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Original Article

The Effectiveness of Medical Prophylactic Treatment on Vestibular Migraine and Its Effect on the Quality Of Life

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OBJECTIVES: The aim of the present study was to determine the efficacy of propranolol treatment in patients with vestibular migraine by the Visual Analog Scale, Dizziness Handicap Inventory (DHI), Vertigo Symptom Scale, and Vestibular Disorders Activities of Daily Living Scale (VADL) and its effect on the quality of life.

MATERIALS and METHODS: The study population consisted of 38 patients with vertigo/dizziness who underwent routine evaluation and vestibular examinations, were diagnosed with definitive vestibular migraine, and received the same medical treatment protocol (propranolol). The questionnaires and scales that were applied to the patients before and after treatment were evaluated. The results were evaluated with 95% confidence interval, and $p<0.05$ was accepted as statistically significant.

RESULTS: The mean age of the patients was 47.55 (18-75) years, and 27 (71%) patients were female, and 11 (29%) were male. The mean total scores of the DHI before and after treatment were 50.21±22.39 (range: 8-92) and 9.31±9.86 (range: 0-58), respectively ($p<0.001$). The degree of disability after treatment was low in all patients ($p<0.001$). The total scores of the VADL before and after treatment were 186.63±79.65 (range: 32-280) and 55.52±51.89 (range: 28-273), respectively ($p<0.001$). There was no correlation between these two scales ($p=0.235$).

CONCLUSION: To our knowledge, this is the first study to evaluate both the efficacy of propranolol treatment and its effects on the quality of life in vestibular migraine. The severity, frequency, and number of attacks and disability scores were reduced, and the quality of life was improved in patients with vestibular migraine with propranolol treatment.

KEYWORDS: Vestibular migraine, vertigo, dizziness, propranolol, quality of life

INTRODUCTION

Vestibular migraine is a form of episodic vertigo associated with migrainous symptoms. Although it is a common cause of dizziness and vertigo, it is not easy to diagnose because of the variety of different symptoms [1]. Patients may have spontaneous or positional vertigo, dizziness, and episodic vertigo attacks due to head movements or visual stimuli. The majority of cases have positional vertigo that is different from benign paroxysmal positional vertigo (BPPV). There is also a strong association with psychiatric disorders, anxiety and depressive disorders [2]. This variety of symptomatology results in patients being treated based on different diagnoses in different clinics. In fact, vestibular migraine should be considered secondarily after BPPV in the differential diagnosis of patients presenting with vertigo/dizziness [3].

Several studies have reported the coexistence of migraine and vertigo [4-6], which was initially named by Boenheim [7] as "vestibular migraine." Thereafter, it was defined as "migraine-associated vertigo/dizziness" [8, 9], "migraine-related vestibulopathy" [10, 11], and "migrainous vertigo" [12]. Eventually, the definition of vestibular migraine was revisited by Dieterich and Brandt in 1999[6]. Although the diagnostic criteria of vestibular migraine were initially identified in 2001, a more accurate description of the disease was reported

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in the Consensus Report of the Bárány Society and the International Headache Society in 2012 [13].

Vestibular migraine, which has a prevalence of 3.2% [1], is 1.5-5 times more common in women than in men [14]. In vestibular migraine, episodic vertigo attacks show a peak in men in the fourth decade and in the third and fifth decades in women.

Currently, there is no optimal accepted method for treatment. First-line treatments involve lifestyle and dietary changes. Propranolol is a non-selective beta-blocker that is primarily used to treat hypertension. According to the Cochrane review, there is a high degree of evidence that propranolol is an effective prophylactic drug for migraine headache [9]. However, there are insufficient data regarding its efficacy in the prophylaxis of vestibular migraine. Therefore, the aim of the present study was to evaluate the efficacy of propranolol treatment in patients with vestibular migraine using the Visual Analog Scale (VAS), Dizziness Handicap Inventory (DHI), Vertigo Symptom Scale (VSS), and Vestibular Disorders Activities of Daily Living Scale (VADL) and to determine the improvement in the quality of life (QOL).

