Presence and Clinical Value of Vestibular Symptoms in Migraine

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Abstract

Objective: To evaluate the correlations between the characteristics of vestibular symptoms and migraine, and to explore the clinical value of vestibular symptoms in patients with migraine.

Methods: Consecutive patients who visited the outpatient Department of Neurology and presented with a principal complaint of headache were enrolled. Patients with primary headache diagnosed according to International Classification of Headache Disorders (ICHD-3) were divided into the episodic migraine group (EM), chronic migraine group (CM) and tension-type headache group (TTH). Information on clinical symptoms was collected with a semistructured questionnaire, and the characteristics of the vestibular symptoms were recorded.

Results: 451 patients were recruited, with 235 EM, 187 CM and 29 TTH. The proportion of patients with vestibular symptoms in the migraine (108/422) was higher than that in the TTH (1/29), and the frequency of vestibular symptoms in the CM was higher. 2-8 days per month was the highest in the EM (131/235), and the migraine features and accompanying symptoms were the most typical. The highest proportion of patients with separate attacks of headache and vestibular symptoms was observed in the low-frequency headache (68.8%) (p<0.05). With an increase in headache frequency, the proportion of concurrent attacks of headache and vestibular symptoms gradually increased, a headache frequency of 8 days per month was a cut-off point for migraine.

Conclusion: Vestibular symptoms occur frequently in patients with CM, and the presence of concurrent attacks of vestibular symptoms and headache was significantly related to the headache frequency. A headache frequency of 8 days per month is recommended as a warning sign for CM. Patients with headaches 2-8 days per month have the most typical characteristics and should be selected for clinical trial.

Introduction

Headache and vestibular symptoms are common symptoms in neurology. The lifetime prevalence of migraine is 16% (1), and the lifetime prevalence of vertigo is 7% (2). In fact, concurrence of headache and vestibular symptoms was found in 3.2% of patients (3). Studies have found that migraine is more common than other primary headache diseases with episodic vestibular symptoms or vestibular diseases (such as benign paroxysmal positional vertigo, vestibular neuritis, and Meniere's disease) (4, 5, 6). Although the International Headache Society and the International Vertigo Society proposed the occurrence and diagnostic criteria for vestibular migraine in recent years, the standard is still in the appendix of the International Classification of Headache Disorders (ICHD-3) (7).

The relationship between vestibular symptoms and migraine is complex and extends, far beyond the diagnosis of vestibular migraine (8, 9). At present, there are few studies on migraine with dizziness or vertigo as related symptoms, and there are few reports on the temporal relationship between migraine and vestibular symptoms; such a temporal relationship is likely to affect the mechanistic study of the
correlation between vestibular symptoms and migraine. Vestibular symptoms are common side effects of medications taken to prevent migraines, such as antihypertensives and anticonvulsants (10). We need to fully understand the relationship between vestibular symptoms and migraine to guide treatment.

Therefore, the purpose of this study was to analyze the prevalence of vestibular symptoms in patients with episodic migraine, chronic migraine and tension-type headache; to study the correlations between vestibular symptoms and migraine characteristics; to explore the clinical value of vestibular symptoms in migraine; and to provide a clinical basis for further understanding the pathogenesis of migraine.

