

# Assessment of Vestibular and Oculomotor Function in Patients with Vestibular Migraine: A Preliminary Study

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## Research article

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# Abstract

**Background:** The purpose of the study is to assess the vestibular and oculomotor function in patients with vestibular migraine (VM). And we also investigate the relationship between test results and effectiveness of prophylactic medication.

**Methods:** We recruited 41 patients with VM. They were examined with vestibular-evoked myogenic potentials (VEMP), video head impulse test (vHIT) and video nystagmography (VNG), including spontaneous or positional nystagmus, gaze-evoked nystagmus, smooth pursuit and caloric irrigation testing. All VM patients were treated with prophylactic medications. The intensity of vertigo were evaluated with dizziness handicap inventory (DHI) before and after treatment. After 6 months, we evaluate the effectiveness of prophylactic medication. We analyzed the relationship between test results and effectiveness of prophylactic medication.

**Results:** In vestibular function test, 71% of VM patients showed abnormal result. 20% showed abnormal air-conducted cVEMP and 42% showed abnormal air-conducted oVEMP. 32% showed abnormal vHIT and 56% showed abnormal caloric irrigation test. The abnormal rate of oVEMP was significantly higher than cVEMP ( $p < 0.05$ ). And the abnormal rate of caloric irrigation test was significantly higher than vHIT ( $p < 0.05$ ). In oculomotor function test, 42% showed pathological result. The abnormal rate of oculomotor function test was significantly lower than vestibular function test ( $p < 0.05$ ). After 6 months follow-up, rate of good effectiveness was significantly higher in normal vestibular function test group compared with the abnormal vestibular function test group ( $p < 0.05$ ). Rate of good effectiveness was no statistically significant difference between normal oculomotor function test group and abnormal oculomotor function test group ( $p > 0.05$ ).

**Conclusions:** Abnormal vestibular and oculomotor function are commonly observed in VM patients. And VM patients with abnormal vestibular function have a weak effectiveness of prophylaxis medications.

## Background

Vestibular migraine (VM) is a common cause of attacks of episodic vertigo [1]. It can account for 7% of patients seen in dizziness clinics and 9% of patients seen in headache clinics [1]. Although the committee of the Bárány Society and a subcommittee of the International Headache Society (IHS) have developed a clearer criteria for VM [2, 3]. Diagnosis of vestibular migraine is challenging. Since the criteria for VM is based on clinical manifestations. And symptoms associated with vestibular migraine are varied. It is difficult that clinical diagnosis completely fulfill the diagnostic criteria of VM. And the pathophysiology of VM is not uncertain. Some studies reported that it was likely of a central nervous system origin [4, 5]. Other studies considered that peripheral vestibular was probably involved [6]. Therefore, clinical tests, such as vestibular function and oculomotor function test, would be helpful on VM understanding.

During the last decade, vestibular function test has evolved such that the semicircular canals and the otolith system [7]. Vestibular-evoked myogenic potentials (VEMP) is a useful

method for evaluating function from the otolith system [8]. And video head impulse test (vHIT) evaluates the semicircular canal function in response to high-frequency head movements and caloric irrigation test, and low-frequency head movements [9]. Recording and measurement of oculomotor is performed with video nystagmography (VNG) [7]. These tests have provided clinicians with useful diagnostic tools to identify dysfunctions of different vestibular pathways. However, there is not adequate assessment in VM patients.

In this study, we assess the vestibular and oculomotor function in patients with VM. And we also investigate the relationship between test result and effectiveness of prophylactic medication.

## Methods

### Participants

We recruited 41 patients with VM from the period between 2017 and 2019 (26 females, 15 males; mean age 49.3 years; range 19–76 years). They were diagnosed to VM according to the criteria of the committee of the Bárány Society and a subcommittee of the IHS [2, 3]. All patients were assessed using VEMP, vHIT and VNG (including spontaneous or positional nystagmus, gaze-evoked nystagmus, smooth pursuit, saccade test and caloric irrigation test). And all VM patients were treated with prophylactic medications. After 6 months, we evaluate the effectiveness of prophylactic medication. All VM patients were inquired the intensity of vertigo and completed the Chinese version of the Dizziness Handicap Inventory (DHI) questionnaire before and after treatment. And VM patients were then classified as good effectiveness (symptomatic improvement  $\geq 50\%$ ), partial effectiveness ( $30\% \leq$  symptomatic improvement  $< 50\%$ ) and poor effectiveness (symptomatic improvement  $< 30\%$ ).