MATERIALS AND METHODS

Study Design

Patient records between January 2015 and September 2017 were examined. The study was approved by the local institutional ethics committee (19.12.2017-11).

Patients

The study population consisted of 38 patients with vertigo/dizziness who underwent routine evaluation and vestibular examinations, were diagnosed with definitive vestibular migraine, and received the same medical treatment protocol. The number of patients met the calculated sample size at α=0.05, d=0.60 determined by pre-study power analysis, and the power of the study was determined as 83%. VAS, VSS, DHI, and VADL were applied to patients before and after treatment. The pre- and post-treatment values of these questionnaires and scales were compared, and the correlations between them were evaluated.

Medical Prophylactic Treatment Protocol

Propranolol hydrochloride (Dideral®; Sanofi-Synthelabo, Istanbul, Turkey) treatment was started at 20 mg twice a day in patients who had not received any treatment for previous complaints. After 1 month, the dose was increased to 40 mg or 60 mg twice a day in patients ≤60 kg or >60 kg in body weight, respectively.

Duration of Symptoms

The patients were asked about the duration of symptoms before and after treatment. For standardization of responses, the duration was calculated as day/year (e.g., the duration for patients whose dizziness/vertigo started 1 year ago and who had an attack for 1 day in 1 month was calculated as 12 days/year).

Determination of Vertigo Severity

The severity of vertigo was evaluated before and after treatment by the VAS and was classified as follows: 0-3, mild; 4-6, moderate; and 7-10, severe [15]. This scale was formerly reported to be reliable and valid not only for pain but also for migraine-associated vestibulopathy [11]. Therefore, it was used as the measurement method for assessing the severity of patients' complaints and converted subjective complaints of patients to quantitative values.

Questionnaires

The VSS, which was administered to the patients before and after treatment, is a questionnaire regarding the frequencies of vertigo/dizziness and/or other complaints. Patients respond to the symptoms described in the questions giving a score of 1-4 points according to the frequency experienced as follows: 0 point, never; 1 point, very rarely; 2 points, most of the time; 3 points, very often (every week); and 4 points, always (every day) [16]. In the present study, the effect of treatment on symptom frequency was evaluated using the short form of this scale consisting of 15 questions.

The degree of disability due to their complaints was evaluated by the DHI consisting of 25 items with physical, emotional, and functional subcomponents, with each question scored as follows: yes, 4 points; sometimes, 2 points; and no, 0 point. The total score is between 0 (minimum) and 100 (maximum). The patients were divided into three groups according to the total score as follows: 0-30 points, low; 31-60 points, moderate; and 61-100 points, high. A score >60 points on the scale indicates impairment of functionality [17, 18].

The effects of the disease on patients' QOL and the effects of propranolol treatment on the QOL have been evaluated using the VADL, which is a questionnaire that examines how vestibular system disorders affect the ability to perform activities of daily living independently. The questionnaire consists of a total of 28 questions, including nine questions evaluating ambulatory activity (e.g., walking and climbing stairs) and seven questions evaluating instrumental activity (e.g., housework and leisure activities). Patients give a score from 1 to 10 according to their degree of vertigo/dizziness and their daily activities.

Inclusion Criteria

- Patients diagnosed with definitive vestibular migraine according to the Bárány Association and the International Headache Society Vestibular Migraine Diagnosis Criteria Consensus Document [13]
- Patients who have not received any other treatment and have been given only propranolol
- Patients who provided signed informed consent
- Patients administered the scale and questionnaires both before and after treatment.

Exclusion Criteria

- Any previous treatment of vestibular symptoms
- Patients who received medical treatment that may have an effect on the symptoms (e.g., antidepressants and anxiolytics) or who underwent vestibular rehabilitation
- Patients who refused to sign an informed consent form, even though they wished to participate in the study
- Absence of one or more scales and questionnaires.