Patients And Methods

Patients

Consecutive patients presenting with a principal complaint of headache from Jan.2019 to Jan.2020 at the headache clinic of the Department of Neurology of the First Affiliated Hospital of Chongqing Medical University were enrolled. To avoid statistical bias due to multiple visits by 1 individual, only the first visit by each patient during this time frame was recorded. The diagnosis of migraine was based on the ICHD-3, and the diagnosis of TTH was based on the relatively more strict criteria included in the ICHD-3. The exclusion criteria adopted for all subjects were as follows: 1. age less than 16 years; 2. age at migraine onset more than 60 years; 3. migraine complicated by other secondary headache diseases (such as hypertension, stroke, epilepsy, mental illness, head trauma, cancer, and sinusitis); 4. pregnancy; and 5. migraine complicated by other vestibular diseases (such as vestibular migraine, vestibular neuritis, benign paroxysmal positional vertigo, Meniere's disease, and vestibular paroxysmal disorder). The classification of vestibular symptoms was based on the definition of vestibular symptoms in vestibular migraine, including 1. spontaneous vertigo including (1) internal vertigo (a false sensation of self-motion); and (2) external vertigo (a false sensation that the visual surroundings are spinning or flowing); 2. positional vertigo, occurring after a change in head position; 3. visually induced vertigo, triggered by a complex or large moving visual stimulus; 4. head-motion-induced vertigo, occurring during head motion; and 5. head-motion-induced dizziness with nausea (dizziness characterized by a sensation of disturbed spatial orientation) (7). The ethics board of the hospital approved the study, and all patients were informed about the purpose of the study and provided informed consent prior to participation.

Methods

Each patient completed a semistructured questionnaire under the guidance of a neurologist. The questionnaire consisted of three parts: the first part obtained information on demographics (personal situation and family history); the second part obtained information on migraine, including the age of onset, course of migraine, triggers, duration of headache (divided into four stages: <1 hour, 1–24 hours, 24–72 hours, >72 hours), frequency of attacks (days of attacks per month), intensity of pain on a 1–10 Visual Analog Scale (VAS), accompanying symptoms and the use of acute medication; and the third part obtained information on vestibular symptoms, including the age of onset, course, frequency of attacks, and temporal relationship with headache attacks (three answers: always, sometimes, never) (11, 12). The
patients were divided into three groups: the episodic migraine group (EM), chronic migraine group (CM) and tension-type headache group (TTH).

**Statistical analysis**

SPSS 22.0 software was used for the statistical analysis. Continuous variables are expressed as the mean ± standard deviation and were compared using one-way ANOVA with the Student–Newman–Keuls (SNK) post-hoc test. Categorical variables are presented as the frequencies (N,%), and the chi-squared test was used to analyze the differences between groups. When the sample size was less than 40, Fisher’s exact test was performed. All statistical analyses were two-sided, and statistical significance was defined as p < 0.05.

**Results**

A total of 726 headache patients visited during the study period: 20 patients who had incomplete data, 18 patients who had other primary headaches, 93 patients who had secondary headaches, 15 patients who had unclear diagnoses, 41 patients who had migraines complicated by conditions listed in the exclusion criteria, and 88 patients who had other vestibular diseases were excluded. A total of 451 patients were included in the study groups. In total, 75.8% of the patients (342/451) were female, and the study population ranged in age from 16 to 83 years old (43.38 ± 13.94). With regard to headache classification, 235 (52.1%) patients had EM, 187 (41.5%) patients had CM, and 29 (6.4%) patients had TTH (Fig. 1).

1. Comparative analysis of EM, CM and TTH

The basic conditions of the patients with EM, CM and TTH are shown in Table 1. The ages of the patients with CM and TTH were older than that of the patients with EM (p < 0.05), but there was no significant difference in the sex ratio. The intensity of pain was mainly mild in patients with TTH and that in patients with migraine was moderate to severe (p < 0.05). The proportions of patients with a family history of headache, a family history of vestibular symptoms, migraine features and the associated symptoms were higher in the migraine group than in the TTH (p < 0.05). Additionally, the proportions of patients who had vestibular symptoms and used acute medication were significantly higher in the CM than in the EM (p < 0.05).
Table 1
Demographics and clinical characteristics of patients with migraine and tension-type headache.