### VEMP

VEMP recordings were performed with an evoked potential instrument (GN Otometrics EP200; version 6.2.1). 500 Hz air-conducted tone bursts were presented monaurally via a pair of calibrated insert earphones at an intensity of 100 dB nHL. We used the following stimulus profile: 2 ms rise time, 2 ms plateau time and 2 ms fall time. The stimulation rate was 5/s, with the analysis time for each response of 60 ms, and 100 repetitions per trial were delivered. The EMG signals were amplified and bandpass-filtered between 1 and 1000 Hz. In cVEMP, after the patients were laid supine, an active electrode was placed on the upper third of the sternocleidomastoid muscle. The forehead served as the site for the ground electrode. The electrode impedance was kept under 5 k $\Omega$ . During recording, patients were asked to elevate their heads. In oVEMP, an active electrode was placed on the face just inferior to each eye, around 1 cm below the center of the lower eyelid. The reference electrode was positioned on the cheek, about 1–2 cm below the corresponding active electrode, and the ground electrode was placed on the forehead. The electrode impedance was kept under 5 k $\Omega$ . During recording, the subject was instructed to look upward at a small fixed point approximately 30° at a distance of approximately 60 cm from the eyes. And the biphasic waveform were performed to confirm the reproducibility at least 3 times. Peak-to-peak amplitudes were calculated from the mean value of the replicate waveforms for each condition. The

asymmetry ratio (AR) = (Left amplitude - Right amplitude) / (Left amplitude + Right amplitude) × 100. In cVEMP, abnormal criteria is the AR > 20%. And in oVEMP, abnormal criteria is the AR > 30% [10].

## **vHIT**

The vHIT was recorded using the ICS Impulse system (Otometrics, Denmark). All horizontal and vertical canals were evaluated. The subject was instructed to gaze at a target that was 1.2 m away. First, calibration is performed. In each trial, the examiner stood behind the patients and performed head impulses by a small angle (10–20°) and an appropriate velocity (150–200°/s). And 20 impulses were recorded for each direction. The lowest and highest values of the normal gain were 0.8 and 1.2 at horizontal vHIT and 0.63 and 1.15 at vertical vHIT. Besides, a corrective saccades peak velocity > 100°/s was considered pathologic [11–13].

## **Videonystagmography**

Videonystagmography was performed using the Chart 200 VEG/ENG system (Otometrics, Denmark). Calibration with the patient seated was done as the first step. Oculomotor test battery including spontaneous or positional nystagmus, gaze-evoked nystagmus, smooth pursuit, saccade test and caloric irrigation test. The bithermal air caloric irrigations were performed with the patient in the supine position. Each ear were irrigated with a airflow of 8 L/min at 50°C and 24°C for seconds. Unilateral weakness (UW) making was based on Jongkee's formula. Abnormal criteria is the UW values ≥ 25% [14].

## **Statistical Analysis**

Chi-square or Fisher exact test was used to compare rate of abnormal vestibular and oculomotor tests. Statistical comparisons of symptomatic improvement in different test groups were made using the Chi-square or Fisher exact.  $p < 0.05$  was considered statistically significant. Statistical analysis were done by using SPSS software (version 19, SPSS Inc., Chicago, IL, USA).

## **Results**

### **Clinical characteristics of patients with vestibular migraine**

Among the 41 VM patients, 24 (59%) patients showed spontaneous vertigo, 7 (17%) had positional vertigo, 5 (12%) had head motion-induced vertigo, and 5 (12%) had unsteadiness. In most patients, severity of vestibular symptom was moderate to severe (DHI score > 30). Vestibular symptoms lasted less than 1 minute in 1 (2%) patients, 1 minute to less than 1 hour in 16 (39%) patients, 1 hour to less than 24 hours in 21 (51%) patients, and more than 24 hours in 3 (7%) patients. One or more migraine features with at least 50% of the vestibular episodes such as one sided location 32 (78%), pulsating quality 23 (56%), moderate or severe pain intensity 28 (68%), aggravation by routine physical activity 17 (42%), photophobia 16 (39%), phonophobia 18 (44%) or visual aura 7 (17%). Tinnitus and hearing loss were reported in 20 (49%) and 16 (39%) patients, respectively. The characteristics of VM patients are summarized in Table 1.

