



An open/pilot trial of cognitive behavioral therapy in Turkish patients with refractory chronic migraine

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Abstract

Cognitive behavioral therapy (CBT) for pain management is a therapy that aims to modify thoughts and behavior to be more realistic and balanced. There are limited number of studies to assess the efficacy of CBT for patients with pharmacotherapy-resistant chronic migraine in our population. We aimed to investigate the effects of CBT for patients with refractory chronic migraine on pain attack frequency, disability, severity, anxiety and depression. Fourteen patients with refractory chronic migraine who were referred from the headache clinic to the psychiatry department and regularly attended CBT sessions at least once every 2 weeks for at least 6 months, were included in the study. After 2 sessions of psychiatric evaluation, the subjects had 12 40-min CBT sessions and were given relaxation exercises. The Hamilton depression and anxiety inventories, visual analogue scale for assessing the severity of pain, and the Migraine disability assessment (MIDAS) test were used before and after CBT. The mean Hamilton depression scores before and after CBT were 29.07 ± 7.74 and 14.21 ± 7.7 , respectively ($p < 0.0001$). The mean Hamilton anxiety scores before and after CBT were 26.8 ± 11.7 and 11.7 ± 2.6 , respectively ($p < 0.0001$). The mean VAS scores before and after CBT were 8.07 ± 0.91 and 3.71 ± 1.32 , respectively ($p < 0.0001$). The mean MIDAS scores before and after CBT were 55.5 ± 20.4 and 20.12 ± 16.6 , respectively ($p < 0.0001$). Our results showed that CBT had made a statistically significant difference on pain severity, number of migraine attacks and disability in patients with refractory chronic migraine. CBT should be considered in this patient group.

Keywords Anxiety · Cognitive behavioral therapy · Depression · Disability · Migraine

Introduction

Chronic migraine is a major public health issue that causes significant disability, excessive drug use, and burdens hospitals with regular admissions (Steiner et al. 2003). In Turkey, the prevalence of certain and probable migraine is 28.8%, and more than half of patients with migraine have at least 4 headache attacks per month (Baykan et al. 2015; Sullivan et al. 2016). Chronic migraine, described as headache occurring on 15 or more days per month for more than 3 months, which has the features of migraine headache according to the international classification of headache disorders (ICHD-III beta version) on at least 8 days per month, negatively affects patients' quality of lives and in turn increases the risk of psychiatric conditions such as depression and anxiety (Antonaci et al. 2011; Baykan et al. 2015; Bıçakcı 2013; Headache classification committee of

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the international headache society (IHS 2013). It has been reported that psychiatric conditions may be related to the chronicity of migraine-type headache, which is known to be associated with temperament traits such as perfectionism, neuroticism, and suppressed aggression, and that early recognition of these comorbid conditions can lead to success in the treatment of the disease (Antonaci et al. 2011; Tombul et al. 2015). Depression and anxiety scores were reported higher in patients with chronic obstructive pulmonary disease than in healthy controls, and it was proposed that the chronicity might have an impact on these findings (Aras et al. 2017). Stress reduction has become a key focus in research area owing to the increasingly demanding nature of modern lifestyles. New physiologic measures have been used to identify stress, and recent related research has paved the way for new methods in objective stress treatment (Subhani et al. 2018). In a meta-analysis that evaluated the relationship between migraine and depression, it was reported that depression was approximately twice as common in migraineurs than in those without headache. According to the study results, the prevalence of depression varies between 3.4 and 24.4% (Antonaci et al. 2011). In addition to depressive disorders, there are studies reporting that migraine is more common in psychiatric disorders such as generalized anxiety disorders, obsessive compulsive disorders, increased alcohol and substance abuse, and bipolar disorders, especially among those with migraine with aura (D'Souza et al. 2008; Eccleston et al. 2015; Thorn et al. 2007a, b).