|                                | EM (235 patients) | CM (187 patients) | TTH (29 patients) |
|--------------------------------|-------------------|-------------------|-------------------|
| Demographics                   |                   |                   |                   |
| Age (mean ± SD)                | 40.07 ± 13.24     | 46.51 ± 13.25     | 47.24 ± 14.18     |
| Female sex (%)                 | 174 (74.0%)       | 149 (79.7%)       | 19 (65.5%)        |
| Family history (%)             |                   |                   |                   |
| Migraine (%)                   | 159 (67.7%)       | 141 (70.1%)       | 5 (17.2%)         |
| Vestibular symptoms (%)        | 73 (31.1%)        | 50 (26.7%)        | 0 (0%)            |
| Migraine features (%)          |                   |                   |                   |
| Unilateral location (%)        | 92 (38.7%)        | 69 (36.9%)        | 5 (17.2%)         |
| Pulsating quality (%)          | 74 (31.5%)        | 54 (28.9%)        | 0 (0%)            |
| Aggravation by physical activity | 144 (61.3%)   | 134 (71.7%)       | 0 (0%)            |
| Intensity of pain (VAS)        |                   |                   |                   |
| 0–3 points (%)                 | 9 (3.8%)          | 5 (2.7%)          | 20 (72.4%)        |
| 4–6 points (%)                 | 121 (51.5%)       | 90 (48.1%)        | 8 (27.6%)         |
| 7–10 points (%)                | 105 (44.7%)       | 92 (49.2%)        | 0 (0%)            |
| Accompanying symptoms (%)      |                   |                   |                   |
| Nausea (%)                     | 119 (50.6%)       | 100 (53.5%)       | 0 (0%)            |
| Vomiting (%)                   | 59 (25.1%)        | 42 (22.5%)        | 0 (0%)            |
| Phonophobia (%)                | 101 (43%)         | 88 (47.1%)        | 1 (3.4%)          |
| Photophobia (%)                | 64 (27.2%)        | 45 (24.1%)        | 0 (0%)            |
| Nausea or vomiting (%)         | 123 (52.3%)       | 105 (56.1%)       | 0 (0%)            |
| Phonophobia and photophobia (%)| 49 (20.9%)        | 34 (18.2%)        | 0 (0%)            |
| Vestibular symptoms (%)        | 49 (20.9%)        | 59 (31.6%)        | 1 (3.4%)          |

Statistical significance: ▲ p < 0.05 vs. EM; ▲ p < 0.05 vs. TTH.
2. Comparative analysis of low-frequency, medium-frequency and high-frequency headaches in EM

According to the frequency of headaches, the patients with EM were divided into a low-frequency group (≤ 1 day per month), a medium-frequency group (2–8 days per month) and a high-frequency group (9–14 days per month), the number of people in the medium-frequency was the most (55.7%). No differences were observed among the three groups in terms of age, sex ratio, family history, vestibular symptoms, and migraine and vestibular symptoms age of onset and course. However, migraine features (unilateral location, pulsating quality, aggravation by physical activity) and accompanying symptoms were the most typical in the medium-frequency group, especially when compared with the low-frequency group (p < 0.05). In the low-frequency group, the intensity of pain was moderate (72.1%), while the intensity of pain was severe in the medium-frequency and high-frequency groups (p < 0.05). It was also found that the use of acute medication increased with the increasing frequency of headaches (Table 2).
Table 2
Demographics and clinical characteristics of patients with episodic migraine