Statistical Analysis

The number of attacks, duration of complaints, vertigo severity, and VAS, VSS, DHI, and VADL scores were recorded before and after the

treatment protocol and analyzed. Chi-square test was used to compare the pre- and post-treatment values, and Pearson's correlation analysis was used to evaluate the correlation between questionnaires. Student's *t* test was used for pairwise comparison of the questionnaires. The changes before and after treatment were evaluated, and the change value in response to treatment was calculated by receiver operating characteristic (ROC) curve analysis. All statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) for Windows, version 21.0. (IBM Corp., Armonk, NY, USA). Data are presented as mean±standard deviation. The results were evaluated with 95% confidence interval. A p<0.05 was considered as statistically significant.

RESULTS

Descriptive Data

Of the 38 patients, 27 (71.1%) were female, and 11 (28.9%) were male. The mean age of the patients was 47.55±13.59 (18-75) years.

Duration of Complaints

The mean duration of vertigo/dizziness symptoms was 115.15±23.60 days before treatment and 12.86±7.92 days after treatment (p<0.001) (Figure 1). The patients were followed up for 6–32 months after treatment.

Number of Vertigo/Dizziness Attacks

The number of vertigo/dizziness episodes was two times a day before treatment and once every 2 months after treatment (p<0.001) (Figure 1). Full control was achieved in 23 (60%) patients, high control (>50% reduction) in 29 (29%) patients, moderate control (25%-50% reduction) in 1 (3%) patient, and minimal control (<25% reduction) in 3 (8%) patients after treatment.

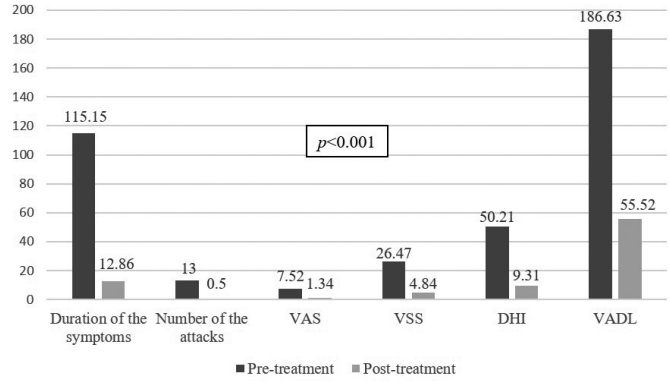

Figure 1. Comparison of all parameters evaluated before and after treatment (all data are mean values).
VAS: Visual Analog Scale; VSS: Vertigo Symptom Scale; DHI: Dizziness Handicap Inventory; VADL: Vestibular Disorders Activities of Daily Living Scale.

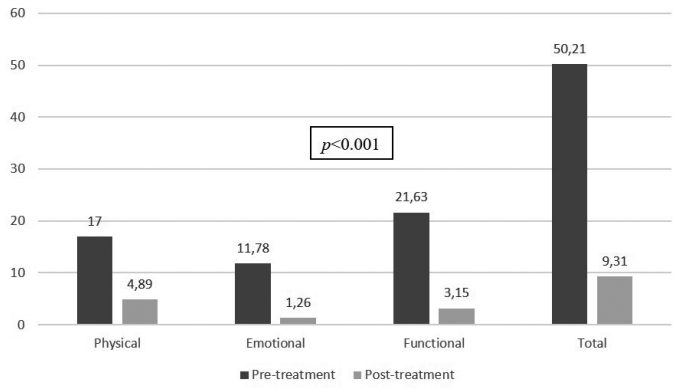

Figure 2. Pre- and post-treatment scores of Dizziness Handicap Inventory.

Vertigo Severity

The mean VAS scores before and after treatment were 7.52±2.28 (range: 3-10) and 1.34±2.05 (range: 0-7), respectively, and the change value was 6.18±3.24 (range: 5.11-7.25) (p<0.001) (Figure 1). The severity of symptoms was mild in four patients, moderate in six patients, and severe in 28 patients before treatment and mild in 31 patients, moderate in five patients, and severe in two patients after treatment.

