

Living with Burden of Migraine: The Analysis of “My Migraine Voice” Survey Results in Turkey

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ABSTRACT

Introduction: Migraine is a common, chronic neurologic disease which causes serious social and economical disability at both the individual and the community level. The aim of this study was to interpret the data for Turkey from “My Migraine Voice,” an online survey of individuals suffering from frequent migraine attacks (≥ 4 days/month with migraine headaches) who had not benefited from existing prophylactic therapies, conducted in 31 countries to investigate the burden of migraine for the individual and the society.

Methods: Based on a set of predetermined criteria (90% of the patients must have used prophylactic therapy, and 80% of them must have needed to change therapy), patients who had ≥ 4 days in a month with migraine headache in the past 3 months were asked to take an online survey of 88 questions. The study included questions aimed at determining the burden of disease during not only the headache phase, but also the prodrome and postdrome phases, as well as a questionnaire for determining the Reduction of Overall Activity and Productivity at Work ((WPAI: GH).

Results: A total of 237 patients from Turkey were included in the study.

62% of the patients stated that they were severely or very severely disabled in their daily activities during the headache phase of migraine, and 31% and 34% of the patients reported that they were disabled during the prodrome and postdrome phases, respectively. 28% of the patients stated they had been receiving prophylactic therapy for more than 2 years, and only 84% of these patients reported complete or partial satisfaction with their current therapies. This value was as low as ~70% in patients in whom 2 or more previous drug treatments or therapies had failed. Actively-working patients reported that they had lost 21% of their time at work due to migraine, and the overall loss of workforce was 67%.

Conclusion: This study showed that migraine can cause disability in an individual's private and professional lives during every stage of migraine, including the prodrome and postdrome phases. This finding will be important for designing future treatments aimed at enhancing the quality of life and productivity of patients who cannot adequately benefit from existing therapies.

Keywords: Migraine, survey, quality of life, burden of migraine

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INTRODUCTION

Migraine is a chronic neurological disease which is quite common in our country as well as all over the world and is the most common cause of admissions to healthcare facilities in general and to neurology outpatient clinics in particular, resulting in significant social and economic burden for both the society and the individual (1-3). Diagnosed according to the ICHD-3 criteria, this condition is characterized by recurrent headache attacks with varying frequency and accompanying hypersensitivity to visual, auditory, olfactory and cutaneous stimuli, nausea and vomiting (4).

Although its prevalence varies across countries, it is reported to be between 5-9% in the male population and 12-25% in the female population in western countries (5,6). The prevalence of migraine, which was 16.4% according to the results of our prevalence study in Turkey in 21 cities in 2008, was reported to increase slightly to around 16.7% in 2013 (1). The incidence studies performed throughout the world report rates of 1.5-2/1000 in men and 3-6/1000 in women, whereas the rates for Turkey is much higher due to both the genetic background and the impact of environmental factors, and was reported as 2.98% in women and 1.93%

in men (1,7). Migraine is hence the most important primary neurological problem for our country.

According to the results of Global Burden of Disease Study 2016 (GBD2016), which is the largest study to determine the social burden of diseases, migraine ranks first among the causes of limitation in adults below the age of 50 years (8). In Turkey, there is a limited number of studies on the social burden of migraine and, based on the results of a study carried out with 41 different centers simultaneously to investigate the headache burden, headache was the main symptom of 35.1% of individuals presenting to neurology outpatient clinics, while 31.3% had other causes for presenting to outpatient clinics but also had accompanying headache (2,9,10).