|                           | EM (235 patients) |
|---------------------------|-------------------|
| Frequency of attacks      | ≤ 1 d/m (61 patients) | 2–8 d/m (131 patients) | 9–14 d/m (43 patients) |
| Age (years)               | 42.33 ± 14.62     | 39.60 ± 13.59          | 42.83 ± 13.89          |
| Female sex (%)            | 46 (75.4%)        | 99 (75.6%)             | 29 (67.4%)             |
| Family history (%)        |                  |                    |                          |
| Migraine                  | 37 (60.7%)        | 92 (70.2%)            | 30 (69.8%)             |
| Vestibular symptoms       | 21 (34.4%)        | 39 (29.8%)            | 13 (30.2%)             |
| Migraine onset (years)    | 29.10 ± 11.15     | 28.92 ± 11.13         | 29.44 ± 13.37          |
| Course of migraine (years)| 12.89 ± 11.36     | 11.91 ± 10.06         | 11.58 ± 11.67          |
| Vestibular symptoms onset (years)| 38.50 ± 15.37  | 39.14 ± 12.80         | 32.00 ± 13.93          |
| Course of vestibular symptoms (years)| 5.16 ± 6.53 | 7.37 ± 8.27            | 9.29 ± 10.36          |
| Migraine features (%)     |                  |                    |                          |
| Unilateral location       | 18 (29.5%)        | 61 (46.6%)            | 12 (27.9%)             |
| Pulsating quality         | 11 (18.0%)        | 52 (39.7%)            | 11 (25.6%)             |
| Aggravation by physical activity | 30 (49.2%)    | 90 (68.7%)            | 24 (55.8%)             |
| Intensity of pain (VAS)   |                  |                    |                          |
| 0–3 points                | 3 (4.9%)          | 5 (3.8%)              | 1 (2.3%)               |
| 4–6 points                | 44 (72.1%)        | 58 (44.3%)            | 19 (44.2%)             |
| 7–10 points               | 14 (23.0%)        | 68 (51.9%)            | 23 (53.5%)             |
| Accompanying symptoms (%) |                  |                    |                          |
| Nausea                    | 24 (39.3%)        | 79 (60.3%)            | 16 (37.2%)             |
| Vomiting                  | 10 (16.4%)        | 40 (30.5%)            | 9 (20.9%)              |
| Phonophobia               | 19 (31.1%)        | 64 (48.9%)            | 18 (41.9%)             |

Statistical significance: ◁ p < 0.05 vs. ≤ 1 d/m; ▲ p < 0.05 vs. 9–14 d/m.
|                          | EM (235 patients) |
|--------------------------|-------------------|
| Photophobia              | 10(16.4%)         | 41(31.3%)       | 13(30.2%) |
| Nausea or vomiting       | 25(41.0%)         | 80(61.1%)       | 18(41.9%) |
| Phonophobia and photophobia | 7(11.5%)         | 32(24.4%)       | 10(23.3%) |
| Vestibular symptoms (%)  | 16(26.2%)         | 26(19.8%)       | 7(16.3%)  |
| Acute medication (%)     | 38(62.3%)         | 89(67.9%)       | 32(74.4%) |

Statistical significance: p < 0.05 vs. ≤1 d/m; p < 0.05 vs. 9–14 d/m.

3. Comparative analysis of the two frequency groups in CM patients

We further divided CM patients into two groups according to the frequency of headache: 15–29 days per month and persistent headache (30 days per month). No significant difference in demographics, family history, clinical features, vestibular symptoms or the use of acute medication was observed between the two groups (Table 3).
| Demographics and clinical characteristics of patients with chronic migraine. |
|---------------------------------|------------------|------------------|
| **CM**                         | **15–29 d/m**    | **30 d/m**       |
| **Age (years)**                | **48.60 ± 12.14**| **47.14 ± 12.36**|
| **Female sex (%)**             | **53(77.9%)**    | **96(80.7%)**    |
| **Family history (%)**         |                  |                  |
| Migraine                       | **49(72.1%)**    | **82(68.9%)**    |
| Vestibular symptoms            | **20(29.4%)**    | **30(25.2%)**    |
| Migraine onset (years)         | **31.58 ± 12.14**| **30.68 ± 11.62**|
| Course of migraine (years)     | **16.98 ± 11.32**| **15.55 ± 12.45**|
| Vestibular symptoms onset (years) | **33.85 ± 11.36**| **37.07 ± 12.43**|
| Course of vestibular symptoms (years) | **10.33 ± 9.73** | **11.27 ± 9.92**|
| Migraine features (%)          |                  |                  |
| Unilateral location            | **24(35.3%)**    | **45(37.8%)**    |
| Pulsating quality              | **21(30.9%)**    | **33(27.7%)**    |
| Aggravation by physical activity| **51(75.0%)**    | **83(69.7%)**    |
| Intensity of pain (VAS)        |                  |                  |
| 0–3 points                     | **0(0.0%)**      | **5(4.2%)**      |
| 4–6 points                     | **35(51.5%)**    | **55(46.2%)**    |
| 7–10 points                    | **33(48.5%)**    | **59(49.6%)**    |
| Accompanying symptoms (%)      |                  |                  |
| Nausea                         | **35(51.5%)**    | **65(54.6%)**    |
| Vomiting                       | **16(23.5%)**    | **26(21.8%)**    |
| Phonophobia                    | **33(48.5%)**    | **55(46.2%)**    |
| Photophobia                    | **18(26.5%)**    | **27(22.7%)**    |
| Nausea or vomiting             | **38(55.9%)**    | **67(56.3%)**    |
| Phonophobia and photophobia    | **14(20.6%)**    | **20(16.8%)**    |
4. Categories and comparison of vestibular symptoms

