Beyond conventional therapies - an overview of the alternative approaches in migraine management

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ABSTRACT

Introduction: Migraine remains one of the most prevalent chronic neurological conditions that significantly impacts the quality of life. The treatment aims to help with the symptoms and prevent further attacks. There are several pharmacological methods, but because of their side
effects, sometimes lower-than-expected effectiveness, costs, and long-term dependency, non-pharmacological approaches have gained popularity.

**Review methods:** We conducted our study as a literature review, with data gathered via PubMed and Embase.

**The state of knowledge:** Managing migraine is hard to achieve based only on pharmacological therapy. Recently, the development of alternative approaches, such as cognitive behavioral therapy, acupuncture, or butterbur, has been observed. Many studies try to assess its effectiveness. Biofeedback is a promising treatment method, however, it is expensive and requires special equipment. Aerobic training is essential in the prevention and therapy of many illnesses and proper intensity can be helpful with migraines, while yoga is a great lower-intensity option.

**Conclusions:** Alternative methods may be a great alternative or support in migraine management. However, there is still a need for standardized investigations to evaluate effectiveness and safety.

**KEYWORDS:** migraine; headache; pain management; yoga

**INTRODUCTION**
Migraine, which, according to the results of the latest Global Burden study, remains the second cause of disability in the world, is characterized by intense throbbing accompanied by unilateral headaches and reversible neurological and systemic symptoms, such as phonophobia, photophobia, nausea, and vomiting. [1] [2] It has two major types: with or without aura. Aura can be defined as neurological symptoms that are focal and transient and generally occur before the headache, though sometimes they can accompany it. According to the definition, if a headache appears at least 15 or more days per month for more than 3 months, with migraine features on 8 days, it is classified as a chronic migraine. [3]

In recent years, migraine has become an increasingly significant issue with more than 1.1 billion people worldwide living with this disability, representing a 1.7% increase in prevalence since 1990. [4] The study mentioned above, which was conducted worldwide, provides information indicating that migraine particularly affects individuals aged 15-39 years, and women are more likely to experience this disorder than men across all age groups. [1]
The evolving understanding of migraine pathophysiology in recent years has spurred the development of novel treatment strategies targeting specific molecular and neural pathways. Additionally, it has enabled the exploration of numerous alternative treatment methods. Although the exact pathomechanism of migraine is still not fully understood, current studies indicate that the excessive activation of the trigeminovascular system is the main contributing factor. This leads to the release of inflammatory markers, triggering a meningeal vasodilatation and inflammation. Moreover, scientists suggest that serotonin may also play a critical role, given its receptors' presence throughout the brain's pain signaling circuits, which offers potential targets for therapeutic intervention. Several brain imaging studies have demonstrated that the sub-cortical structures are active during spontaneous migraine, which could mean that we should also take into consideration dysfunction within these regions in patient assessment. Additionally, both genetic and environmental factors play significant roles in migraine susceptibility and development.

By addressing the underlying mechanisms driving migraine, clinicians can offer more effective and tailored interventions to improve patient outcomes and quality of life. Unfortunately, it is already known that some patients may find the currently available oral pharmacological treatments for migraines difficult to tolerate. Unfavorable side effects and lower-than-expected effectiveness can result in poor treatment adherence and other complications, including the chronicization of headaches and excessive use of acute medications. This all indicates that, in clinical practice, there is a significant demand for alternative approaches to both acute and preventive migraine treatment.

**REVIEW METHODS**

This study was conducted as a literature review, with data being gathered via PubMed and Embase, and explores the latest non-drug therapeutic approaches in managing migraines and evaluates their effectiveness.

**THE STATE OF KNOWLEDGE**

Managing migraines aims not only to relieve the symptoms but also to prevent further attacks. Pharmacological treatment includes several drugs, that are divided into two main groups: pain-relieving and preventive medications. The therapy should suit the patient's needs, frequency, severity of attacks, and potential side effects. For example, pain relievers, when taken too long, may cause medication-overuse headaches. Many factors could be responsible for
the onset of migraine attacks. Apart from the above-mentioned medication-related episodes researchers recognized stress, anxiety, diet, sleep habits, hormones, and irregular lifestyle as possible causes. [12] Managing them improves the quality of life of patients suffering from migraine but is hard to achieve based only on medication therapy. [13] That has led to the development of alternative, non-pharmacological approaches.

**Cognitive behavioral therapy (CBT)**

Cognitive behavioral therapy (CBT) is a structured psychotherapeutic intervention that targets maladaptive cognitive factors to improve mental disorders and psychological distress. It is widely used in problems ranging from depression, anxiety, and personality disorders to nonpsychiatric disorders, including irritable bowel syndrome, insomnia, and chronic pain conditions, such as migraine and fibromyalgia. [14,15].