The purpose of this study was to analyze the Turkish data from the survey study called “My Migraine Voice” that aimed to investigate the individual and social burden of migraine and was performed online in 31 countries with individuals who had ≥ 4 migraine days a month, failed

to benefit from available prophylactic therapies and were suffering from conditions classifiable as serious migraine. Given that this group may be more susceptible to the negative effects of migraine, there is a clear need for new studies on the burden of migraine on quality of life, social and professional life and on the society. The secondary aim was to demonstrate the negative effects of migraine on patients' daily activities during the phase preceding the pain (prodrome) and after the pain (postdrome) and to show that migraine burden is not limited to the pain phase only but that it was involved in all phases of the pathogenesis of migraine. There is only one study performed for this purpose worldwide (11), and current study was the first to investigate the problems in the prodrome and postdrome phases reported from Turkey. In addition, patients completed the General Work Productivity and Activity Impairment Questionnaire: General Health V2.0 (WPAI: GH) and it was thus aimed to study the impact of the condition on work productivity and daily activities in migraine patients, and hence to investigate loss of work force on the social level.

METHOD

Patient Selection and Inclusion Criteria

Performed with 11,266 adult patients in 31 countries, this study constitutes the Turkey leg of the study that was conducted between September 2017 and February 2018. Patients were included in the study on a voluntary basis, mainly through online surveys. Given the research format, the study was exempted from ethics committee appraisal (11). Prior to enrolment, the patients were asked to first to specify how many days a month they had had headache/migraine, and they were asked screening questions to verify the diagnosis of migraine, and based on the responses, diagnoses were made by headache specialists based on the ICHD III classification (4). The data of 237 adult patients aged between 18–75 years, with ≥ 4 migraine headache days per month in the last 3 months were included in this study. Informed consent forms were obtained from all patients before they answered the study questions, and patients read and completed the questionnaires in their native languages. In addition, the following criteria were adopted as additional criteria in patient selection based on the recommendations of the committee conducting the study: 90% of patients had used at least 1 prophylactic treatment, At least 80% of this patient group needed to change treatment; of the group of patients who changed treatment, 10% required treatment switch after experiencing at least one treatment failure (TF), and approximately 90% required treatment switch after experiencing TF with ≥ 2 drugs. (Figure 1)

These additional criteria were included in the study in order to ensure that TF was adequately represented among the individuals enrolled in the study. The study was planned as an online questionnaire with a total of 88 questions and the details of the protocol related to the study were consistent with the international study previously published elsewhere (11).

Because of the limited data available in the literature on the burden of disease in the prodrome and postdrome phases of migraine attacks, the questionnaire included questions to determine the migraine impact and burden in each phase of migraine. The participants were informed in detail about the migraine phases before the survey.

In addition, the Turkish version of the "Work Productivity and Activity Impairment Survey (WPAI-GH), i.e. Overall Work Productivity and Activity Impairment: General Health V2.0 (WPAI:GH) was used as part of the questionnaire to evaluate the impact of migraine on work productivity and daily activities in working individuals with the aim of studying the impairment in the individual's productivity and activities (12). The validity