The 70–85% prevalence of vestibular symptoms found in the present study includes all categories of vestibular symptoms described by the Bárány Society’s Classification of Vestibular Symptoms (9, 13). We classified the vestibular symptoms of 108 patients with EM and CM. Vertigo accounted for the smallest proportions of vestibular symptoms in the two groups (8.9%, 14.3%, respectively), while dizziness and postural symptoms accounted for the highest proportions (42.3%, 41.6%, respectively), followed by vestibulo-visual symptoms. However, there was no significant difference between the two groups (Fig. 2).

5. The temporal relationship between vestibular symptoms and headache in each headache frequency group

In migraine patients, we analyzed the temporal relationship between vestibular symptoms and headache in each group according to the frequency of headache. We found that the incidence of vestibular symptoms separate from headache was the highest in patients with a low frequency of headaches (68.8%) (p < 0.05); with an increase in headache frequency, the frequency of concurrent vestibular symptoms and headache increased, especially in CM (p < 0.05) (Table 4).

| Migraine with vestibular symptoms | ≤ 1 day/month (16 patients) | 2–8 days/month (26 patients) | 9–14 days/month (7 patients) | 15–29 days/month (22 patients) | 30 days/month (37 patients) |
|----------------------------------|------------------------------|------------------------------|-----------------------------|-------------------------------|----------------------------|
| Vestibular symptoms during migraine attacks (%) | Never 11 (68.8%) | 9 (34.6%)* | 1 (14.3%)* | 4 (18.2%)* | 8 (21.6%)* |
| | Sometimes 2 (12.5%) | 6 (23.1%) | 2 (28.6%) | 6 (27.3%) | 10 (27.0%) |
| | Always 3 (18.8%) | 11 (42.3%) | 4 (57.1%) | 12 (54.5%)* | 19 (51.4%)* |

Statistical significance: * p < 0.05 vs. ≤1 day/month.

To further analyze the temporal relationship between vestibular symptoms and headache and whether there is a cut-off point for frequency, patients were divided into four groups according to headache frequency.
frequency (<8 days per month, 8–14 days per month, 15–29 days per month and 30 days per month). We found that the highest proportion of patients with vestibular symptoms separate from headache was the group with a headache frequency <8 days per month (p < 0.05). This group had the lowest proportion of patients with concurrent vestibular symptoms and headache (p < 0.05). There was no difference among the three groups with headache frequencies >8 days per month. Moreover, when headache and vestibular symptoms occurred at the same time, the course of vestibular symptoms gradually increased with an increase in headache frequency (p < 0.05). Compared with patients with a headache frequency less than 8 days per month, the course of headache was significantly longer in patients with persistent daily pain (p < 0.05) (Table 5).
Table 5
The temporal relationship between vestibular symptoms and headache in each headache frequency group.