Patients who have received appropriate prophylactic treatments for their pain management such as anticonvulsant, beta blockers, calcium channel blockers, and tricyclic anti-depressants, but whose quality of life is negatively affected even though they are administered at adequate doses and periods of time can be considered as treatment-resistant. In 2008, the American headache society (AHS) proposed naming patients with chronic migraine who have modified triggers, lifestyle factors, and those who have taken adequate amounts of acute and prophylactic drug combinations but still have no significant change in their quality of life as “Refractory chronic migraine patients” (Schulman et al. 2008).

Rational emotive behavior therapy, thought to be founded by Albert Ellis, and Cognitive Therapy theorized by Aaron T. Beck, demonstrated the indisputable role of thought in the conceptualization of the psychopathologies in the fields of psychology and psychiatry. Cognitive therapy, in addition to the techniques of behaviorism, have found extensive use and effective treatment approaches in various clinical situations such as depression, anxiety disorders, personality disorders, and eating disorders (Beck 1995). In the cognitive model, the aim is to achieve realistic, valid, and balanced thoughts with therapeutic

interventions and to change feelings and behaviors by modifying thoughts (Alford and Beck 1997).

There have been studies carried out to demonstrate the use of cognitive behavioral therapy (CBT) in migraine (Christiansen et al. 2015; Seng and Holroyd 2014; Göksel 2013). A recent meta-analysis showed that CBT was beneficial for migraine conditions, had lasting effects, and might also increase the efficacy of standard medications such as amitriptyline (Ng et al. 2017a, b). CBT used for migraine focuses on two main points. The first of these is the arrangement of behavioral interventions the individual undertakes to prevent migraine or control episodes. The other is to organize an individual's automated thoughts on migraine. Even though it has been suggested that regulation at the cognitive and behavioral level towards migraine might work, little is known regarding the management of patients with refractory migraine and it is unclear if CBT would work in this patient group (Morley et al. 1999). In a study comparing two groups of 34 patients with migraine who underwent CBT and another group of 11 patients who received no CBT, no statistically significant difference was found in terms of pain severity and frequency (Seng and Holroyd 2014). In this study, cognitive techniques were used to reduce catastrophizing cognitive errors. On the other hand, there are other studies suggesting that CBT may be useful for patients with chronic headache (Thorn et al. 2007a, b). In a study evaluating the efficacy of acceptance and commitment therapy (one of the third-wave psychotherapies) on chronic tension-type headache and migraine without aura; significant decreases were found in disability and stress rates (Mo'tamedi et al. 2012). Approaches based on Awareness and Acceptance and Commitment Therapy, which are claimed to be effective in migraine treatment, are mostly behavioral approaches and aim to heal functionality and decrease stress levels, rather than decreasing the severity of pain (Smitherman et al. 2015). It has been suggested that CBT is more effective when compared with biofeedback and relaxation methods (Seng and Holroyd 2014). There is a need for further research in this area because the impact of CBT on headache is controversial. In this study, we aimed to investigate the effects of CBT for patients with refractory chronic migraine on pain severity, migraine attack frequency, disability, anxiety, and depression.

Methods

Patients who fulfilled the International classification of headache disorders (2013 ICHD-III beta version) criteria for chronic migraine and had normal physical and neurologic examinations were selected. The patients with chronic migraine were consulted at our psychiatry clinics

between July 2014 and June 2016. The migraineurs included in the study were aged between 18 and 65 years, gave consent after being informed about the study, and attended cognitive behavioral therapies regularly, at least once every 2 weeks for at least 6 months, and had sufficient intelligence and language competence levels for cooperation. Patients with alcohol and substance use were excluded from the study. Among the 35 patients who presented in this time period, 6 expressed that they would not come regularly, 6 had alcohol abuse, 3 did not have the required mental capacity, 1 did not have the required language skills, and 5 did not continue their therapy regularly, and thus were excluded from the study.