CBT’s goals are to develop preventive and acute care strategies and coping skills, such as trigger identification, stress management, modification of maladaptive disease-related thoughts and behaviors, and physiological autoregulation. [14,15,16] It is achieved through various psychological methods including stress management, relaxation, and sometimes even biofeedback techniques. Relaxation seems to be the main efficient core of CBT treatment, as a trial comparing programmed for migraine CBT and only relaxation techniques indicated high efficacy of both with no significant difference between them. [16] The assistance of an expert in the initial phase is crucial to evade the fear-avoidance cycle, where catastrophizing thoughts and excessive avoidance of potential triggers can worsen symptoms, as fear of pain is associated with increased migraine-related disability. Behavior changes should be tailored for each patient, focusing on identifying individual premonitory symptoms, improving medication adherence such as early intake of medication during an attack and avoiding its overuse, and lifestyle changes to minimize risk factors such as inconsistent eating schedule, dehydration, overdose of caffeine or alcohol, sleep disturbances. Also, highly comorbid with migraine, mood and anxiety disorders increase migraine disability therefore, addressing their psychological symptoms improves the course of migraine. [17]

CBT has a favourable risk profile with almost no negative side effects. Reported adverse effects occurred rarely, and temporarily, and included status migrainosus or worsening of migraine intensity and frequency, respiratory symptoms, and vivid recollection of a traumatic event. [14,18]
CBT is available for all ages and has proved to be highly effective in treating pediatric headaches and migraine, making it a recommended first-line preventive treatment option either alone or with pharmacotherapy. [15,18] However, some patients may struggle with continuing therapy due to the declared extensive treatment burden, stigma against psychological treatment, and barriers such as time, cost, and low accessibility. [18,19] A solution to this problem can be alternative methods of CBT delivery, such as telephone or electronic methods, which have shown similar efficacy to face-to-face therapy. [15,18]

Several meta-analyses support CBT as an effective form of treatment for adults and children producing clinically significant reduction in headache frequency and MIDAS score with long-term maintenance of benefits shown in follow-up studies. [14,16,18]

**Mindfulness**

Mindfulness is a meditation technique that focuses awareness on a present moment and usually includes concentrating on physical sensations, like feeling one’s breathing or listening to surrounding sounds. Mindfulness-based stress reduction (MBSR) was first developed to relieve chronic pain, while mindfulness-based cognitive therapy (MBCT) to decrease the risk of depression relapse. [20]

Neuroimaging studies suggest that in addition to enhanced self-awareness and better coping with pain, mindfulness practices can influence neuroplastic changes in specific parts of the brain. [21] It can also help with effective heart rate regulation and stress management in patients with headaches, who because of the parasympathetic dysregulation are usually more vulnerable to stress. [22] Mindfulness was also proven to relieve anticipatory anxiety and reduce pain catastrophizing. Possibly because of the enhanced sensitivity to interoceptive signals earlier recognition of migraine attack was also noticed. [23] Although in a randomized clinical trial, MBSR proved to positively influence disability, self-efficacy, and getting through pain headache education was shown to decrease migraine frequency to a similar degree. [24] A recent study on MBCT efficiency showed a reduced migraine-related disability in patients but did not influence headache frequency. [25]

Migraines can not be cured with only mindfulness practice, but they potentially can significantly benefit patients’ emotional regulation, pain management, and life quality. [23,24,25]

**Biofeedback**
Biofeedback is a non-invasive technique that uses various instruments to measure changes in body processes and feed them back, which allows patients to increase awareness and teach them to modify specific physiological functions. [26] The most common types of biofeedback used in migraine treatment include EMG biofeedback (EMG-FB), peripheral skin temperature biofeedback (TEMP-FB), and blood-volume pulse biofeedback (BVP-FB) monitored in the temporal artery. Meta-analytic studies show that these methods can have a moderate influence on the frequency, severity, and length of migraine episodes, but combining them with medication may improve the overall outcome of treatment. [27,28] There is also some evidence indicating that systematic biofeedback practice can lead to a lower relapse rate in patients with analgesic overuse. [28]

Some studies show that simpler relaxation techniques give similar results with less money and time invested in treatment. [29] Other issues, especially patients' weak compliance, need to be considered when selecting this therapy. [30] New methods, such as using a surface EMG (sEMG) at-home device are promising for future potential use in headache treatment. [31]

**Aerobic Exercise**

Aerobic exercise defines rhythmic and repetitive physical activity that activates large muscle groups and increases heart rate. These exercises include cycling, walking, running, and swimming. They prevent or reduce symptoms of many chronic conditions, including heart disease, diabetes, and high cholesterol. [32] Recent studies indicate that aerobic exercises may also improve the quality of life of patients suffering from migraine. [32] However, there are also indications, that excessive training may trigger attacks. [33] It raises the question of how to establish a proper exercise strategy.