### **Vestibular and oculomotor function in VM patients**

In vestibular function test, 29(71%) VM patients showed abnormal result.8(20%) showed abnormal air-conducted cVEMP and 17(42%) had abnormal air-conducted oVEMP. In vHIT, Abnormal results were observed in 13(32%).Abnormal horizontal canal vHIT were recorded in 6(15%) patients and abnormal vertical canal vHIT were recorded in 11(27%) patients. In caloric irrigation test,23(56%) exhibited abnormal UW. The abnormal rate of oVEMP was significantly higher than cVEMP ( $p < 0.05$ ,Fig. 1). And the abnormal rate of caloric irrigation test was significantly higher than vHIT( $p \leq 0.05$ , Fig. 1).

In oculomotor function test, 17(42%) VM patients showed pathological result such as 4(10%) with spontaneous nystagmus,10(24%) with positional nystagmus,1(2%) with gaze-evoked nystagmus, and 7(17%) with smooth pursuit. The abnormal rate of oculomotor function test were significantly lower than vestibular function test ( $p \leq 0.05$ ).

## **Symptomatic improvement in VM patients at the follow-up**

After 6 months follow-up, 21(51%) VM patients reported a good effectiveness in their symptoms and 17(42%) reported a partial effectiveness in their symptoms while 3(7%) experienced poor effectiveness. Rate of good effectiveness was significantly higher in normal vestibular function test group compared with the abnormal vestibular function test group ( $p < 0.05$ , Table 2, Fig. 2). Rate of good effectiveness was no statistically significant difference between normal oculomotor function test group and abnormal oculomotor function test group( $p > 0.05$ , Table 3, Fig. 3).

Table 1  
The clinical characteristics of VM patients(n = 41).

Type	n(%)
Vestibular symptoms	
Spontaneous vertigo	24(59)
Positional vertigo	7(17)
Head motion-induced vertigo	5(12)
Unsteadiness	5(12)
Severity of vestibular symptom	
Mild(DHI ≤ 30)	7(17)
Moderate to severe(DHI > 30)	34(83)
Duration of episodes	
Lasting seconds	1(3)
Lasting minutes	16(39)
Lasting hours	21(51)
Lasting days	3(7)
Migraine featuresofthe vestibular episodes	
one sided location	32(78)
pulsatingquality	23(56)
moderate or severe pain intensity	28(68)
aggravation byroutine physical activity	17(42)
photophobia	16(39)
phonophobia	18(44)
visual aura	7(17)
Auditory symptoms	
Tinnitus	20(49)
Hearing loss	16(39)

Table 2  
Effectiveness of prophylaxis medications in different vestibular test group.

	n	good effectiveness(%)	partial effectiveness(%)	poor effectiveness(%)
Vestibular normal group	12	10(83)	2(17)	0
Vestibular abnormal group	29	11(38)	15(52)	3(10)

Table 3  
Effectiveness of prophylaxis medications in different oculomotor test group.

	n	good effectiveness(%)	partial effectiveness(%)	poor effectiveness(%)
Oculomotor normal group	24	14(58)	8(34)	2(8)
Oculomotor abnormal group	17	7(41)	9(53)	1(6)

## Discussion

VM is a distinct clinical entity that accounts for a high proportion of vestibular symptoms. Diagnosis of VM mainly depends on recurrent vestibular symptoms, a history of migraine, a temporal association between vestibular symptoms and migraine symptoms and exclusion of other reasons [2]. And vestibular symptoms is based on the Bárány society's classification of vestibular symptoms such as spontaneous vertigo, positional vertigo, visually-induced vertigo, head motion-induced vertigo and head motion-induced dizziness with nausea [15]. In our studies, more than half of VM patients are found spontaneous vertigo. 10–20% VM patients have other forms of vertigo. We can find that the most common vestibular symptom is spontaneous vertigo. Findings of most of studies are similar our results [1, 16, 17]. Although most of VM patients have moderate to severe vestibular symptoms. We still found some mild VM patients. This may be due to different measurements. In VM diagnostic criteria, vestibular symptoms are rated "moderate" when they interfere with but do not prohibit daily activities and "severe" if daily activities cannot be continued [2]. However, in our studies, vestibular symptoms is assessed with DHI. In VM, duration of episodes have been reported at varying lengths, ranging from seconds to days and most often between minutes to hours [18]. In our study, most VM patients were reported lasting minutes to hours. This is consistent with the previous literature [18]. Besides, different migraine features may occur during vestibular episodes, including unilaterality, pulsating quality, moderate to severe intensity, worsening with physical activity, photophobia, phonophobia and visual aura. In our study, the visual aura is infrequent in VM patients. Furman et al. reported that VM is more common in patients without aura than in patients with aura [19]. The view supports our study result. We also found that auditory symptoms like tinnitus and hearing loss have been found in 49% and 39% of VM patients. It is reported that the number of patients

