal hearing loss at the present time but who display sustained saccular hydrops, harbor sensory cells that are not dead but which are on course for functional loss with time.

The present results are consistent with our previous data [10].
The prior and present results support the view that along with an increasing SP/AP ratio in ECoG, an increasing IAD ratio in VEMP may play a role as a hearing predictor.

The saccule is the second most frequent location for endolymphatic hydrops. Fifty percent of MD involve saccular hydrops [3]. The severe form of endolymphatic hydrops is most frequently found in the saccule [18]. If this hydrops lasts for a long time, it will lead to atrophy of the macula of the saccule [2]. Although the absolute prevalence of macular atrophy is far less than that of healthy macula in patients with hydrops [19], uncontrolled saccular hydrops will inevitably lead to functional loss of sensory cells including hair cells in the cochlea. Thus, long-term endolymphatic hydrops can cause irreversible hearing loss. We can assume this pathologic status with the clinical testing of VEMP.

After 5-10 years of MD onset, hearing loss stabilizes at a mean level of 50-60 dB [20]. Late in the course of the disease, hearing loss is the most common fixed damage [21-24]. Furthermore, major loss is experienced in the first few years of the disease [20]. Therefore, it is important to recognize patients that are at high risk for hearing deterioration before starting treatment. More careful treatment of patients with preserved hearing but impaired saccular function could result, which would be a very important advance, since such individuals have a greater chance of having poor hearing outcomes.

The study had several limitations. VEMP could not be performed at the same time for all patients. Because we severely restricted the study population, greater numbers of subjects are needed for statistical support. As shown in Fig. 5B, four patients with a poor hearing outcome showed a sharply declined hearing level, but three patients maintained a similar hearing level during the follow-up. Also, although we could adjust the timing of the hearing outcome evaluation, it was not strictly the same for all subjects due to the limitations of a prospective study. Accordingly, a large group prospective study is required to confirm the present results.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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