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The Impact of Fibromyalgia on Disability, Anxiety, Depression, Sleep Disturbance, and Quality of Life in Patients with Migraine

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ABSTRACT

Introduction: The aim of the present study was to assess the impact of fibromyalgia (FM) comorbidity on disability, anxiety, depression, sleep disturbance, and quality of life in patients with migraine.

Methods: Eighty-six consecutive migraine patients (age, 35.4±10.3 years; 69 women and 17 men) were enrolled in the study. The headache characteristics of the patients were recorded. FM was diagnosed based on the 1990 American College of Rheumatology classification criteria for the diagnosis of FM. All patients were asked to complete selfreport questionnaires, including the Fibromyalgia Impact Questionnaire (FIQ), Headache Impact Test (HIT-6), Migraine Disability Assessment Questionnaire (MIDAS), Pittsburgh Sleep Quality Index (PSQI), Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), and the 36-Item Short Form Survey (SF-36) to assess their pain-related disability, migraine-related disability, depression, anxiety, sleep disturbance, and quality of life.

Results: Of the migraine patients, 28 (32.6%) met the criteria for FM. Migraine patients with FM showed significantly increased migraine frequency and BDI, BAI, and PSQI scores and decreased quality of life scores for all eight domains of the SF-36 compared to patients with migraine alone, whereas the mean HIT-6 and MIDAS values did not differ between the groups. FIQ score showed statistically significant positive correlations with BDI, BAI, PSQI, and MIDAS scores and with headache frequency ($p<0.001$, $r=0.657$; $p<0.001$, $r=0.730$; $p<0.001$, $r=0.754$; $p=0.005$, $r=0.300$; $p=0.008$, $r=0.286$, respectively); FIQ score showed negative correlations with scores for all domains of the SF-36. In multivariate linear regression analysis, BDI, BAI, and PSQI scores independently predicted FIQ score.

Conclusion: Our study results demonstrate the significant impact of FM comorbidity on anxiety, depression, sleep disturbance, and quality of life in this population. FM evaluation and treatment should be considered in the routine care of patients with migraine to globally improve the patient's quality of life.

Keywords: Chronic pain, migraine, fibromyalgia, comorbidity, quality of life

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INTRODUCTION

Fibromyalgia (FM) is a common condition characterized by widespread pain, tenderness, fatigue, sleep disturbance, mood disturbance, and other somatic complaints (1). The precise causes of FM remain obscure. However, the most supported hypothesis proposes an increased mechanism of central sensitization that results in muscle skeletal pain persistence (2). Consequently, FM tends to have a severe impact on health-related quality of life and has been demonstrated to be associated with high rates of use of healthcare resources (3,4). Migraine is a debilitating headache disorder that affects 14% of the population and up to 18% of women (5). Migraine is currently ranked by the World Health Organization (WHO) as 19th among causes of years lived with disability (6). Migraine has been noted to be comorbid with a number of illnesses, including psychiatric, neurological, vascular, heart, and other diseases, in specialty care patients and in population samples (7). In the Nord-Trondelag study by Hagen et al. (8), participants with headache reported more musculoskeletal pain than those without. The risk was similar between patients with and without migraine; however, headache frequency was a strong predictor for musculoskeletal pain. It has been suggested that FM, chronic daily headache, and episodic migraine may actually be a continuum of the same disorder (9).

A common genetic basis, synergistically working with other agents (personality, emotional features, medication overuse, and stressing events), may create chronic modification of the antinociceptive system, leading to progressive increase (hyperalgesia) and diffusion (panalgesia) of pain. In migraine, activation of the trigeminovascular system stimulates "sterile inflammation" (10), followed by peripheral and central sensitization, with diffusion of pain from the vessel and meninges to the skin and muscles; allodynia also occurs (11). In addition, central sensitization is responsible for migraine pain persistence, leading to the

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development of chronic pain (12). Therefore, both FM and migraine may be characterized by nociceptive inflammatory pain that, regardless of its genesis, may persist due to central sensitization phenomena (2).