with auditory symptoms will be more than doubles as the progression of VM[20]. However, hearing loss does not progress to profound levels[21].

VM is classified entirely on the basis of clinical features as reported by the patient[21]. However, VM patients can also find abnormal results in vestibular and oculomotor function test. In our study, most of VM patients have abnormal vestibular function test. It includes otolith function (VEMP) and semicircular canal function (vHIT and caloric irrigation test). In VEMP, we found that oVEMP has a higher abnormal rate. After testing 39 VM patients with cVEMP and oVEMP, Zaleski et al. reported that oVEMP may be especially vulnerable in patients with VM[22]. This is consistent with our result. In semicircular canal system, vHIT evaluated the semicircular canal function in response to high-frequency head rotation and caloric irrigation test, and low-frequency head rotation[9]. According to our study result, the abnormal rate of caloric irrigation test was higher than vHIT. It suggests that low-frequency semicircular canal function is vulnerable in VM patients. And the results in our study is also in accordance with the previous reports[23, 24]. Apart from vestibular function, oculomotor function is also an important sign in VM. In the symptom-free interval, nearly half of VM patients were found abnormal oculomotor tests in our study. Such signs include spontaneous nystagmus, positional nystagmus, gaze-evoked nystagmus and smooth pursuit. In previous reports, oculomotor abnormalities were reported in 8 to 60% of VM patients[6, 25–27]. There is a wide incidence of oculomotor abnormalities. It may be related to course of disease. Incidence rate of oculomotor abnormalities can increase over time[20]. Besides, oculomotor abnormalities is especially common during attacks of VM[18]. In addition, we further found that positional nystagmus and smooth pursuit are common in oculomotor abnormalities. It is similar to previous studies[20, 28]. These results related to mechanisms of VM. Apart from central mechanisms an inner ear involvement may explain abnormal findings. Trigeminovascular reflex-mediated vasodilatation of cranial blood vessels and subsequently plasma extravasation causing meningeal inflammation are the key reason and trigeminovascular system also innervates the inner ear[1, 19].

Medications used for migraine prophylaxis can be used to treat VM[18]. In our study, we found that half of VM patients reported good effectiveness in their symptoms through prophylactic medications after 6 months follow-up. However, there are still nearly half of VM patients that requiring medication continued or medication change (partial or poor effectiveness). How to identify the possible influencing factors before preventative medications in VM. Therefore, according to vestibular and oculomotor test results, we divided them into different subgroups. Compared with abnormal vestibular function group, we found that most of VM patients with normal vestibular function group were good effectiveness. It suggests that vestibular function abnormalities are closely related to the effectiveness of prophylaxis medication of VM. However, the effectiveness of prophylaxis medication was no significant difference between normal and abnormal oculomotor function test in VM patients. Kang et al. found that abnormal results of vHIT and caloric tests were closely related to the necessity for continued medication in VM patients at 6-month follow-up[29]. Besides, Jung et al. also report that there was a good drug responsiveness in VM patients with normal VEMP[30]. These results were similar to our study. It was proved that there is a weak effectiveness of prophylaxis medications in VM patients with abnormal vestibular function. But the

specific mechanism is not clear. Future basic studies are promising in the prophylaxis medication mechanisms of VM.

## Limitations

There are some limitations in this study. First, the number of VM patients and follow-up time were insufficient. The future study with a large samples and longer follow-up time need to further confirm our results. Second, different prophylaxis medications or a combination of multiple medications requires further evaluation. Last, future studies need to investigate the role of specific parameters in vestibular and oculomotor function tests.

## Conclusion

Abnormal vestibular and oculomotor function are commonly observed in VM patients. And VM patients with abnormal vestibular function have a weak effectiveness of prophylaxis medications.