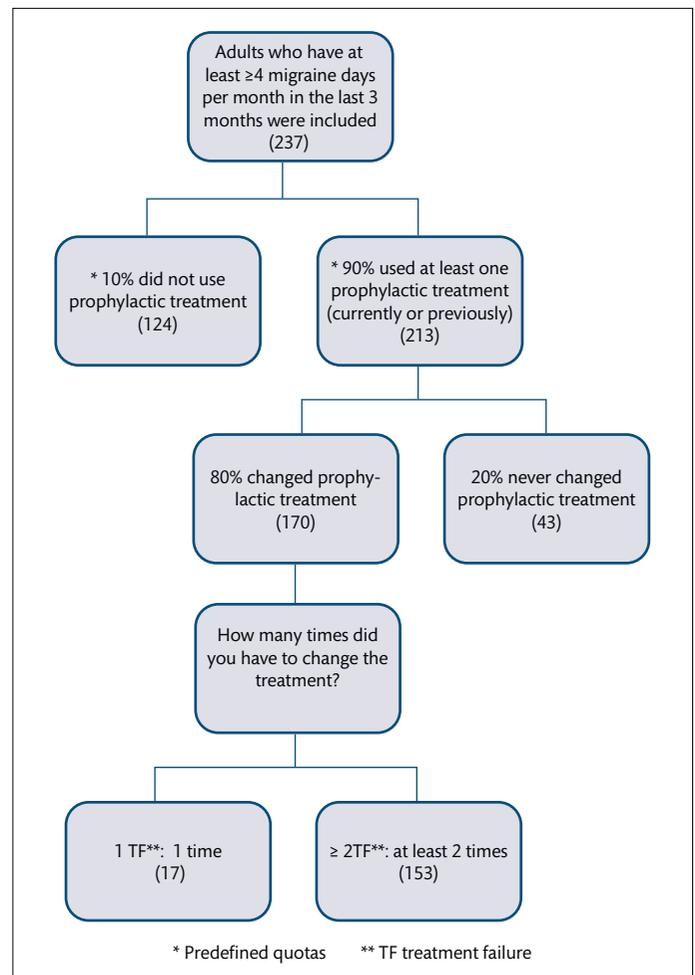


Figure 1. Patient selection criteria for the study questionnaire and flow chart

and reliability study of this questionnaire in Turkish was undertaken. The questionnaire consists of 6 questions and main topics including the number of days/hours lost due to health problems, the number of actual days/hours he/she could work, the extend at which the working individual's productivity was affected due to health problems, and the extend at which normal daily activities were affected due to health problems within the past 7 days. Scores are calculated in percentage values for active time and productivity, over the total worked time.

Data Analysis

IBM SPSS Statistics (version 24) was used to analyze demographical characteristics, to generate summary statistics in analyses and to determine clustering levels. Qlikview software was used to generate graphical data. The quality assessment of the data, including an evaluation of response patterns in the questionnaire, inconsistencies and analysis of open-ended questions, was performed. Frequency, average, median and standard deviation parameters were used in the subgroup analysis of the participants. Reported *p* values were generated using Student's *t*-test to compare the means and the chi-square test to compare percentages and rates.

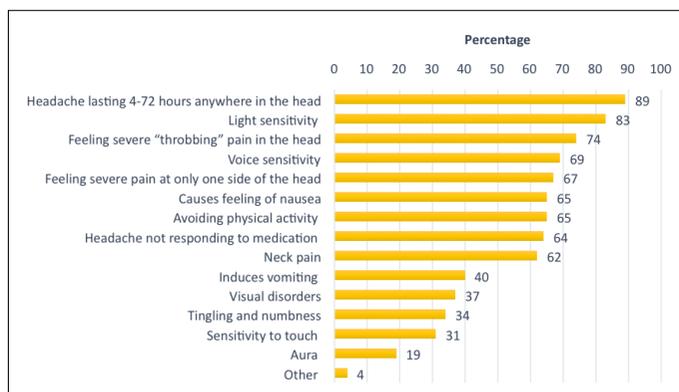
RESULTS

Demographics

Sociodemographic data from 237 patients included in the study from Turkey are summarized in Table 1. The group included 128 women (54%) and 109 men (46%), for total of 237 patients, and their mean age was 34.82 ± 8.31 years.

Table 1. Demographic information of the patients included in the study

Demographics (n=237)	% (n)
Gender (f/m)	54/46 (128/109)
Age	
18-29 years	30 (71)
30-49 years	65 (155)
50-74 years	5 (11)
Marital status	
Single	21 (50)
Married	76 (180)
Divorced	3 (7)
With children	72 (170)
Presence of a family history of migraine	54 (128)
Full-time working in a regular job	73 (173)
Unemployment due to migraine	11 (26)
Disease duration	
>21 years	5 (11)
16-20 years	8 (18)
11-15 years	11 (26)
6-10 years	31 (73)
1-5 years	43 (101)
<1 year	3 (7)
Average number of concomitant chronic diseases reported by participants	2.4
Most frequently reported	Depression 29% (69)
The second most frequently reported	Anxiety 22% (51)
The third most frequently reported	Chronic pain 18% (42)

**Figure 2.** Distribution by symptoms experienced during migraine pain and symptom frequency

Migraine Features and Living with Migraine

The attacks of 35% of the participants lasted 4-12 hours on average. For 29%, headache persisted for 24 hours or longer. Patients' distribution by the symptoms experienced during migraine pain and their frequency is summarized in Figure 2.