Fibromyalgia comorbidity is frequently present in migraine patients and appears to be characterized by more severe migraine (13,14,15,16). Comorbidity in migraine is important from several perspectives: co-occurrence of diseases can complicate diagnoses; one disease can remind clinicians of other diseases; one treatment can be used for two diseases; and comorbidity of illnesses can provide clues to the pathophysiology of migraine (17). Migraine patients with comorbid disease require a multidisciplinary approach to the management of their conditions to achieve global improvement of their quality of life. In this study, we aimed to evaluate the impact of FM comorbidity on disability, anxiety, depression, sleep disturbance, and quality of life in our migraine cohort.

METHODS

This cross-sectional study was conducted between September 2014 and June 2015. The study protocol was approved by the Ethics Committee of Recep Tayyip Erdoğan University, Faculty of Medicine, Turkey. The study was performed in accordance with the principles stated in the Declaration of Helsinki, and written informed consent was obtained from all participants prior to the study. Eighty-six consecutive patients (age, 35.4±10.3 years; 69 women and 17 men) who met the International Headache Society (IHS) criteria (18) for migraine and who had been examined for the first time were enrolled. Patients were excluded from the study if they had other types of headache, had neurological or psychiatric disorders, or showed other known causes of diffuse pain, such as rheumatic, endocrine, or systemic disorders. Sociodemographic characteristics (age, gender, body mass index, education, employment status, marital status) and headache characteristics (age of onset, frequency, headache attack duration, number of years with migraine) were recorded.

Fibromyalgia was diagnosed based on the 1990 American College of Rheumatology classification criteria for the diagnosis of FM (19) by an experienced physiatrist. FM may be confidently diagnosed in patients with widespread musculoskeletal pain and multiple tender points. The FM tender point examinations were performed by an experienced physiatrist with the pulp of the thumb using digital palpation. For a tender point to be considered "positive," the patient was required to state that the palpation was painful. The total tender point score was calculated by adding the individual scores for all 18 tender points.

All patients were asked to complete the following self-report questionnaires for the assessment of pain-related disability, migraine-related disability, anxiety, depression, sleep disturbance, and quality of life.

Headache Impact Test

The Headache Impact Test (HIT-6) (20) is a validated tool to assess the impact of headache (range: 36–78) on the lives of respondents. HIT-6 scores ≤48 reflect little impact; scores between 56 and 59 reflect substantial impact; and scores ≥60 reflect severe impact.

Migraine Disability Assessment Scale

The Migraine Disability Assessment Scale (MIDAS) (21) is a brief and reliable headache-specific tool that is used to quantify headache-related disability. Scores from 0–5 indicate little or no disability, 6–10 indicate mild disability, 11–20 indicate moderate disability, and ≥21 indicate severe disability.

Beck Depression Inventory

The Beck Depression Inventory (BDI) is a 21-item survey that assesses the presence and severity of depression (22). Higher scores reflect more severe depression. The standard cutoff scores are as follows: 0–9: indicates minimal depression; 10–18: indicates mild depression; 19–29: indicates moderate depression; 30–63: indicates severe depression. The validity and reliability of the BDI in the Turkish population has been demonstrated by Hisli et al. (23)

Beck Anxiety Inventory

The Beck Anxiety Inventory (BAI) is a relatively brief, easily administered, and easily scored 21-item survey that assesses the severity of patient anxiety (24). The total score ranges from 0–63. Scores from 0–9 indicate normal or no anxiety, 10–18 indicate mild to moderate anxiety, 19–29 indicate moderate to severe anxiety, and 30–63 indicate severe anxiety. The validity and reliability of the BAI in the Turkish population has been demonstrated by Ulusoy et al. (25)

Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index (PSQI) is an 18-item questionnaire that measures sleep quality and disturbances over a 1-month time interval (26). The PSQI differentiates "poor" sleep from "good" sleep by measuring seven domains, including subjective sleep quality, sleep duration, sleep latency, sleep disturbances, habitual sleep efficiency, daytime dysfunction, and use of sleep medication over the last month. A total score of 5 or higher indicates a "poor" sleeper. The validity and reliability of the PSQI in the Turkish population has been demonstrated by Ağargün et al. (27)

36-Item Short Form Health Survey

The 36-Item Short Form Survey (SF-36) is a 36-item questionnaire which measures quality of life across eight domains that are both physically and emotionally based (28). The eight domains included in the SF-36 are role limitations due to physical health problems (RP), physical functioning (PF), social functioning (SF), bodily pain (BP), general mental health (MH), vitality (VT), role limitations due to emotional problems (RE), and general health perceptions (GH). The validity and reliability of the SF-36 in the Turkish population has been demonstrated by Demiral et al. (29)

