

# The Use of Complementary and Alternative Medicine in Patients with Migraine

## Migrende Tamamlayıcı ve Alternatif Tedavi Yöntemlerinin Kullanımı

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### ABSTRACT

Although many patients with migraine get positive benefits from conventional pharmacological treatments, many others do not benefit sufficiently or experience adverse effects from these treatments. For that reason, these patients usually seek complementary and/or alternative medical (CAM) treatments all over the world. In general, although CAM therapies are not recommended by neurologist in Turkey, most of migraine patients, who do not respond conventional medicine treatments, seek alternative therapy. Acupuncture, botulinum toxin, mind-body interventions, and nutraceutical options are the most popular treatments. In this review, the available evidence for all these treatments will be discussed. (*Archives of Neuropsychiatry 2013; 50 Supplement 1: S41-S46*)

**Key words:** Migraine, complementary and alternative medicine, nutraceuticals, behavioral treatment, acupuncture, biofeedback

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### ÖZET

Migrenli hastaların çoğu geleneksel farmakolojik tedavilerden fayda görseler de, diğerleri yeterince etki görmemekte veya bu tedavilerin yan etkilerini yaşamaktadırlar. Bu nedenle dünyanın pek çok yerinde tamamlayıcı ve alternatif tedavi (TAT) yöntemleri arayışı vardır. Türkiye’de TAT yöntemleri nörologlar tarafından önerilirse de, geleneksel tedavi yöntemlerinden fayda görmeyen hastalar alternatif tedavi yöntemleri aramaktadır. Akupunktur, botulinum toksin, akıl-vücut işbirliğini kullanan yöntemler, elementler ve bitkisel maddeler en sık kullanılanlardır. Bu derlemede bu tedavi yöntemlerinin mevcut kanıtları tartışılacaktır. (*Nöropsikiyatri Arşivi 2013; 50 Özel Sayı 1: S41-S46*)

**Anahtar kelimeler:** Migren, tamamlayıcı ve alternatif tıp, elementler ve bitkiler, davranışçı tedavi, akupunktur, biofeedback

**Çıkar çatışması:** Yazarlar bu makale ile ilgili olarak herhangi bir çıkar çatışması bildirmemişlerdir.

## Introduction

The lifetime prevalence of migraine has been reported to be 11% (1). The prevalence of migraine in Turkey is 16.4% in patients 15-55 years old. It is estimated that 8 million people in Turkey suffer from migraine headaches (2).

Although every year new pharmacological treatments have been developed, 9 million women, 3 million men suffered from migraine with moderate to severe disability in the United States. The economic burden of migraine in the United States totaled \$13 billion. Eight million people visited doctor’s office every year and 157 million workdays each year are lost due to headache (3).

Although pharmacological treatments are the first choice for migraine, adverse effects and inefficiency limit the use of drugs. Therefore, patients are very attentive to complementary and alternative medicine (CAM) therapies for the prophylaxis and treatment of headache attacks.

In recent years, there has been a growing public interest and demand in CAM. For that reason, an increasing number of randomized controlled and prospective studies on this topic are being performed. In various studies it is stated that, the percentage of population who used CAM at least once in the previous year is estimated to be 42% in the United States, 48% in Australia, 20% in England, and 11.6% in Italy. Conventional physicians in the United States refer patients for some CAM treatments (4, 5, 6). In Turkey, there is some conflict about the use of CAM modalities. The use of CAM modalities in Turkish patients with diabetes mellitus, asthma, cancer and pain has been reported (7, 8, 9, 10, 11, 12, 13, 14). However, we did not find any study on the use of CAM in Turkish headache patients. While CAM is becoming increasingly popular worldwide, our population seeks alternative treatments as well.

There are many studies about this subject from other countries, but there is not any in Turkey. However, the use of alternative treatment modalities, particularly, herbal remedies is increasing

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in public, and even there are advertisements in social media. Although there are several reports about the use of CAM modalities in migraine patients, well-designed randomized controlled studies are few in number (15, 16, 17, 18). Considering increasing use of non-prescribed herbal treatments, we need objective and evidence-based data about CAM.

In recent years, evidence-based classification (EBC) has taken place in clinical practice protocols. The aim of EBC is to improve patient outcomes, quality of care, and to provide some standardization of treatment (19).