Following 1–2 sessions of taking history and performing psychiatric examinations, the patients chosen for the study had 12 40-min CBT interviews. The following assessments were undertaken before and 6 months after the therapy initiated: the Hamilton depression rating scale, Hamilton anxiety rating scale, Visual analogue scale (VAS) for grading the intensity of pain, and the Migraine disability assessment (MIDAS) test for disability assessment associated with migraine. The Ethics Committee of Bakirkoy Training and Research Hospital for Psychiatry Neurology and Neurosurgery approved the study protocol (Date: June 3, 2014; Protocol number: 586). All participants were asked to sign the informed consent forms. This research was conducted in accordance with the Declaration of Helsinki and good clinical practice.

Constructed CBT interviews

There have been differences in CBT sessions conducted on patients with chronic migraine in studies thus far. For example, Martin et al. performed 12 sessions of 50 min and Christiansen et al. performed 13 sessions of 50 min (Martin et al. 2015; Christiansen et al. 2015). Based on the CBT sessions of Martin et al. and Christiansen et al. who claimed that CBT performed on patients with migraine was effective, the CBT sessions in our study were structured as follows: the first two sessions were arranged as psycho-teaching sessions; the anatomy and physiology of migraine as well as the rationale of CBT was described to the patients. The patients were asked to keep a pain diary following these sessions. This pain diary is a chart of the severity of the migraine episodes; their frequency; factors that trigger migraine attacks; the events, thoughts and feelings that occurred during the episode; and any actions taken to terminate the attacks. Patients with depressive symptoms accompanying headaches were offered behavioral activation. In doing so, patients were asked to keep a log of scores ranging from 0 to 10 that they associated with their daily activities and the joy they brought them. Cognitive restructuring was performed in patients without

depressive symptoms. In these sessions, the aim is to attempt to replace cognitive distortions that patient's focused on such as negativity, generalization, and catastrophizing with alternative thoughts and thus emphasize the ability to manage migraine attacks. To discover the alternative thoughts, the proof examination method, which does not support or oppose the accuracy of the patients' thoughts, was used. For example, after examining the proof supporting or opposing the thought "I can't withstand this headache episode, it will go on forever and I will never be happy because of these headaches," the patients were taught to place the alternative thought, "These episodes will be over after a while, like the ones prior to these, if I stay calm they will be easier to cope with." Afterwards, the patients were taught relaxation and breathing exercises, focusing on the ability of patients to cope with migraine attacks. Therapies were terminated with the last 1–2 sessions giving information on management of recurrence. After the therapy was ended, the Hamilton Anxiety and depression rating scales, VAS, and MIDAS tests were reevaluated. In order to avoid clinical subjectivity, the first Hamilton anxiety and depression inventory was administered by the therapist practicing CBT, whereas the post-therapy Hamilton anxiety and depression inventory was conducted by a physician who was blinded to the treatment protocol to avoid bias in estimated treatment effects.

Scales for assessments

Sociodemographic data form

This form was constructed for the researchers of this study to discern the sociodemographic characteristics of the participants and to determine suitability according to the inclusion and exclusion criteria.

Visual analogue scale (VAS)

The VAS is a progressive line or band and the patient chooses a point that identifies their pain intensity. In this, patients assign a number to their pain severity or healing (for pain intensity, 0 represents absence of pain and 10 represents the highest possible pain) (Wewers and Lowe 1990).

Hamilton depression rating scale

This test, developed by M. Hamilton and JBW. Williams, measures the severity of depression. It is administered by physicians to individuals with depressive symptoms. The validity and reliability test of the Turkish version was performed by Akdemir et al. (1996).

Hamilton anxiety rating scale

The scale was developed by Hamilton in 1959 to measure anxiety severity as well as the anxiety level and symptom distribution. The validity and reliability of the Turkish version of the scale was established in 1998 (Yazici et al. 1998).