Fibromyalgia Impact Questionnaire

The Fibromyalgia Impact Questionnaire (FIQ) is a 10-item assessment and evaluation instrument developed to measure FM patient status, progress, and outcomes. The total score ranges from 0–100 (30). Higher scores indicate greater impact of FM on functioning. The validity and reliability of the FIQ in the Turkish population has been demonstrated by Sarmer et al. (31)

Statistical Analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences, version 13.0, for Windows (SPSS Inc; Chicago, IL, USA). Continuous variables are expressed as mean±standard deviation. Compliance of the variables with normal distribution was assessed by the Kolmogorov- Smirnov test. Inter-group analyses were performed with Student's t-test for normally distributed variables and the Mann-Whitney U test for non-parametric variables. The chi-square test was used for the comparison of qualitative data. To determine the correlation between the variables, Spearman's rank or Pearson's correlation analyses were performed according to the distribution of the data. Multivariate linear regression analysis was performed to investigate the independent predictors for FIQ scores. Independent factors were BDI, BAI, PSQI, MIDAS, and migraine frequency. The number of independent factors was determined according to the study sample size. A p value of <0.05 was considered to be statistically significant.

RESULTS

The demographic and clinic characteristics of the migraine patients are shown in Table 1. The mean age and disease duration were 35.4±10.3

Table 1. Demographic and clinic characteristics of patients with migraine

Characteristics	Migraine patients (n=86)
Mean age, years (range)	35.4 ± 10.3 (18-58)
Gender (%)	
Female	69 (80.2)
Male	17 (19.8)
Body mass index (kg/m2)	25.9 ± 5.1
Marital status (%)	
Single	25 (29.1)
Married	61 (70.9)
Employed, n (%)	29 (33.7)
Education, years (range)	8.3 ± 4.2 (0-15)
Migraine with aura, n (%)	13 (15.1)
Mean age at migraine onset, years (range)	28.3 ± 9.2 (18-55)
Duration of migraine, years (range)	7.3 ± 6.8 (1-25)
Typical migraine frequency (number per month)	7.3 ± 6.2
Duration of episode, n (%)	
<12 h	22 (25.6)
12-24 h	27 (31.4)
> 24 h	37 (43)
Headache severity, n (%)	
Mild	2 (2.3)
Moderate	20 (23.3)
Severe	43 (50)
Unbearable	21 (24.4)
HIT-6	59.9 ± 12.7
MIDAS	± 21.5
Little or no disability (0-5), n (%)	11 (12.8)
Mild disability (6-10), n (%)	17 (19.8)
Moderate disability (11-20), n (%)	21 (24.5)
Severe disability (≥21), n (%)	37 (43)

Values are expressed as mean ± standard deviation.
HIT-6: Headache Impact Test; MIDAS: Migraine Disability Assessment Scale

Table 2. Characteristics of migraine patients with and without fibromyalgia (FM)

	Migraine patients with FM (n = 28)	Migraine patients without FM (n = 58)	P
Mean age, years	38.6 ± 9.5	33.9 ± 10.3	0.048
Gender (F/M), n (%)	27/1 (96.4/3.6)	42/16 (72.4/27.6)	0.020
Body mass index (kg/m^2)	27.2 ± 5.8	25.3 ± 4.7	0.102
Married, n (%)	24 (85.7)	37 (63.8)	0.065
Education, years	7.0 ± 4.6	8.9 ± 3.9	0.069
Employed, n (%)	6 (21.4)	23 (39.7)	0.152
Migraine with aura, n (%)	9 (32.1)	4 (6.9)	0.004
Mean age at migraine onset, years	30.2 ± 9.2	27.3 ± 9.1	0.172
Duration of migraine, years	8.2 ± 7.3	6.9 ± 6.5	0.516
Accompanying features			
Nausea n (%)	25 (89.3)	49 (84.5)	0.743
Vomiting n (%)	8 (28.6)	20 (34.3)	0.584
Photophobia n (%)	25 (89.3)	48 (82.8)	0.533
Phonophobia n (%)	24 (85.7)	51 (87.9)	0.743
HIT-6	62.8 ± 7.1	58.4 ± 14.5	0.481
MIDAS	27.6 ± 18.9	23.3 ± 22.6	0.390
FIQ	66.5 ± 10.3	24.1 ± 11. 2	<0.001
Tender points count	12.8 ±1.5	2.0 ± 1.8	<0.001
Widespread pain (VAS)	7.5 ± 1.4	2.4 ± 0.5	<0.001
BDI	25.5 ± 9.2	11.9 ± 7.4	<0.001
BAI	30.2 ± 11.1	13.1 ± 7.7	<0.001
PSQI	11.4 ± 2.2	5.1 ± 2.5	<0.001