Frequency of Vertigo and Accompanying Symptoms

According to the VSS, the majority of patients had vertigo >20 min. The most common accompanying symptom of vertigo was dizziness, and headache was often an accompanying symptom. The mean total scores before and after treatment were 26.47±7.97 and 4.84±8.24, respectively, and the change value was 21.63±10.88 (p<0.001) (Figure 1).

Degree of Disability

The mean total scores of the DHI before and after treatment were 50.21±22.39 (range: 8-92) and 9.31±9.86 (range: 0-58), respectively, and the change value was 40.89±20.26 (range: 33.24-48.54) (p<0.001) (Figure 1). The mean values of the physical, emotional, and functional components of the DHI before and after treatment are shown in Figure 2, and the degrees of disability before treatment were moderate, low, and high, respectively. The degree of disability after treatment was low in all patients (p<0.001). The numbers of patients are shown by the degree of disability in Table 1. The mean change values were 12.10±6.34, 10.52±8.97, and 18.47±11.73, respectively (p<0.001).

Activities of Daily Life and the QOL

The total scores of the VADL before and after treatment were 186.63±79.65 (range: 32-280) and 55.52±51.89 (range: 28-273), respectively (p<0.001).

All of these data indicated that the patients' symptoms decreased, and that their QOL improved after treatment.

Analysis of the Correlation between Questionnaires and Scales

In Pearson's correlation analysis, VAS was correlated with VSS (p<0.001), DHI (p=0.023), and VADL (p<0.001), and DHI was correlat-

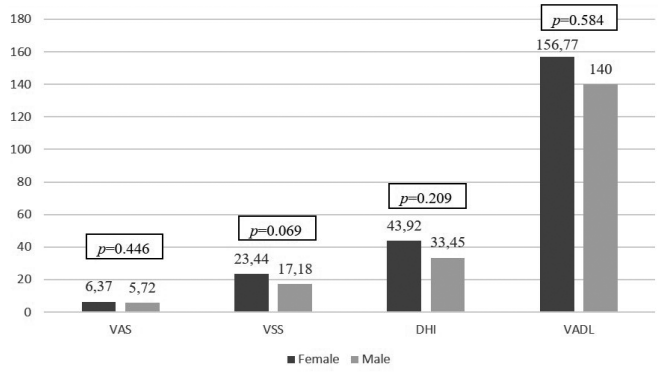

Figure 3. The change values between the genders.
VAS: Visual Analog Scale; VSS: Vertigo Symptom Scale; DHI: Dizziness Handicap Inventory; VADL: Vestibular Disorders Activities of Daily Living Scale.

Table 1. Number of patients according to disability levels in the Dizziness Handicap Inventory

			Post-treatment			
			Low	**Moderate**	**High**	**Total**
Total	Pre-treatment	Low	9	0	0	9
		Moderate	15	1	0	16
		High	13	0	0	13
		Total (%)	37 (97.4%)	1 (2.6%)	0	38
Physical		Low	3	0	0	3
		Moderate	16	4	0	20
		High	12	3	0	15
		Total (%)	31 (81.6%)	7 (18.4%)	0	38
Emotional		Low	24	0	0	24
		Moderate	8	0	0	8
		High	6	0	0	6
		Total (%)	38 (100%)	0	0	38
Functional		Low	9	0	0	9
		Moderate	14	1	0	15
		High	13	1	0	14
		Total (%)	36 (94.7%)	2 (6.3%)	0	38

Table 2. Treatment response change values and sensitivity–specificity ratios of the questionnaires and scales determined by ROC analysis

	Value	**Sensitivity (%)**	**Specificity (%)**	**p**
VAS	1.5	100	100	0.004
VSS	2.0	100	100	0.004
DHI	21	82.9	100	0.017
VADL	16	100	100	0.004

VAS: Visual Analog Scale; VSS: Vertigo Symptom Scale; DHI: Dizziness Handicap Inventory; VADL: Vestibular Disorders Activities of Daily Living Scale.

ed with VSS (p=0.033) and VADL, whereas there was no correlation between DHI and VADL (p=0.235).