When all of the patients were evaluated, 62% reported that they were extremely and very extremely limited in their daily activities during the headache phase of migraine, reporting a limitation of 31% and 34% in prodrome and postdrome phases, respectively. These rates were calculated as 40%, 68% and 40%, respectively, in the group of patients with ≥ 2 TF. This has shown that migraine causes individual limitations in all phases, thus creating a serious burden not only during the headache phase but in all phases (Table 2).

Table 2. Characteristics of migraine phases

	Pre-attack phase % (n)	Headache phase % (n)	Postdromal phase % (n)
Migraine phase duration			
<4 hours	52.3 (124)	22 (52)	36.6 (87)
4-24 hours	30 (71)	56 (143)	40 (95)
>24 hours	17.3 (41)	22 (52)	23 (54)
Has not undergone this phase	0.4 (1)	0	0.4 (1)
In the group of patients who used prophylactic therapy, the proportion of those whose migraine attack phase lasts >24 hours			
Without a history of unsuccessful prophylactic treatment (43)	14 (6)	12 (5)	12 (5)
With history of 1 unsuccessful prophylactic treatment (17)	6 (1)	6 (1)	12 (2)
With history ≥ 2 unsuccessful prophylactic treatments (153)	20 (30)	26 (40)	27 (41)
P value: comparison of the group with history of ≥ 2 prophylactic treatments vs. the group without a history of unsuccessful prophylactic treatment	0.350	0.046	0.038
Those reporting they are extremely and very extremely affected in the corresponding migraine phase	34 (80)	62 (147)	31 (80)

Patient's Journey: From the First Diagnosis to the Current Therapy

Of the respondents, 66% first presented to the neurology specialist with the complaint of headache. The type of physicians the patients first presented were, by order of frequency, general practitioners (21%), headache specialists (10%), emergency department physicians (2%) and other physicians (1%), respectively. Migraine was most commonly diagnosed by neurologists (80%), followed by general practitioners (10%), headache specialists (8%), emergency room physicians (1%) and other physicians. Of the 222 patients diagnosed medically, 25% were diagnosed in less than 1 month, 44% in 1-6 months, 9% in 7-12 months, 11% in 1-2 years and 10% were diagnosed with migraine after more than 2 years and were examined by an average of 2.7 different physicians before being diagnosed and had had 3.7 physician visits. The physicians responsible for the current follow-up and treatment of the patients were neurologists (70%), headache specialists (14%), family physicians (6%), and him/herself (5%) while 5% never received follow-up or treatment. While 59% of the patients were able to reach the family physician who was following their migraine within 1 day, 32% stated that they could reach the specialist physician within a few days.

Questioning of Current Therapies

Overall, 87% of the patients (n=206) reported using medication for acute treatment and this rate was as high as 92% in the group with ≥ 2 TF. Of those who reported receiving treatment, 86% (n=177) were using the drug prescribed by a physician. In addition, 47% of the patients (n=97) used medications that they obtained from the pharmacy without any prescription for acute treatment, while 42% (n=86) benefited from complementary therapies (homeopathy, Ayurveda and massage). The most preferred acute drug treatments were pain medications with 78%, followed by triptans with 59%, ergots with 28% and other drugs with 5%. Some of the patients used one or more of these treatments as combination therapies.

Of the participants who stated that they used acute treatments, 61% defined themselves as partly satisfied and 16% as completely satisfied with acute treatment. When the reasons for this were questioned, 58% responded that it was because the treatments provided rapid relief of symptoms and 48% described that their treatments were comfortable to use. In the group who stated that they were not partially or completely satisfied with their acute treatments (5% and 2%) (n=15), the most common cause of this was the failure of the therapy to rapidly relieve their symptoms (67%).