Values are expressed as mean ± standard deviation.
F: female, M: male, HIT-6: Headache Impact Test, MIDAS: Migraine Disability Assessment Scale, FIQ: Fibromyalgia Impact Questionnaire, VAS: visual analog scale, BDI: Beck Depression Inventory, BAI: Beck Anxiety Inventory, PSQI: Pittsburgh Sleep Quality Index

(range 18–58) and 7.3±6.2 years. Of the 86 participants, 69 (80.2%) were female. The mean migraine frequency, HIT-6, and MIDAS scores were 7.3±6.2 days per month, 59.9±12.7, and 24.7±21.5, respectively. Thirty-seven patients (43%) had severe headache-related disability according to the MIDAS, and 64 patients (74.4%) had severe or unbearable migraine headache. Of the participants, 28 (32.6%) met the criteria for FM.

The comparison of migraine patients with and without FM is shown in Table 2. The mean age and percentage of female participants were significantly higher in migraine patients with FM than without FM (38.6±9.5 vs. 33.9±10.3 years, p=0.048; 96.4% vs. 72.4%, p=0.02, respectively). Other sociodemographic features, including body mass index, marital status, level of education, employment status, and disease duration did not significantly differ between the groups (p>0.05 for all). Migraine patients with FM showed significantly increased migraine headache frequency per month compared to patients without FM, whereas there were no significant differences in accompanying features such as nausea, vomiting, photophobia, and phonophobia between the groups (p>0.05 for all). The percentage of subjects with aura was higher in the migraine group with FM comorbidity compared to the group with migraine alone. Although the mean HIT-6 and MIDAS scores were higher in migraine patients with FM than without FM, the results were not statistically significant (62.8±7.1 vs. 58.4±14.5, p=0.481; 27.6±18.9 vs. 23.3±22.6, p=0.390, respectively). As expected, the mean widespread pain (VAS) scores, tender point counts, and FIQ scores were significantly higher in migraine patients with FM compared to migraine patients without FM (7.5±1.4 vs. 2.4±0.5; 12.8±1.5 vs. 2.0±1.8; 66.5±10.3 vs. 24.1±11.2; respectively, p<0.001 for all). Migraine patients with FM showed significantly increased BDI, BAI, and PSQI scores compared to patients without FM (25.5±9.2 vs. 11.9±7.4, 30.2±11.1 vs. 13.1±7.7, an 11.4±2.2 vs. 5.1±2.5, respectively; p<0.001 for all). Also, the quality of life scores for all eight domains of the SF-36 were significantly lower in migraine patients with FM compared to migraine patients without FM (Table 3) (p<0.001 for all).

The correlation of FIQ scores with other study parameters is shown in Table 4. FIQ score showed statistically significant correlations with BDI, BAI, PSQI, and MIDAS scores and headache frequency in patients with migraine (p<0.001, r=0.657; p<0.001, r=0.730; p<0.001, r=0.754; p=0.005, r=0.300; p=0.008, r=0.286, respectively). However, there was no statistically significant association between HIT-6 and FIQ scores (p=0.085, r=0.187). In addition, scores for all domains of the SF-36 showed statistically significant negative correlations with FIQ score (PF: p<0.001, r=–0.582; VT: p<0.001, r=- 0.633; BP: p<0.001, r=–0.541; GH: p<0.001, r=–0.636; SF: p<0.001, r=–0.521; MH: p<0.001, r=–0.556; RE: p<0.001, r=–0.470; RF: p<0.001, r=–0.453). In the multivariate regression analysis, the BDI, BAI, and PSQI scores independently predicted the FIQ score in our study population (Table 5).