Level (I) has been defined evidence obtained from at least one properly-designed randomized controlled trial. Level II means evidence obtained from well-designed controlled trials without randomization. Level III is evidence included opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees. Level IV evidence is observational trials (case series, case controlled studies etc), and finally Level V is expert opinion not based on critical appraisal but based on reasoning from physiology, bench research, or underlying principles (19, 20).

In this review, the evidence for various CAM therapies in migraine treatment will be discussed.

### **I-CAM Modalities**

#### **IA-Acupuncture**

Traditional Chinese medicine use acupuncture for more than 2000 years. Acupuncture was accepted as a viable alternative for the treatment of chronic headache (21, 22).

According to traditional Chinese medicine, life energy, known as Qi, is believed to flow in the body through channels or meridians connected to all organs and to each other. Disease is explained by an imbalance in the energy flow within the meridians. More than 324 acupuncture points and 12 meridians are defined in human body (21, 22).

Although, the meridians which were believed in Chinese medicine cannot be explained by modern research technologies, there are some theories about how acupuncture works. The insertion of an acupuncture needle stimulates A-delta and C fibers. When this stimulation is perceived by the brain, opioid peptides (dynorphin, endorphin, enkephaline) are produced. The analgesic effect of acupuncture may be related to this mechanism. Serious adverse effects of acupuncture have not been reported. Local pain, small hematoma and, local paresthesia have been reported in 1% of patients (21, 22, 23, 24).

There are some legal requirements to practice acupuncture in Turkey. The physicians should attend a acupuncture course with the permission of the Turkish Ministry of Health. After the course, the participants should be successful in the examination.

A meta-analysis study of acupuncture and prophylaxis for migraine headaches analyzed 22 randomized controlled trials with 4,419 patients. Six of them compared traditional acupuncture with no prophylactic or standard prophylactic treatment; 14 of them compared real acupuncture with sham acupuncture. This study showed that acupuncture provides more benefit than routine care or acute treatment alone. However, there is no evidence that true acupuncture is more effective than sham acupuncture (25).

The general accepted view is acupuncture 'could be valuable

non-pharmacological tool in patients with frequent episodic or chronic tension-type headaches' (Level I) (20, 21, 22, 23, 24, 25)

#### **IB. Botulinum Toxin**

Botulinum toxin A (BTA) is a neurotoxin. BTA is used to induce muscle paralysis and to treat focal dystonia. This effect results from prevention of release of acetylcholine from nerve endings to muscles. The analgesic effects of BTA on migraine are not dependent on changes in muscle tone. BTA injection relieves not only the headache but associated symptoms such as nausea, vomiting, photophobia and phonophobia. It has been known that migraine headache is secondary to neurogenic inflammation of dural and meningeal vessels. BTA prevents substance P release from trigeminal nerve endings, along with activating expression of substance P in the raphe nuclei. In addition, vasoactive intestinal peptide and neuropeptide Y located in parasympathetic neurons are inhibited by BTA injection (26, 27, 28).

Injection sides for migraine are temporal, frontal, glabellar, occipital and cervical regions. 25-195 Unites of BTA have been used for migraine patients in several studies. The most common side effects associated with BTA injections were neck pain, and ptosis (29).

BTA has been used since 2000 for treating chronic migraine. But Onobotulinum toxin A received FDA approval for the treatment of chronic migraine in October 2010. Several randomized control studies have shown that BTA improves headache and associated symptoms. Especially, a randomized double-blind, PREEMPT study (29) which was done on 1384 patients resulted in significant improvements compared with placebo in multiple headache symptom measures, and significantly reduced headache-related disability, and improved functioning, vitality, and overall health-related quality of life. The dose of 155-195 units of onabotulinum toxin A every 12 weeks over 24 weeks was well tolerated. A comparative study (30) on onabotulinum toxin A and topiramate showed significant reductions from baseline in the frequency of headache and migraine days and improved quality of life with each treatment. However, it was found that the risk of discontinuity of topiramate was much higher.

There is no enough positive data available about BTA in episodic migraine patients. In addition, onabotulinum toxin A cannot be considered as a standard treatment for chronic migraine.