| Migraine with vestibular symptoms | <8 days/month | 8–14 days/month | 15–29 days/month | 30 days/month |
|----------------------------------|--------------|----------------|-----------------|--------------|
| Vestibular symptoms during migraine attacks (%) | (39 patients) | (10 patients) | (22 patients) | (37 patients) |
| Never | 19 (48.7%) | 1 (10.0%)* | 4 (18.2%)* | 8 (21.6%)* |
| Family history (%) | | | | |
| Migraine | 12 (63.2%) | 1 (100%) | 2 (50.0%) | 4 (50.0%) |
| Vestibular symptoms | 8 (42.1%) | 0 (0%) | 2 (50.9%) | 3 (37.5%) |
| Migraine onset (years) | 33.2 ± 14.89 | 31.00 | 36.37 ± 10.43 | 36.32 ± 11.01 |
| Course of migraine (years) | 15.58 ± 10.67 | 13.00 | 16.23 ± 9.06 | 18.10 ± 8.98 |
| Vestibular symptoms onset (years) | 39.04 ± 16.32 | 39.00 | 38.07 ± 12.43 | 39.67 ± 12.72 |
| Course of vestibular symptoms (years) | 5.63 ± 6.64 | 5.00 | 8.23 ± 8.01 | 8.34 ± 10.26 |
| Sometimes | 9 (23.1%) | 2 (20.0%) | 6 (27.3%) | 10 (27.0%) |
| Family history (%) | | | | |
| Migraine | 5 (55.6%) | 1 (50.0%) | 4 (66.7%) | 5 (50.0%) |
| Vestibular symptoms | 3 (33.3%) | 1 (50.0%) | 3 (50.0%) | 4 (40.0%) |
| Migraine onset (years) | 29.05 ± 4.72 | 28.95 ± 13.54 | 25.5 ± 5.54 | 29.15 ± 12.42 |
| Course of migraine (years) | 12.13 ± 6.06 | 11.50 ± 5.47 | 18.50 ± 7.36 | 17.03 ± 10.58 |
| Vestibular symptoms onset (years) | 34.24 ± 4.03 | 33.00 ± 5.66 | 39.17 ± 9.03 | 38.65 ± 12.72 |
| Course of vestibular symptoms (years) | 5.45 ± 6.64 | 7.50 ± 8.32 | 6.67 ± 5.64 | 8.03 ± 5.27 |
| Always | 11 (28.2%) | 7 (70.0%)* | 12 (54.5%)* | 19 (51.4%)* |

Statistical significance: *p < 0.05 vs. <8 days/month.
|                                | Migraine with vestibular symptoms |
|--------------------------------|-----------------------------------|
|                                | (108 patients)                    |

| Family history (%)            |                                   |
|--------------------------------|-----------------------------------|
| Migraine                       | 6(54.5%) 4(57.1%) 7(58.3%) 10(51.4%) |
| Vestibular symptoms            | 4(36.4%) 2(28.6%) 4(33.3%) 5(26.3%) |

| Migraine onset (years)         | 27.71 ± 6.36 28.05 ± 8.34 26.65 ± 10.03 28.63 ± 10.31 |
| Course of migraine (years)     | 9.43 ± 10.65 11.35 ± 9.13 13.92 ± 9.16 20.05 ± 9.43* |
| Vestibular symptoms onset (years) | 30.86 ± 11.02 30.15 ± 9.23 28.75 ± 11.51 33.42 ± 11.18 |
| Course of vestibular symptoms (years) | 4.38 ± 2.83 10.08 ± 9.34* 11.66 ± 6.91* 15.79 ± 10.35* |

Statistical significance: *p < 0.05 vs. <8 days/month.

**Discussion**

The association between vestibular symptoms and migraine has been established in previous studies (9, 14, 15), which led the International Headache Society and the International Vertigo Society to propose research criteria for vestibular migraine (16). Our previous studies showed that 10% of migraine patients fulfilled the research criteria for vestibular migraine (11, 17). Another clinical-based study found that 72% of migraine patients reported dizziness as a symptom associated with migraine attacks (18). A recent meta-analysis also described the relationship between vestibular symptoms and migraine, but there was no clear conclusion (15). In the present study, the criteria may have been too strict to cover the full range of migraine and vestibular symptoms.