Midas migraine disability assessment questionnaire (MIDAS)

MIDAS is an easy to apply, widely used scale developed for assessing the disabling effects of migraine on a patient's life. It questions the number of times headache has limited their ability to participate in activities and their productivity at work/school/home and social-family activities in the last 3 months. The Turkish validity and reliability of the form was studied by Ertaş et al. (2004) According to the MIDAS scale, the limitation degrees are as follows: 0–5: None, 6–10: Mild, 11–20: Moderate, 21 and higher: Severe disability.

Statistical analysis

SPSS 18.0 was used in the study as the statistical analysis program. The paired-sample *t* test was used to compare repeated quantitative measurements in the group, as well as descriptive statistical methods (mean, standard deviation, frequency). Statistical significance was evaluated as $p < 0.05$.

Results

The participants' demographic and clinical characteristics were as follow: 5 males (35.7%) and 9 (64.3%) females aged between 24 and 47 years. The mean age of the patients was 34.35 ± 8.17 years. Among the patients, 5 (35.7%) were single, 6 (42.9%) were married, and 3 (21.4%) were divorced. The education levels were listed as: 5 (35.7%) primary school, 2 (14.3%) middle school, 2 (14.3%) high school, and 5 (35.7%) university. Only 4 (28.6%) patients did not have a regular job. The mean duration of headache was 13.07 ± 7.18 years.

Twelve (85.7%) patients had previous psychiatric admissions. Among those with prior psychiatric admission, 7 patients had been diagnosed as having depression, 1 patient was diagnosed as having obsessive–compulsive disorder (OCD), 2 patients had been diagnosed as having panic disorder, 1 patient had been diagnosed as having generalized anxiety disorder, and 1 patient was diagnosed as having post-traumatic stress disorder. There was only 1 patient with migraine with aura, the remainder had

migraine without aura. All patients met the International classification of headache disorders [ICHD-III beta version] chronic migraine criteria. Nine (64.3%) patients received prophylactic treatment for migraine [botulinum toxin injection ($n = 3$), beta blocker (propranolol) and amitriptyline combination ($n = 3$), topiramate and duloxetine combination ($n = 2$), and topiramate ($n = 1$)], whereas 5 (35.7%) received no prophylactic treatment (Table 1).

The Hamilton depression scores of the patients showed a statistically significant difference before (29.07 ± 7.74) and after (14.21 ± 7.17) CBT, and there was a significant decrease in Hamilton depression scores after CBT ($p < 0.0001$). Hamilton anxiety scores were statistically significant before CBT (26.8 ± 11.7) and after (11.7 ± 2.6); there was a significant decrease in Hamilton anxiety scores after CBT ($p < 0.0001$).

VAS scores showed a statistically significant difference before (8.07 ± 0.91) and after (3.71 ± 1.32) CBT; there was a significant decrease in VAS scores after CBT ($p < 0.0001$). There was a statistically significant difference in the number of migraine attacks before (10.85 ± 3.50) and after CBT (4.92 ± 2.70), and there was a significant decrease in migraine attack frequency after CBT ($p < 0.0001$). We found a significant decrease in MIDAS disability scores between the pre-CBT (55.5 ± 20.4) and post-CBT scores (20.12 ± 16.6)

Table 1 Clinical characteristics of Turkish patients with migraine

Migraine patients n (%)	
Migraine duration (year)	
Mean \pm standard deviation	13.07 \pm 7.18
Previous psychiatric referral	
Yes	12 (85.7%)
No	2 (14.3%)
Previous psychiatric diagnoses	
Depression	7 (50.0%)
Anxiety disorders	4 (28.6%)
Post traumatic stress disorder	1 (7.1%)
Prophylactic treatment	
Yes	
Botulinum toxin injection	3 (21.5%)
Beta blocker (Propranolol) + Amitriptyline	3 (21.5%)
Topiramate + Duloxetine	2 (14.3%)
Topiramate	1 (7.1%)
No	5 (35.7%)
Smoking	
Yes	5 (35.7%)
No	9 (64.3%)

($p = 0.012$). The clinical characteristics of the patients before and after CBT are shown in Table 2.