Onabotulinum toxin A may be used in patients with chronic migraine under the following conditions:

Migraine is a leading cause of disability

Chronic/frequent episodic migraine patients who do not respond to conventional therapy

Conventional therapy is contraindicated

The presence of medication overuse headache

Associated with neck and jaw spasm

#### **IC. Massage**

Massage therapy is beneficial in relieving pain due to muscle strain. It reduces subcutaneous adhesions and fibrosis. Massage therapies also regulate the circulation of blood and lymph and helps regulate the sleeping patterns. A randomized controlled study (20) which investigated the effect of massage therapy in 26 chronic migraine patients (12 control patients) revealed that massage therapy had a statistically significant effect on pain intensity as

compared with controls. Pain intensity was reduced 71% in the massage group and was unchanged in the control group. Another study (31) on 48 patients (25 controls) showed that migraine attack frequency was significantly reduced in the massage group as compared with control group, while the intensity of attacks was unchanged. However, there is no enough evidence to recommend massage as a primary treatment (Level IV) (20, 31).

#### **ID. Yoga**

Yoga is an ancient technique which includes breathing techniques, mindfulness and meditation. Yoga may have positive effects on blood pressure, blood glucose, intraocular pressure and breath regulation (20). There is only one study performed on the effectiveness of yoga in migraine patients (32). 72 migraine patients were included in this randomized-controlled study. The headache intensity, symptomatic medication consumption, pain rating index, anxiety and depression scores were significantly lower in the yoga group compared to the self-care group (Level II) (32).

#### **IE. Aerobic Exercise**

The knowledge about the effect of aerobic exercise in patients with migraine is based on anecdotal reports. In the year 2008, 4 case studies and eight studies investigated the therapeutic role of aerobic exercise on migraine headache. The majority of studies did not find a significant reduction of headache attacks or headache duration but indicated only a reduction of pain intensities in migraine patients due to regular exercise (33). Another study (34) from Turkey showed that regular aerobic exercise reduced migraine pain severity, frequency and duration.

Recently, a prospective, randomized, controlled study which included 99 patients with migraine showed that aerobic exercise (3 times per week, 40 minutes) was as effective as topiramate and relaxation training. They concluded that exercise was found to be equal to the well-documented methods of relaxation and topiramate with regard to the reduction of migraine frequency (Level II). (35)

#### **II- Cognitive Therapies**

These therapies included bio-feedback, cognitive-behavioral treatment, meditation, relaxation training, and hypnosis (15, 20, 36).

##### **II A. Biofeedback**

Biofeedback (BFB) involves monitoring and voluntary control of physiologic processes, allowing patients to take an active role in managing their pain. Different types of BFB such as EMG BFB, positional BFB, thermal BFB, electrogoniometer BFB, EEG BFB, and blood-volume-pulse BFB are used. In migraine, thermal, blood-volume-pulse feedback and EMG BFB are most commonly used. EMG BFB is used to detect the feedback of electrical activity from muscles. Thermal BFB provide thermal feedback by attaching a temperature-sensing device to a finger. It has been reported that emotional stress increases temperature of the finger. Thermal BF regulates blood flow throughout the body, including blood flow to the brain. If the patient can relax, the finger gets warmer. Another BFB technique is blood- volume-pulse feedback method which is specifically designed for migraine. Patients are trained how they constrict the temporal artery (37, 38).

A meta-analysis study by Nestoriuc and Martin (37) showed that BFB was effective in patients with migraine (Level I). This meta-analysis report included 55 studies. In addition, this study showed

that blood-volume-pulse feedback yielded higher effect sizes than peripheral skin temperature feedback and electromyography feedback (20, 36, 37, 38).

##### **IIB. Cognitive-Behavioral Therapy**

In this method, the patient focuses on cognitive, affective and behavioral stimuli of headache. Cognitive-behavioral therapy (CBT) increases patient awareness of headache. CBT aims include the development of self-efficacy and internal locus of control in headache patient. Patients observe the situations in which their headache occurs, including their thought and feelings. Once headache-related stressful situations are recognized, the patient and therapist work together via collaboration. Several studies have reported that CBT was effective for migraine, with studies showing that 40% to 50% of individuals experience 50% or greater reduction in headache frequency (Level I) (20, 36).

##### **IIC. Meditation**

All types of meditation effects focus on attention and mental activity. Cerebral electrical activity and neurotransmitter and immune system changes during the meditation have been reported. In addition, frontal/prefrontal, dorsolateral prefrontal cortex, and anterior cingulate cortex activation during meditation have been shown. We found only one study performed on meditation and migraine (39). 83 migraine patients practiced spiritual meditation, secular meditation or muscle relaxation. The results of this study showed that the spiritual meditation group had greater decreases in migraine frequency and anxiety than other groups. Limitations of this study were small group and short duration (the monitoring of patients were 1 months), besides, the unique diagnosis method for migraine was ID-migraine screening tool (39).