DISCUSSION

In the present study, 28 (32.6%) of the migraine patients met the criteria for FM; also, migraine patients with FM comorbidity tended to be older,

Table 3. Quality of life between migraine patients with and without fibromyalgia (FM) according to Short Form-36

	Migraine patients with FM (n = 28)	Migraine patients without FM (n = 58)	P
Physical functioning	55.6 ± 18.6	82.4 ± 15.3	<0.001
Role-physical	19.5 ± 26.5	54.6 ± 37.2	<0.001
Bodily pain	30.7 ± 13.6	49.9 ± 21.1	<0.001
General health	35.9 ± 14.6	56.9 ± 17.9	<0.001
Vitality	30.7 ± 15.7	56.1 ± 18.6	<0.001
Social functioning	40.4 ± 19.1	66.6 ± 20.5	<0.001
Role- emational	28.1 ± 31.8	54.8 ± 32.2	<0.001
Mental health	44.2 ± 14.2	65.4 ± 16.1	<0.001

Values are expressed as mean ± standard deviation. FM: fibromyalgia

Table 4. The correlation of Fibromyalgia Impact Questionnaire (FIQ) scores with other variables

	FIQ	
	r	p
Migraibe duration	0.06	0.576
Headache frequency	0.286	0.008
MIDAS	0.300	0.005
HIT-6	0.187	0.085
BDI	0.657	<0.001
BAI	0.730	<0.001
PSQI	0.754	<0.001
Physical functioning	-0.582	<0.001
Role-physical	-0.453	<0.001
Bodily pain	-0.541	<0.001
General health	-0.636	<0.001
Vitality	-0.633	<0.001
Social functioning	-0.521	<0.001
Role- emational	-0.470	<0.001
Mental health	-0.556	<0.001

MIDAS: Migraine Disability Assessment Scale, HIT-6: Headache Impact Test, BDI: Beck Depression Inventory, BAI: Beck Anxiety Inventory, PSQI: Pittsburgh Sleep Quality Index, FIQ: Fibromyalgia Impact Questionnaire

and most were female. The prevalence of FM in the general population in our country is 3.6% (32). In a survey of five countries, it was demonstrated that the prevalence of FM is age- and sex-related and varies between countries (33). There is general agreement that FM is uncommon in young subjects (25–30 years). Tietjen et al. (34) reported that female gender was significantly associated with symptoms of central sensitization in migraine patients. FM is recognized as a common condition in the clinic and a major cause of morbidity worldwide (33). The prevalence of FM ranges from 22% in patients with episodic migraine (14) to 35.6% in chronic migraine patients (12). Similar to our results, in a recent study on patients with episodic migraine, Küçükşen et al. (35) demonstrated that 31.4% of migraine patients present with FM comorbidity. Contrastingly, Vij et al. (36) evaluated the frequency of migraine headache in a large cohort of patients with FM using a brief migraine headache-screening tool; they found that 966 (55.8%) of the respondents met the criteria for migraine headaches.

The frequency of migraine headache was significantly higher in patients with FM than in those without FM in our study. However, linear regression analysis did not identify headache frequency as an independent predictor of FIQ score. Although migraine patients with FM had numerically higher

Table 5. The effect of different variables on Fibromyalgia Impact Questionnaire (FIQ) scores in patients with migraine

FIQ (dependent variable)	B	SE	Beta	p[a]
Migraine frequency	-0.187	0.249	-0.051	0.453
MIDAS	0.019	0.069	0.018	0.780
BDI	0.546	0.192	0.244	0.006
BAI	0.572	0.174	0.301	0.001
PSQI	2.577	0.497	0.432	<0.001
constant	0.909	3.240	-	0.780

R^2=0.70 (p<0.001)
[a]The multivariate linear regression analysis was performed to investigate the independent predictors for FIQ scores; Independent variables are as follows: migraine frequency, MIDAS, BDI, BAI, PSQI
MIDAS: Migraine Disability Assessment Scale, BDI: Beck Depression Inventory, BAI: Beck Anxiety Inventory, PSQI: Pittsburgh Sleep Quality Index