## Abbreviations

VM

vestibular migraine; VEMP: vestibular-evoked myogenic potentials; vHIT: video head impulse test; VNG: videonystagmography; DHI: dizziness handicap inventory

## Declarations

### Acknowledgements

Not applicable.

### Authors' contributions

WF, JH, YB and NC designed the experiment, analyzed the data, and wrote the article. FH, DW, and YS collected data and prepared figures. YW guided the study. All authors have read and approved the final document.

### Funding

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### Availability of data and materials

The retrospective datasets are available by request from the corresponding author of this manuscript.

### Ethics approval and consent to participate

All subjects provided written informed consents to participate in this study. This study was approved by the Institutional Review Board of Xijing Hospital, Fourth Military Medical University.

### Consent for publication

Not applicable.

### Competing Interests

The authors declare that there is no conflict of interest.

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## Figures

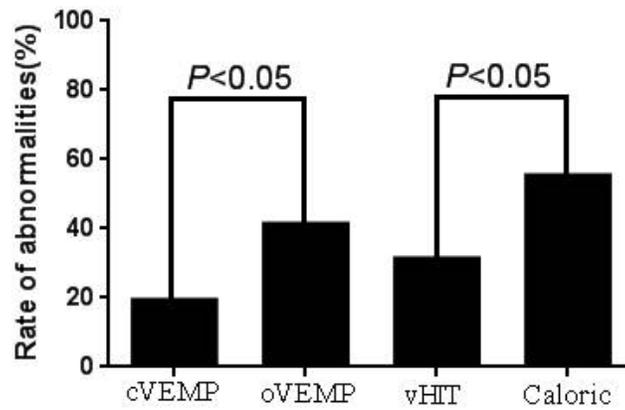


FIGURE 1|Comparison of abnormalities rate in VM patients with otolith tests(cVEMP and oVEMP) and canal tests(vHIT and caloric irrigation test).

### Figure 1

Comparison of abnormalities rate in VM patients with otolith tests(cVEMP and oVEMP) and canal tests(vHIT and caloric irrigation test).

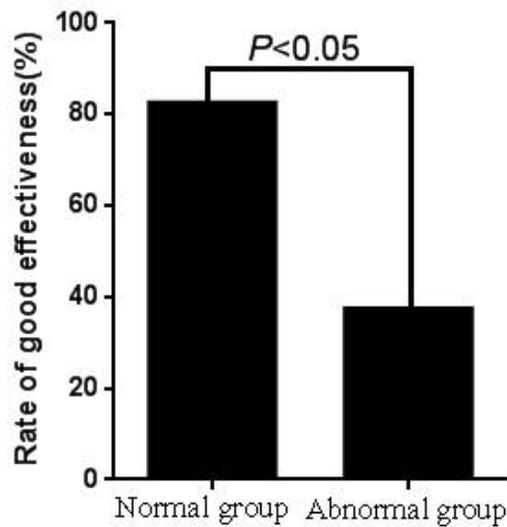
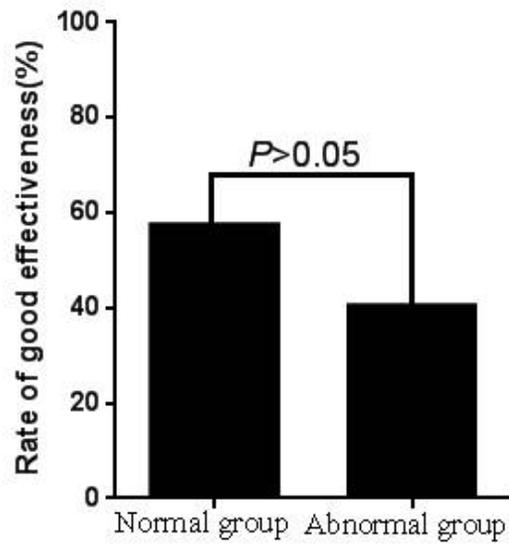


FIGURE 2|Comparison of VM patients with good effectiveness in normal vestibular test and abnormal test.

### Figure 2

Comparison of VM patients with good effectiveness in normal vestibular test and abnormal test.



**FIGURE 3** Comparison of VM patients with good effectiveness in normal oculomotor test and abnormal test.

**Figure 3**

Comparison of VM patients with good effectiveness in normal oculomotor test and abnormal test.