##### **IID. Relaxation Training**

Relaxation training focuses on breathing rate, rhythm and muscle relaxation. These exercises are used to decrease physiologic responses to stress and sympathetic tone. The most popular technique is progressive relaxation training. The patient is aware of the tense and relaxed muscles. This technique takes 20 to 30 minutes per day. Initially 16 muscle groups are involved, and as treatment proceeds, muscle groups are progressively combined, resulting in 4 groups at the end of the therapy.

Several analyses have reported that relaxation training is effective in relieving both migraine and tension type headache, with studies showing that on average, 43% to 55% of individuals experience 50% or greater reduction in headache frequency (20, 36, 40, 41).

##### **IIE. Hypnosis**

Hypnosis is a method which focuses on attention and concentration with relative suspension of peripheral awareness. Anderson et al. (42) showed that the number of attacks was significantly lower for the group receiving hypnotherapy than for the group receiving prochlorperazine. Hypnotherapy consisted of six sessions at intervals of 10 to 14 days. One year later, hypnotherapy was found to be more effective than other treatments. Self-hypnosis training was shown to be effective when compared with propranolol. They found no statistically significant difference between the two groups. More studies are needed and there is not enough evidence to recommend hypnosis as the first-line option for headache prevention (Level IV) (43).

### III- Elements and Natural Therapies

#### IIIA-Coenzyme Q10

Coenzyme Q10 is an enzyme cofactor in the mitochondrial electron transport chain which had a role in aerobic cellular respiration. It may play prophylactic role in patients with migraine as an antioxidant. Magnetic resonance spectroscopy and DNA analyses suggested that mitochondrial dysfunction is related to the genesis of migraine. The rationale for Coenzyme Q10 in migraine is based on this theory (36).

There are two studies on adult use of Coenzyme Q10 in migraine patients. One of them was an open-label study which was conducted on 31 migraine patients (44). The patients received 150 mg/day of Coenzyme Q10 for 3 months. 61.3% of patients had a greater than 50% reduction in number of days with migraine headache. There were no adverse effects noted with this therapy. The other study (45), which was a double-blind, randomized, placebo-controlled study, was performed on 42 patients. It was observed that 100 mg of Coenzyme Q10 3 times daily significantly decreased attack frequency, headache days, and days with nausea.

Coenzyme Q10 treatment may be used effectively especially in childhood migraine. Coenzyme Q10 levels were measured in 1550 pediatric migraine patients with frequent headache (46). Coenzyme Q10 levels in 32.9% of patients were below the reference range. Patients with low Coenzyme Q10 were treated with 1 to 3 mg/kg per day of Coenzyme Q10 in liquid gel capsule formulation. The headache frequency and Headache Disability Index scores were improved with Coenzyme Q10 supplementation.

The Coenzyme Q10 treatment may be chosen in pediatric migraine patients as an alternative treatment (20, 36) (Level II).

#### IIIB. Riboflavin

Riboflavin, also known as vitamin B2, is a cofactor in the electron transport chain of the Krebs cycle. In addition, it plays a role in membrane stability and the maintenance of energy-related cellular functions (36).

Riboflavin in a dose of 400 mg for 3 months has been compared with beta blockers (47). The proportion of responders regarding headache frequency (ie, patients having a decrease of 50% or more of attack frequency) was similar in the beta-blocker (55%) and the riboflavin (53%) group.

Another study showed that 400 mg of riboflavin daily was effective in migraine treatment compared to placebo. Two minor side effects were diarrhea and polyuria (Level II) (48).

#### IIIC. Magnesium

Magnesium inhibits platelet aggregation and vasospasm. It also stabilizes cell membrane and supports cerebrovascular tone. Magnesium concentration has an effect on serotonin receptors and inflammatory mediators, release and synthesis of nitric oxide. It has been known that low magnesium level may be detected in migraine patients during attacks. Routine laboratory testing generally measures total magnesium level, but ionized magnesium level is important for evaluating migraine (36, 49).

Magnesium deficiency may be common especially in women with menstrual-related migraine. It has been shown that 600 mg/day oral magnesium citrate supplementation is useful to decrease headache frequency and severity. On the other hand, 3x360 mg/day magnesium supplementation (from the 15th day of the menstrual

cycle to the onset of menstrual flow) was shown to be effective in patients with menstrual-related migraine (36,49).