When the patients were questioned for prophylactic treatment, the most commonly used prophylaxis treatment options were beta blockers with 41% and anti-epileptics with 31%. Forty percent of the patients had been receiving prophylactic treatment for less than 6 months, 19% between 7 and 12 months, 13% between 1 and 2 years, and 28% had been receiving prophylactic treatment for more than 2 years, with 71% of them being completely or partially satisfied with their treatments. This rate was found to be 70% in the group with ≥ 2 TF. The main reason for the satisfaction of the patients was that their prophylactic treatment reduced symptom severity substantially (42%).

Effects on Personal, Social and Professional Life and Results of General Work Productivity and Activity Impairment Questionnaire

Of the patients, 78% (n=185) were working full- or part-time on a regular basis and for 80% (n=148), their employer was aware of the fact they had migraine and only 24% (n=37) could receive their employer's support regarding their condition. Twenty-two percent of patients in the group with ≥ 2 TF were able to receive support. While 77% of the participants stated that migraine affected their professional lives, this rate was 84% in the group with ≥ 2 TF. Approximately 78% of the patients with migraine had to use at least one day off (3.4 days on average) in the last month, while patients in the ≥ 2 TF group had an average of 3.5 days off in the last month because of migraine-related reasons. On average, 68% of the patients were able to get paid sick leave for 1 to 5 days in the previous month (mean 2 days). The most frequent effect of migraine on work life was the difficulty in concentrating on work (38%). Interestingly, up to 11% of the patients reported that migraine had a positive effect on their profession lives in that it increased their individual flexibility and coping capacity.

Looking at the results of General Work Productivity and Activity Impairment Questionnaire; 191 patients were currently working, and 186 of them had worked actively within the last 7 days. In this active group (n=186), 21% of the working time was lost due to migraine pain (absenteeism) (8% in the group with 1 TF, 24% in the group with ≥ 2 TF) and overall labor loss rate was 67% (absenteeism + presenteeism) (57% in 1 TF group and 72% in ≥ 2 TF group) and overall labor loss rate was 67% (absenteeism + presenteeism) (57% in 1 TF group, 72% in ≥ 2 TF group). In the group of patients who were still working (n = 191), migraine-related

Table 3. Use of health resources according to the number of failed migraine prophylactic treatment in the past

	Total (n=237)	1 TF group (n=17)	≥ 2 TF group (n=153)
Brain imaging			
Percentage of respondents (n)	80 (189)	65 (11)	88 (134)
Average number of scans	2.3	2.1	2.5
ED visit in the last 12 months			
Percentage of respondents (n)	80 (190)	71 (12)	89 (136)
Average number of visits	4.1	3.8	4.5
Hospitalization rate in the last 12 months			
Percentage of respondents (n)	62 (146)	41 (7)	70 (107)
Average number of hospital stay	3.9	3.7	4.4

ED, emergency department; TF, treatment failure

performance loss rate was 61% (presenteeism) (59% in group 1, 67% in patients with ≥ 2 TF) and daily activity loss rate was calculated as 64%, (1 TF, 64%, ≥ 2 TF 69%).

Effects on Healthcare Resource Utilization

Brain imaging was performed in 80% of the participants (n=237), and this rate was about 65% in 1 TF group (mean: 2.1 images), and increased to 88% (mean: 2.5 images) in the group with ≥ 2 TF. Of the 189 patients with brain imaging, 31% had 1, 37% had 2, 16% had 3, 2% had 4 and 14% had >5 imaging assays. Of the respondents, 80% (n=190) presented to the emergency department within the last 12 months and the average number of emergency services was 4.1. Of the patients, 62% had to spend the night in the hospital due to migraine and the average number of hospitalized days was 3.9 nights (Table 3).