Discussion

There are studies reporting that CBT and relaxation techniques are effective when migraine treatment is addressed from a psychological perspective (Sullivan et al. 2016; Harris et al. 2015). In this study, the effects of CBT on migraine treatment in cases of treatment-resistant migraine were evaluated using the Hamilton depression and anxiety scales, VAS, migraine attack frequency, and MIDAS disability scores before and after CBT, and we detected a statistically significant improvement in our sample.

Behavioral techniques that may be effective in coping with migraines include relaxation techniques, which reduce the level of stress aimed at preventing the appearance of migraine attacks, as well as techniques aimed to reducing the severity of pain during a migraine attack (such as going to a dark room). That is, the behavioral techniques necessary for coping with pain are positive strategies such as relaxation, stress management, and negative strategies such as isolation and avoidance aimed at reducing the severity of pain (Sullivan et al. 2016). Adler et al. reported that gaining new cognitive coping skills was correlated with reduced depressive symptoms, even if negative beliefs remained. Moreover, once people learned these skills, they could use them for the rest of their lives, which might explain why the benefits of CBT remain long after treatment cessation (Adler et al. 2015). In the long run, the impacts of positive strategies on quality of life are different from those of negative strategies. For example, the use of isolation to prevent the emergence of migraine attacks seems to work initially, but it can be harmful in the long term (Martin et al. 2007). The goal of cognitive therapy in patients with migraine is to change their inappropriate thinking mechanisms, including catastrophizing.

Thorn et al. (2007a, b) found no statistically significant difference in migraine frequency between a control group

and migraineurs who underwent CBT. Our research differs from this study in some features. First, we used the Hamilton anxiety and depression rating scales, which were conducted by a physician who was blinded to the treatment, not self-report assessments such as the Beck depression and Beck anxiety scales. This may have led to differences in assessing anxiety and depression. In addition, in our research, individual CBT was applied, differing further from the study of (Thorn et al. 2007a, b). CBT was rationally described to all patients initially, and patients with predominant depression were first introduced to behavioral activation techniques. Thorn et al. may have obtained different results because they used the same approach with group CBT (i.e. not individualized). For this reason, we think that individualization of the CBT in migraine patients may be important. Similar to our findings, Christiansen et al.'s study had results indicating that individual CBT in addition to group CBT might be effective in reducing pain intensity and severity in patients with migraine (Christiansen et al. 2015).

Martin et al. (2015) reported a statistically significant reduction in the frequency of migraine attacks in the treatment of migraine and tension-type headaches by adding relaxation to CBT. In Martin et al.'s study, Beck depression and anxiety inventory scores were decreased significantly. The CBT session configuration used in our study was based on Martin et al.'s study. Although Hamilton depression and anxiety inventories were used in our study, the difference between scores prior to CBT and after were close to 50%, similar to Martin et al.'s study. However, D'Souza et al. found no significant results in terms of the frequency of migraine attacks; however, their study comprised relaxation techniques only (D'Souza et al. 2008). In our study, adding cognitive restructuring to relaxation in patients with migraine may have resulted in different outcomes compared with their study.

Regarding the reasons for treatment drop-out in our follow-up study, 6 patients stated that they could not come regularly from the beginning and 5 patients did not come to therapy sessions regularly. These patients had refractory

Table 2 Clinical characteristics of patients before and after cognitive behavioral therapy

		Pre-CBT n	Post-CBT n	<i>p</i> value
HAM-A	Mean ± SD	26.8 ± 11.70	11.7 ± 2.60	< 0.0001
HAM-D	Mean ± SD	29.07 ± 7.74	14.21 ± 7.17	< 0.0001
VAS	Mean ± SD	8.07 ± 0.91	3.71 ± 1.32	< 0.0001
Migraine attack frequency	Mean ± SD	10.85 ± 3.50	4.92 ± 2.70	< 0.0001
MIDAS	Mean ± SD	55.5 ± 20.4	20.12 ± 16.6	< 0.0001