Numerous studies are trying to answer that question and confirm, that aerobic training may be an effective, alternative therapy. For example, a trial by Darabaneanu et al. reveals that an exercise group of migraine patients experienced both a reduction in the number of migraine days per month and the intensity of the attacks. [34] The exact mechanism of training on headaches is unknown. Some research suggests that the level of beta-endorphin, which is an endogenous opioid, is decreased in patients with migraine. [35] Exercise is known to increase beta-endorphin levels, which may explain the positive correlations with headaches. In a study by Köseoglu et al., exercise was found to have beneficial effects on all 40 female patients with
migraine and increased beta-endorphin levels were observed among them after the treadmill practice. [36]

Multiple health benefits, low costs, and minimal side effects are the reasons why aerobic exercises are recommended for patients with migraine, especially as adjuvant therapy. However, the exact intensity and frequency needed to be established. uu

Yoga

Yoga is recognized by the National Health Institute as a complementary medical approach and consists of asanas (physical postures), meditation, breathing techniques, lifestyle, and diet.[37] It is widely used not only as an exercise technique, but also to reduce stress and anxiety levels and help with chronic pain, and sleeplessness, all of which are known to be headache risk factors.[38] Recent studies have shown that yoga alone also reduces migraine frequency, migraine duration, and pain intensity.[38,39]

In the migraine treatment yoga is mostly used as an adjuvant therapy. A major advantage is the low cost and accessibility of this approach, however, it is important to mention, that it may take several months to be effective and requires a long-term commitment. Regardless, practicing yoga helps with many chronic diseases and leads to an improved quality of life. [40] In a study conducted by Kisan et al., migraine patients were given for 6 weeks either conventional care or yoga with conventional care. Also, both groups have shown improvement in monthly migraine frequency, average pain intensity, and migraine-related disability, in the second group (patients receiving conventional care and yoga) clinical outcome measures were more significant. [41] Another investigation by Kumar et al. evaluates that yoga as an add-on therapy for migraine is superior to medical therapy alone. [42] In the group of patients, who were exercising yoga in addition to pharmacological treatment, a significant reduction in headache frequency, headache intensity, HIT score, MIDAS score, and pill count was observed. [42]

It is important to emphasize that the diversity of yoga techniques and practicing methods makes it difficult to compare the findings of different studies. [40] However, it remains a promising approach, that needs further investigation. Noteworthy is the stability and calmness of yoga, especially in contrast to intense exercises, which are known to be a trigger factor for around 22% of migraine patients. [40,41]
**Melatonin**

Endogenous melatonin is a neurohormone produced and secreted in the pineal gland and it was shown to have multiple ways of influencing headache pathophysiology. Its reduced levels in the blood have been found in many patients with headache disorders. [43] In one study, three out of six women with status migrainosus had disturbed plasma melatonin profiles. Four patients claimed relief from pain in the morning after the first infusion of exogenous melatonin and the remaining two after the third infusion. [44] Forty people with episodic migraine took part in an open-label trial and were given 3mg melatonin half an hour before their bedtime. Out of the patients, who completed the study, twenty-five showed at least half reduction and none showed an increase in headaches. [45] Although mostly small studies showed the benefits of taking melatonin by migraine patients, it can potentially be beneficial, especially in patients with comorbid disorders like depression or insomnia. [43,46]

**Butterbur**

Butterbur is an herbal product derived from the rhizomes and stems of the perennial butterbur bush (Petasites hybridus) belonging to the *Asteraceae*. For centuries has been used in traditional folk medicine for various purported uses. [47,48] Nowadays the American Headache Society has given it a level A recommendation declaring it effective in preventing migraine headaches. Recently researchers have also used the herb in allergic rhinitis, asthma, and its potential neuroprotective effect in Alzheimer’s disease. [49]

Among many chemical components of butterbur, petasins (petasin, isopetasin), are considered accountable for the anti-migraine effects of the herbal extract. [48] Various hypotheses have been developed to explain the action of butterbur, including its anti-inflammatory effect, particularly in the neuro-inflammatory process, antioxidant activity, neuroprotection function, and influence on ion channels. There was noted desensitization of nociception by acting on calcium-conducting transient receptor potential (TRP) ion channels (selectively TRPA1 and TRPPV1) of primary sensory neurons impairing their dual function of signaling pain and releasing the neuropeptides, substance P, and calcitonin-gene related peptide (CGRP), which mediate neurogenic inflammation. [48,50]