Previous studies have found a prevalence of dizziness or vertigo ranging from 12–72% among patients with migraine (8, 18, 19, 20). However, patients with vestibular migraine were not excluded. To further analyze the relationship between vestibular symptoms and headache, we did not include patients with vestibular migraine in this study. Even after this exclusion, the results still show that there is an association between migraine and vestibular symptoms, which is more common in patients with chronic headache; this finding is consistent with the results of previous studies (8, 9). However, the chronicity of migraine was not accounted for in the proposed vestibular migraine criteria (7, 9), and it is poorly explored by studies on the topic (9, 21, 22). The correlation between vestibular symptoms and headache needs to be further researched.

In drug clinical trials, the choice of the frequency of headache used to define episodic migraine in trials of new drugs has always been a difficult problem. Some clinical trials chose a headache frequency from 3
to 8 days per month (23), some chose from 1 to 6 days per month (24), and some chose from 2 to 8 days per month (25). However, there is no relevant clinical research indicating the number of days that should be selected as the standard, the number of days that would be appropriate to select based on the study design, and the number of days that is the most common frequency among patients in the clinical setting. In our study, we found that the frequency of headache was 2–8 days per month in approximately 55.7% of patients with episodic migraine and the headache characteristics and accompanying symptoms in this group of patients were the most typical. If this group of patients is selected for drug clinical trials, the therapeutic effects will be easily comparable, and the results will be more clinically applicable than if patients in other frequency groups are selected.

The estimated prevalence of chronic migraine worldwide ranges from 0.9 to 5%, and approximately 2.5% of patients with episodic migraine progress to chronic migraine each year (26, 27). A study found that patients with episodic migraine were most likely to progress to chronic migraine if they had a high frequency of migraine attacks (9–14 days per month) (28). While the chronicity of migraine has been established, few studies have examined whether there are differences in clinical characteristics based on headache frequency. In our study, patients were divided into two groups according to headache frequency, and it was found that there was no significant difference in clinical characteristics between patients with headaches 15–29 days per month and those with persistent daily pain (30 days per month). This supported the established chronicity of migraine, and chronic migraine and episodic migraine patients were different not only in terms of the number of days with migraine, but also in terms of fundamental pathophysiological characteristics.

In our study, to analyze the temporal relationship between vestibular symptoms and headache, patients were divided into three groups, and it was found that the frequency of concurrent attacks of vestibular symptoms and headache increased with increasing headache frequency. After further investigation of headache frequency, a cut-off point was found (8 days per month). A significant difference was observed in the temporal relationship between vestibular symptoms and headache before and after this point. However, there was no significant difference between patients with a headache frequency between 8 and 29 days per month and those with persistent daily pain, which may be related to the critical cut-off value for chronic migraine.

Chronic migraine was proposed in 1994 (29). From 1988 to 2018, when the Classification Committee of the International Headache Society published the diagnostic criteria for a series of headache diseases, including migraine, the chronic migraine was defined as a headache frequency ≥ 15 days per month, while migraine-like headache attacks were defined as a headache frequency ≥ 8 days per month for at least three months (7, 30–33). However, recent studies have proposed that a headache frequency ≥ 8 days per month is the diagnostic criterion for chronic migraine (34). In our study, we also found that 8 days was a warning sign. Whether vestibular symptoms such as allodynia are a sign of chronic migraine needs to be confirmed by basic research.
Patients with migraine are often found to have a vestibular disorder, but the mechanisms underlying the pathogenesis of vestibular symptoms and migraine in patients with vestibular migraine, brainstem aura migraine, and benign recurrent vertigo are still unclear. Is the pathophysiology of vestibular symptoms and migraine independent in migraine patients without these diseases? Previous studies suggested that the etiology of vestibular symptoms in migraine patients may be related to the overlap of the trigeminal nerve and the vestibular pathway (35). Our previous animal experiments found behavioral manifestations of vestibular injury in chronic migraine models; the development of vestibular injury was consistent with the trend in the development of allodynia, and we observed that the structure of the vestibular afferent terminal organs in a chronic migraine rat model was preserved (36). In addition, the activation of neurons in the spinal trigeminal nucleus and vestibular nucleus in the animal model of chronic migraine, and further, the activation of the trigeminal nucleus in the chronic migraine model were mainly due to the activation of the vestibular nucleus mediated by the spinal trigeminal nucleus (36). These studies suggested that the vestibular disorders associated with chronic migraine may be due to the activation of the trigeminal neurovascular system caused by the activation of the vestibular nucleus during chronic migraine. Moreover, migraine neurotransmitters play a role in the modulation of vestibular neuron activity (37). It was confirmed that CGRP in the trigeminal ganglion could alleviate the damage to vestibular function in rats, suggesting that anti-CGRP therapy could play an important role in the treatment of CM-related vestibular symptoms (35). The limitations of the present study include its preliminary nature, and we need to design a more in-depth study to explore the pathophysiology of vestibular symptoms in migraine.