A single-blind randomized controlled study showed that 1 g intravenous magnesium sulfate was superior to placebo in 30 patients with moderate to severe migraine attacks (50).

Magnesium was probably effective for migraine prophylaxis on the basis of 2 positive Level II studies and 1 negative Level III study. Because of contradictory results in these trials, magnesium treatment is not a first-line treatment in migraine patients (51). However, it may be advised in patients with menstrual-related migraine.

The most common side effect associated with oral magnesium supplementation is diarrhea. Magnesium toxicity is characterized by the loss of deep tendon reflexes followed by muscle weakness, respiratory paralysis, and death. Renal failure patients are at higher risk of developing toxicity (36).

#### IIID. Feverfew

Feverfew (*Tanacetum parthenium*) is a member of the daisy family. Feverfew products usually contain feverfew leaves. The name feverfew comes from a Latin word meaning "fever reducer". It has been used as an anti-inflammatory agent for centuries. Feverfew has been used for migraine prophylaxis. This prophylactic effect may be related to inhibition of platelet aggregation as well as release of serotonin from platelets and white blood cells. In addition, it inhibits prostaglandin and phospholipase A synthesis (36).

There are several randomized controlled studies on the efficacy of feverfew in migraine prophylaxis. However, the results of the studies about use of feverfew in patients with migraine are controversial. These different results may be due to wide variations in the strength of the parthenolides and differences in the stability of feverfew preparation. Recently, a new stable feverfew extract (MIG-99) was created. A multicenter, double-blind, placebo controlled study reported benefit from feverfew in migraine. The most common reported adverse effects were gastrointestinal disturbance and mouth ulcers. "Post-feverfew syndrome" including anxiety, headaches, insomnia, and muscle and joint stiffness may arise with long-term use of feverfew (36, 52).

Feverfew should not be used by pregnant women. It should not be used concomitantly with anticoagulant drugs because of platelet inhibitory effect of feverfew (19)

#### IIIE. Butterbur (*Petasites Officinalis*)

Butterbur has been used to treat fewer, spasm and pain in some parts of Europe and Asia. Although its action mechanism is not fully understood, butterbur acts through calcium channel regulation and inhibition of peptide leukotriene biosynthesis, thus, influence the inflammatory cascade and therefore reduces inflammation associated with migraine headache (20, 36).

The butterbur plant contains pyrrolizidine alkaloids which is carcinogenic and hepatotoxic. The commercially available preparations do not include this substance. For that reason, patients should be advised to use only butterbur products that are certified and labeled "PA-free." A study showed that 50 mg of Petadolex® taken twice daily may significantly reduce number of migraine attacks and migraine days per month compared to placebo (53). A multicenter prospective, open-label study on 109 children and

adolescents with migraine demonstrated that Petadolex® reduces the frequency of migraine (54).

### III.F. Ginger

Ginger has been used in China for centuries to treat pain, inflammation and muscle spasm. Ginger has been used as a potential anti-inflammatory and antithrombotic agent due to inhibition of prostaglandin and leukotrienes synthesis. Some reports suggest that it is effective on nausea and headache.

Recently, a multicenter, placebo-controlled study (54) revealed that sublingual feverfew/ginger was safe and effective as a first-line abortive treatment in migraine patients who frequently experience mild headache prior to the onset of moderate to severe headache. The most frequently adverse effects are oral numbness and nausea (20, 36, 55).

### Other Alternative Treatments

#### Cold Therapy

Although the first information about the use cold therapy in migraine was reported many years ago, there are not lots of studies related to cold therapies in patients with migraine. It has been known that it can reduce pain approximately 10-20% (12). Cold therapy may have local anesthetic effect, can decrease pain stimuli and contraction. The gate theory suggests that the cold sensations overwhelm and block transmission of the pain stimuli into the cerebral cortex. It reduces the release of histamine and vasoactive subjects. Ucler et al. reported in 28 patients that cold application alone may be effective in migraine patients (12).

#### Hyperbaric Oxygen Treatment

The use of hyperbaric oxygen treatment (HBOT) involves the intermittent inhalation of 100% oxygen at environmental pressures greater than one atmosphere. Five trials compared HBOT with sham. There was no evidence that it was useful in preventing migraine (36).

In conclusion, CAM therapies may be used in some migraine patients if pharmacological treatment is ineffective. More well-designed studies are needed to evaluate the use of alternative therapies as the first-line treatment.

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