Change Values

The change values between pre- and post-treatment scores of all of the parameters evaluated are shown under the heading of each parameter. In addition, the change values were compared between the sexes by the Mann–Whitney U test. The difference in the emotional subcomponent of the DHI was significantly higher in females than in males (p=0.025). The differences in functional and physical subcomponents of the DHI (p=0.478 and p=0.674, respectively), VAS (p=0.446), VSS (p=0.069), and VADL (p=0.584) were not statistically significant (Figure 3).

ROC Analysis

Three patients reported no response to treatment, whereas the remaining patients reported a partial or complete response. ROC analysis was performed to determine the degree of difference between pre- and post-treatment values in the questionnaires and scales (Table 2).

Evaluation of Treatment Efficacy

The differences between pre- and post-treatment values were statistically significant for all parameters evaluated. Propranolol treatment decreased the duration of symptoms, vertigo severity, and number of attacks, as well as providing significant control of attacks in vestibular migraine. There was a significant decrease in the degree of disability, indicating a positive contribution to the QOL.

DISCUSSION

In vestibular migraine, QOL is generally affected by chronic illness rather than vertigo/dizziness [1]. Therefore, QOL measurements in vestibular migraine are important to determine the effects of the disease on patients and to evaluate the response to treatment. The DHI used in the present study was reported to be strongly correlated with Short Form 36 [19], which is an overall QOL inventory. Although not a QOL questionnaire, the results of this inventory can indirectly provide an insight into the QOL. Nevertheless, VADL, which is a scale of QOL specific to vestibular diseases, was also used in the present study. The lack of a statistically significant correlation between these two scales showed that the DHI in vestibular migraine could provide limited insight into the QOL. There was no correlation between the objective tests and the DHI scores in patients with balance disorders [20], indicating that the DHI alone was not enough for assessment of the QOL in vestibular migraine, and that it should be supported by QOL scales, such as the VADL.

A limited number of studies have been reported regarding the treatment of vestibular migraine. Beta-blockers, antidepressants, and anticonvulsants used in migraine prophylaxis are also recommended for vestibular migraine prophylaxis [21]. It was reported that amitriptyline and topiramate were more appropriate in patients who experienced

multiple episodes [22]. In addition, venlafaxine has been reported to be an effective drug in the prophylaxis of vestibular migraine, but is known to be closely related to psychiatric comorbidities. Although it has not been shown to be superior to propranolol, venlafaxine is recommended for use in patients with vestibular migraine presenting with severe depressive symptoms [23, 24].

The beta-blocker, propranolol, is preferred for prophylactic treatment. Several retrospective studies provided limited data on the efficacy of propranolol in vestibular migraine prophylaxis [2, 21, 25, 26], and only two prospective, randomized controlled trials [23, 27] have been reported to date. In one of the randomized controlled trials, 36 patients who received propranolol, metoprolol, flunarizine, clonazepam, or amitriptyline were evaluated. Only 12 of these patients received propranolol, which limited the power of the study. In another study, propranolol (n=26) and venlafaxine (n=26) were compared as prophylactic treatment in 52 patients. Both drugs were shown to provide clinically significant benefits for patients with vestibular migraine, and venlafaxine is recommended in patients with severe depressive symptoms [23]. In retrospective studies, treatment response rates for propranolol ranged from 72% to 100%, but very few of these studies used definitive vestibular migraine diagnostic criteria, and/or the number of patients was sufficient [25, 26]. Our study was retrospective, and definitive vestibular migraine criteria were used in the diagnosis. Propranolol treatment showed complete control in 60% of cases and high control in 29%. In addition, the power of the study was 83%, thus making our results meaningful.

Although there is no clear consensus in the literature regarding the evaluation of the efficacy of treatment, symptom control, attack frequency and intensity, and the DHI were used. In the present study, the duration of symptoms, number of attacks, VAS, VSS, and DHI were used for evaluation of treatment efficacy, and all were shown to be correlated with each other. Therefore, instead of discussing all of these parameters individually, the results that may contribute to the literature will be emphasized.