**Conclusions**

Vestibular symptoms are very common in patients with migraine, especially in patients with chronic migraine. The presence of concurrent attacks of vestibular symptoms and headache was significantly related to the frequency of headache. In particular, a headache frequency of 8 days per month is recommended as a warning sign for chronic migraine. Patients with headache attack frequencies of 2–8 days per month should be enrolled in drug clinical trials to better observe the treatment effects.

**Abbreviations**

ICHД-3: International Classification of Headache Disorders; EM: episodic migraine; CM: chronic migraine; TTH: tension-type headache; VAS: Visual Analog Scale; ANOVA: analysis of variance; SNK: Student–Newman–Keuls; CGRP: Calcitonin gene-related peptide; SUNCT: short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing; OSAHS: obstructive sleep apnea-hypopnea syndrome; PCI: posterior circulation ischemia; RCVS: reversible cerebral vasoconstriction syndrome; EM: episodic migraine; CM: chronic migraine; TTH: tension-type headache.

**Declarations**

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**Authors’ contributions**

JL, QP and JYZ designed the study. JL, QP, YLF, YZ, XPF and JZT collected and analyzed the data. JL, QP, YXZ and JYZ drafted the manuscript.

Critically revising the article was done by JL, QP, YXZ and JZT. All authors read and approved the final manuscript.

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**Availability of data and materials**

The data used and analyzed in this article are available from on reasonable request.

**Ethics approval and consent to participate**

In this study were approved by the First Affiliated Hospital of Chongqing Medical University.

**Consent for publication**

Not applicable.

**Competing interests**

The authors declare that they have no conflict of interest.

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**Figures**

Figure 1

726 consecutive headache patients were questioned at the headache outpatient clinic (Jan. 2019–Jan. 2020)

Excluded

- 4 patients: hypnic headache, PCI
- 6 patients: RCVS
- 7 patients: cervicogenic headache, headache due to rhinosinusitis
- 8 patients: occipital neuralgia
- 11 patients: hypertension
- 13 patients: cold headache, cluster headache
- 14 patients: algopsychia
- 15 patients: unclear diagnosis
- 19 patients: incomplete data

1 patient each (SUNCT, primary stabbing headache, fibromyalgia, postoperative pituitary adenoma, hyperthyroidism, vascular headache, epilepsy, primary cough headache, meningitis, autoimmune encephalitis, traumatic headache, OSAHS, infectious mononucleosis, alcohol-induced headache, neuropathic pain after operation on left eye, Chiari malformation)

2 patients each (climacteric syndrome, prosopalgia, temporal arteritis, left mandibular arthritis)

- EM: 333 patients
  - excluded 98 patients
  - EM: 235 patients
- CM: 214 patients
  - excluded 27 patients
  - CM: 187 patients
- TTH: 33 patients
  - excluded 4 patients
  - TTH: 29 patients
Figure 2