DISCUSSION

This is the first study performed online in Turkey to assess in detail the personal, social and professional and economic burden of migraine in patients who failed on previous prophylactic treatments and still have ≥ 4 days of migraine-type headaches and could be classified as to have a severe disease course.

The results of the study support the fact that migraine poses a serious burden on people and society, both socially and economically, and that this burden is more pronounced in the subgroup of patients who have had migraine headache attacks ≥ 4 per month and had not benefited from prophylactic treatment. A particularly striking result is that migraine could lead to a limitation in the functionality of the person not only in the headache phase, but also in the pre- and post-episode phases, and that the extent of the migraine burden is therefore much extensive than is known. Again, losses as high as 77% in work performance due to migraine pain and the increase in this rate up to 84% in the ≥ 2 TF group are important results in that the accentuate the serious negative effects of migraine on professional life.

The major largest community-based studies in the world reviewing migraine burden include the International Burden of Migraine Study (IBMS) (13), Chronic Migraine Epidemiology and Outcomes (CaMEO) (14) and American Migraine Prevalence and Prevention Study (AMPP) (15) the American Migraine Prevalence and Prevention Study (AMPP) (15), while the most prominent of the limited number of studies that have been reported from Turkey is a multicenter study by Baykan B et al. performed with 3862 patients to assess headache burden in patients presenting to neurology outpatient clinics (2).

According to the data from this study, 50-70% of patients suffering from headache in Turkey presented to a doctor, but the majority of new-onset migraine patients could not be diagnosed in the early stages because they presented to internal medicine physicians first, thus leading to increased tendency to chronicity. Initial physician referral rates were reported as 66% in this study, consistent with the rates reported in the above-mentioned study, whereas it was found that the first physician the patients presented was neurologists with a rate of 80%. This can be interpreted that the awareness of migraine in our society may have increased over time and therefore the preference of the physician who the patients present may have shifted to the direction of neurologists. This is a very positive development in terms of initiating appropriate treatment in early migraine patients and reducing chronicity rates. When we look at the worldwide data of the "My Migraine Voice" health survey, the first physician type the patients present was reported as general practitioner (53%), which differs from the data from our country and can be explained by the fact that the patients are encouraged to apply to primary health care services compared to health policies of other countries around the world. (11). Based on the data from the same study, emergency department admission rates in the last 12 months was 38%, and average number of visits was 3.3. The corresponding figures in Turkey are much higher, i.e. 80% and 4.1 respectively, and this is a striking finding demonstrating that patients with ≥ 4 days of migraine headache per month could lead to much larger healthcare resources utilization and economic burden. This is more pronounced in the group with ≥ 2 TF per month. Similarly, the average number of brain imaging in Turkey per person was 2.3 (≥ 2.5 TF group), also supporting this finding.

When we look from the perspective of work loss and decrease in productivity, the rates of patients in our country whose lives were impacted by migraine and had at least one work day loss in the last month due to migraine were found to be significantly higher compared with the world average (70% and 60% vs. 77% and 78% in our country, respectively). These rates were reported to be much higher in the group with ≥ 2 TF compared with both Turkey and the world in general. The WPAI survey results showed similar results with the above ratios. The most common adverse effect the patients experienced associated with migraine was difficulty in concentrating to work and the data did not differ between Turkey and the world in general. Baykan B. et al. reported in their study they performed in 2017 a work loss rate of 29% for new-onset migraine cases, which emphasizes that negative consequences on professional life and migraine-associated indirect work losses could lead to much more severe implications in patients with ≥ 4 migraine headaches a month, especially in those with ≥ 2 TFs, compared with new-onset patients and highlights the need that clinicians should act timely in diagnosing and treating this group of patients (2).