MIDAS and HIT-6 scores than those without FM, the differences were not statistically significant. In accordance with our results, there were no significant differences in migraine severity indices (MIDAS and HIT-6) between migraine patients with and without FM in a study by Ifergane et al. (14) However, there was no information with regard to headache frequency in that study. Headache frequency was identified as one of the best discriminating factors for FM comorbidity in a study by de Tommaso et al. (15). In another study, FM was more common among patients with migraine, who reported more frequent migraines and comorbid mood disorders (37). Küçükşen et al. (35) demonstrated no significant differences in headache frequency and MIDAS score between migraine patients with and without FM; however, their study found higher HIT-6 scores in migraine patients with FM compared to those without FM. However, only episodic migraine patients were included in that study. In addition, the presence of aura was significantly higher in migraine patients with FM than in those without FM in our study.

Migraine is comorbid with several psychiatric disorders, including depression, anxiety disorder, and post-traumatic stress disorder, as well as other conditions (38). Some theories have been suggested to clarify the etiology of the relationship between psychiatric conditions and migraine, including shared environmental or genetic risk factors, unidirectional causal and bidirectional causal models, and latent brain state models. In addition, affective disorders and sleep disturbances are also significantly common among patients with migraine (39,40). In the present study, migraine patients with FM comorbidity showed higher PSQI, BDI, and BAI scores than patients without FM. Also, FIQ score was significantly associated with BDI, BAI, and PSQI scores. Similar results were reported in other studies (14,15,35,41). Although there was no difference in terms of depression between migraine patients with and without FM, migraine patients with FM showed higher BAI scores than those without FM in the study by Küçüksen et al. (35) In addition, anxiety and reduced sleep adequacy were found to be among the best discriminating factors for FM comorbidity in the study de Tommaso et al. (15) Decreased habituation to pain is common in migraine and FM and may facilitate central sensitization and myofacial pain persistence in the existence of other favoring situations, such as sleep disturbances and anxiety (41). Mongini et al. (42) have reported that in particular episodic migraine, the presence of anxiety or of anxiety combined with depression significantly enhances the severity of muscle tenderness in the neck and, to a lesser extent, in the head; this may simplify the progress toward chronic migraine. Therefore, anxiety may also facilitate FM and diffuse myofascial pain comorbidity in headache patients who present with increased pericranial muscle tenderness. Contrastingly, muscle tenderness pain may trigger central sensitization and is also likely to increase depression and anxiety. Sleep disturbance may cause hyperalgesia; despite the broadly overlapping and distributed neural networks which manage situations such as pain and

sleep, the exact brain mechanism remains to be clarified (2). Decreased sleep quality induces dissemination of myofascial pain in patients with headache; however, which sleep phase is most responsible for the formation of widespread pain remains obscure.

Our migraine patients with FM comorbidity also exhibited poorer quality of life for all domains of the SF-36 than patients without FM. In addition, FIQ score showed strong correlations with all domains of the SF-36. It has been demonstrated that FM patients present worse quality of life than patients affected by other conditions and the general population (4,43,44). In the study by de Tommaso et al. (41), the physical component of life quality was determined to be one of the best discriminating variables for FM comorbidity. Ifergani et al. (14) reported significantly decreased scores for only the PF, PR, GH, and VT domains of the SF-36 in migraine patients with FM than for those without FM, whereas Küçüksen et al. (35) reported that migraine patients with FM had decreased quality of life scores for all domains of the SF-36, with the exception of VT, compared to patients with migraine alone. In contrast, Marcus et al. (13) reported no significant differences in SF-36 scores between FM patients with and without headache; they concluded that FM patients with headache do not appear to represent a significantly different subgroup compared to FM patients without headache.

A major limitation of our study was the small number of participants. Also, we did not evaluate the differences in the frequency of FM comorbidity and other study parameters between patients with chronic and episodic migraine. In conclusion, our study results demonstrated the significant impact of FM comorbidity on anxiety, depression, sleep disturbance, and quality of life in patients with migraine. FM evaluation and treatment should be considered in the management of migraine patients to globally improve the patients' quality of life.

Committee Approval: Ethics committee approval was received for this study from the ethics committee of Recep Tayyip Erdoğan University School of Medicine.

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

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