Paired samples *t* test Bold indicates statistical significant value

HAM-A Hamilton anxiety rating scale, *HAM-D* Hamilton depression rating scale, *MIDAS* midas migraine disability assessment questionnaire, *Mean ± SD* mean ± standard deviation

chronic migraine and as a result of their catastrophizing thinking that may have concluded that they would not benefit from treatment, which could also have influenced their treatment discontinuation.

The mean migraine duration in this patient group was 13 years. Given this extended period, ‘learned helplessness’ may have played a role, especially in the context of CBT intervention, because this is a common phenomenon in patients who become conditioned to believe that a situation is unchangeable or inescapable (Frediani and Villani 2007). Also, it can be said that in cases of accompanying depression, the treatment motivation of the patients increased and the frequency and severity of the migraine attacks decreased with time as a result of applying the methods such as behavior activation, regulation of activity schedules, and increasing activities that gave pleasure.

According to the results of our research, we found a statistically significant decrease in MIDAS scores after CBT in patients with refractory chronic migraine who reported no benefit from medical or interventional treatments. There are not enough studies evaluating the effects of CBT and MIDAS scores in the current literature. Bromberg et al. reported that the MIDAS scores in their study were reduced with CBT treatment compared with the control group, but the decrease was not statistically significant (Bromberg et al. 2012). Mérelle et al. (2008) assessed the outcome of 51 patients who were given cognitive training comprising relaxation and trigger management to be practiced at home, and reported no significant changes in disability scores and no reduction in the number of migraine attacks. The fact that these studies differ from our study’s method, that these patients managed their own treatments either via the internet or at home, and the lack of professional help may be the reason of unchanged MIDAS scores and therefore the same level of disability.

The patients in our study were selected from among patients with high-frequency and severe attacks despite several medications and/or interventional treatments. We saw that some of our patients were in despair, believing no response to treatment would be available and that they did not practice the treatments we suggested. We observed that patients with decreased frequency and severity of migraine attacks after CBT were more responsive and more eager about treatment after CBT in our neurology clinic. We think that psychiatric evaluation of patients with migraine in routine neurology clinics, referring them to related units, and teaching methods of coping with disease will prevent loss of time in the treatment process of headache.

Our study has several limitations. These include the small sample size, the statistical evaluation of sex not being performed, not having a control group, and the heterogeneity caused by patients having CBT with or without migraine prophylaxis. Nevertheless, our study has some

strengths; the objective criteria used in our study showing CBT reduces levels of depression and anxiety among patients with refractory chronic migraine, also reduces the number of disability days as well as the degree of disability. Furthermore, other strengths of our study include the planning of the patients’ first CBT with a semi-structured interview with a psychiatrist, a migraine pain diary keeping patients’ pain frequency, duration and severity and individualization of CBT according to these logs. The sample appears small and limited to a convenience sample (subject to a high likelihood of sampling error, selection bias and other influence).

Research on CBT’s efficiency on episodic migraine just like research on chronic migraine may guide us in better understanding the relationship of CBT and migraine. For future studies, participants could be followed up to ensure that the improvements observed are stable. In addition, other non-pharmacologic options should be explored as well in this difficult-to-manage patient group. For example, physical exercise is recommended by most physicians; however, there is scant evidence supporting this recommendation (Narin et al. 2003). Headache and ADHD are also known to be associated and physical exercise has been shown to provide benefits in ADHD (Paolino et al. 2015; Ng et al. 2017a, b).

Conforming to the results of our research, it could be concluded that in patients with refractory chronic migraine, CBT reduces the severity of pain attacks and also significantly reduces disability. Cognitive therapy can organize automatic thinking and shape behavior. CBT should be considered in this patient group.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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