An opposite result with interesting and striking implications is that about 11% of the respondents reported that migraine caused an increase in individual flexibility and coping capacity during work. This can be interpreted as that as the individual learns to cope with migraine symptoms, his/her individual development is favorably affected, and the life perspective is expanded. An individual who builds correct sleep and food pattern and learns how to cope with stress to reduce frequent migraine attacks may also be benefiting from these strategies in business life. This result can provide an explanation for the researches which question why migraine is a common disease which is reserved in the evolutionary process.

In the study, it was noted that migraine caused limitations in daily life not only during the headache phase but in all phases (prodrome, headache and postdrome) (34%, 62% and 31%, respectively). These rates were found to be even higher in the group with a low success rate of prophylactic treatment (≥ 2 TF) (40%, 68% and 40%, respectively). Although the most

pronounced limitation was reported during the headache phase, the findings are striking in that they demonstrate the migraine burden extend far beyond the headache phase.

There are some limitations of the study. First of all, this was an online, questionnaire-based study and patients with ≥ 4 migraine headaches per month were included in the study on a voluntary basis. Therefore, although there are a large number of participants, the study may be inadequate to represent patients with migraine throughout the society. In addition, patients with limited access to online resources in our country and those having less than 4 migraine headaches per month were not included in the study, which may have contributed to patient selection bias. Another limitation was that the diagnosis of migraine and accompanying comorbid diseases were not clinically confirmed due to the fact that the data are based on individual statements. However, since all patients were diagnosed with migraine by a physician previously, the individual reports were not likely to be inaccurate and the symptoms were checked. Finally, the fact that the study was planned for a specific population (a group of patients with migraine headaches ≥ 4 days a month who previously failed on prophylactic treatment) and that it could not evaluate the temporal change of migraine and the personal and social burden it might bring over in time due to its cross-sectional nature could also be considered a limitation.

Despite all these above-mentioned limitations, the study is valuable because it was a well-designed study performed on a large population of patients, and is one of the rare studies conducted in a group of patients who were resistant to treatment and had ≥ 4 migraine headaches per month and particularly because it reflects the individual and social burden of migraine for the patient not only in the attack phase of migraine but also in the prodrome and postdrome phases.

CONCLUSION

Migraine is a not disease consisting of only headache but a neurological disease that can affect people and society in all its dimensions and can cause serious disability. This study shows that migraine may lead to limitations in both individual and professional life at each stage, including prodrome, headache and postdrome phases, particularly in a patient group who have ≥ 4 days with migraine headaches a month and failed to achieve sufficient benefit from the prophylactic therapies they have used who can be classified as to have "severe" disease. It is noteworthy that health expenditures such as physician visits and imaging studies are increased significantly in this group with the increase being more pronounced than it is in the whole world, and that migraine thus constitutes an important social economic burden in our country. In the future, it is especially important to plan treatment for patients who cannot benefit from the current treatments in order to increase the quality of life and productivity of these individuals.

Ethics Committee Approval: Participants were recruited by means of existing online panels (GfK Health). Participants' consent was obtained prior to participation in the survey. Survey data were handled confidentially and anonymity of respondents was maintained throughout the study. As such, and due to its research format, this study was exempted from ethics committee review.

Informed Consent: Participants' consent was obtained prior to participation.

Peer-review: Externally peer-reviewed

Author Contributions: Concept - PV; Design - AÇA MB, ZÇ, PV, ME, BB; Supervision - AÇA, MB, ZÇ, PV, ME, BB; Resource - GfK Health; Material- PV; Data Collection and/or Processing - AÇA, MB, ZÇ, PV, ME, BB; Analysis and/or Interpretation - AÇA, MB, ZÇ, PV, ME, BB; Literature Search - AÇA, MB, ZÇ, PV, ME, BB; Writing - AÇA, MB, ZÇ, PV, ME, BB; Critical Reviews - AÇA, MB, ZÇ, PV, ME, BB; Availability of data and materials: The datasets generated and analyzed during the study are not publically available for data confidentiality reasons.

Conflict of Interest: Manal Bozkurt, Zeynep Çalışkan and Pamela Vo are the employees of Novartis.

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