In the DHI, the degree of disability can be defined as low, medium, or high, and the rate of patients with a low grade after treatment can provide an insight into the response to treatment. However, in our study, patients with low-grade disability were identified before treatment. A significant difference between the scores before and after treatment in these patients indicates the benefit of treatment. However, ROC analysis was performed for a more effective evaluation. The results of this analysis indicated that there was a response with a 21-point change in the DHI after treatment. Only one study reported a difference of >18 points after treatment [17], whereas another study indicated a difference of >10 points, indicating that the treatment was effective [28].

The DHI was evaluated by examining not only the total score but also its subcomponents. The lower response rate in the physical component, as compared with the other components, may be explained by the episodic nature of vestibular migraine and because it is most affected by physical activity. The change value for physical scores was less, or pre-treatment scores were bad than in other subcomponents. However, emotional scores showed different findings. In the literature, the best scores were found in the physical component, whereas the emotional scores were better in the present study. It has been reported that the rates of depression and anxiety are higher in patients with vestibular migraine than in those with other causes of vertigo [29]. Although this appeared to contradict our findings, anxiety and depression scales showed weak or no correlations with the DHI in the literature [19, 23]. Therefore, the DHI was insufficient for evaluation of emotional scores.

The change values between genders were compared for all parameters, and the differences were not statistically significant. However, when the subcomponents of DHI were compared according to gender, there were statistically significant differences in emotional scores before and after treatment. These data suggested that vestibular migraine, which occurs more frequently in women, does not discriminate between genders with regard to the clinical picture and response to treatment, but vestibular migraine shows greater effects on emotional components in women. There were no comparisons between sexes in previous studies evaluating vestibular migraine with the DHI. In studies comparing more than one drug, subcomponents were evaluated based on drugs, and the superiority of antidepressants was emphasized, especially for emotional function [30].

Even in the absence of symptoms, the likelihood of experiencing an attack may limit the activities of daily living in vestibular migraine [31]. DHI, which evaluates disability degree because of vertigo/dizziness and, partly, QOL, was used in the present study. However, as only nine items were related to functionality and we assessed self-care skills and daily movements, it was assumed to be more appropriate to combine them with another scale. Therefore, VADL was used. This scale was developed specifically for patients with vestibular disorders to determine the degree of independence during daily living activities regardless of underlying pathophysiology [18]. Independence in daily living activities is one of the factors contributing to QOL. Therefore, the contribution of treatment to patients' QOL can also be evaluated using this scale [32]. Other scales specific to vestibular diseases, including DHI, measure perceived QOL rather than independence in activities of daily living. In the present study, the significant difference between the total scores of the scale before and after treatment indicated that the treatment contributed positively to QOL.

To the best of our knowledge, this is the first study in which the efficacy of propranolol treatment in vestibular migraine and its effectiveness on QOL was comprehensively evaluated and analyzed. As a matter of fact, one of the limitations of the present study is the lack of placebo-controlled design. However, a previously reported meta-analysis indicated that the placebo effect in migraine could not be >21% [33].

CONCLUSION

The various questionnaires and scales used in the present study clearly showed that the duration of symptoms and the severity, frequency, and number of attacks were reduced. Additionally, disability scores were significantly reduced, and QOL was improved in patients with vestibular migraine with propranolol treatment.

Ethics Committee Approval: Ethics Committee Approval was received for this study from the Ethics Committee of Eskisehir Osmangazi University (19.12.2017-11).

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – O.Ç., G.T.T., A.İ.; Design - O.Ç., G.T.T., A.İ.; Supervision - O.Ç., G.E., A.İ.; Resource - O.Ç., G.E., N.Ş.S; Materials - G.T.T., G.E., N.Ş.S.; Data Collection and/or Processing - O.Ç., G.T.T., N.Ş.S.; Analysis and/or Interpretation - G.T.T., G.E., A.İ.; Literature Search - G.T.T., G.E., A.İ.; Writing - G.T.T., G.E., A.İ.; Critical Reviews - O.Ç., G.E., A.İ.

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Conflict of Interest: The authors have no conflict of interest to declare.

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