Petadolex, introduced in 1972 in Germany and 1998 in the USA, is the only one among many of butterbur extracts, whose clinical efficacy and safety were amply evaluated in the preventive treatment of migraine. [50] Adverse effects of butterbur generally are rare, mild, and well-
tolerated, and include gastrointestinal upset, eructation, nausea, diarrhea, headache, dizziness, increased bleeding tendency, and rash. [47] One major safety concern is hepatotoxicity. 40 reported cases of usually reversible hepatotoxicity, although including two liver transplants, are associated with the use of Petasites products [51]. Research places responsibility for these issues on the presence of naturally occurring plant pyrrolizidine alkaloids (PA), as PA-free butterbur products, including Petadolex, were confirmed not to cause liver injury, either in the form of serum enzyme elevations or clinical cases of acute liver injury. [47,49] However liver injury cases have been reported due to residual PA contamination in some butterbur products. The analysis found toxic PA levels in 7 out of 21 commercially available compounds. [51] Therefore patients experiencing any unusual symptoms should undergo liver tests and stop using the herb. There is no known antidote for butterbur overdose, so use should be discontinued in such cases. Given possible interaction with anticholinergic medications butterbur should not be used with these drugs. Butterbur is also not recommended in children under six or pregnant or lactating women due to a lack of safety studies in these groups. [47,49,50]

The recommended oral dosage of butterbur’s extract in migraine prophylaxis has been established as 50 to 75 mg twice a day. [51] A randomized, double-blinded, and placebo-controlled trial with Petadolex® dosages of 150mg daily, 100mg daily, and placebo group induced a ≥50% reduction in attack frequency at 4 months in 68%, 56%, and 49% of patients respectively. [52] Another independent 12-week study of Petadolex confirms this efficacy with a dose of 100mg/day in ≥50% frequency attack reduction in 45% of patients versus 15% in the placebo group. [53] Trials in pediatric patients also confirm the efficacy of butterbur by at least halving the frequency of attacks in 77% of children in the experimental group in one study and reduction by 59% versus 31% in the placebo group in the second study. [49]

Several studies confirm butterbur’s efficacy in prophylaxis and treatment of migraine, as well as its safety if a used extract is PA-free and the recommended doses are administered. Therefore, it should be recommended, however with caution of choosing only labeled and certified products.

**Acupuncture**

Acupuncture is one of the main treatment methods in Traditional Chinese Medicine, reported also as one of the most common complementary therapies worldwide. In recent years, it has
gained popularity in Western countries as a non-pharmacological approach for pain conditions. [54,55]

Manual acupuncture involves inserting the penetrating needles into the skin at specific acupuncture points and manipulating them through intermittent rotation, lift, and thrust. [56] While traditional acupuncture concepts involve non-anatomical structures and non-physiological processes, modern research aims to integrate acupuncture with neurophysiology. Studies have shown the short-term effects of acupuncture on a variety of physiological variables, several of which are relevant to pain and analgesia, but the physiological effects behind long-term pain reduction are still unclear. [57,58] Assumptions are that many various compounds are leading to the final effect of pain relief. Besides local effects of needling some research reported that stimulating different types of afferent nerves could cause inhibition in pain transmission within the central nervous system and release of some pain suppressors such as endorphin, serotonin, dopamine, neurotrophins, and nitric oxide in the brain. [55] In the particular case of migraine, an interesting result is also a decrease of serum matrix metalloproteinase which is a helpful factor in migraine headaches [59]. Also, functional magnetic resonance imaging gave answers that acupuncture could elicit cerebral responses in patients with migraine by modulation the pain systems engaged in the pathology of migraine. [60]

Acupuncture treatment is a relatively safe procedure and induces fewer and milder adverse events than drug use. [54] In two overviews average of about 8% of patients reported at least one acupuncture-related adverse event. Recorded adverse events included: bleeding, subcutaneous hemorrhage, subcutaneous hematoma, serious pain, palpitation, fainting, and local infection. All adverse effects were reported as mild or moderate, and none required special medical interventions. [56,57]

Data from research are not fully coherent, however, the overall agreement is that acupuncture has a significant influence on reducing the duration and frequency of both chronic and acute migraines. Multiple studies noted that it was at least non-inferior to standard drug therapy. [55] Conclusions from the overview [54] of 15 systematic reviews published between 2011 and 2019 present that acupuncture had a better long-term effective rate for migraine in reduced headache days, the severity of headaches and the times of using painkillers than Western medicine and sham acupuncture, both in short-term and long-term follow-up. A trial [56] with 150 randomized patients supervised for 20 weeks reported a significantly greater reduction in migraine days and
migraine attacks by manual acupuncture in several weeks. Independent research [58] has shown that in comparison with drug prophylaxis manual acupuncture was significantly more effective (57% versus 46%), but the significance was not maintained at follow-up after 6 months (59% and 54% respectively). In the other four trials, acupuncture as an [58] addition to usual care or treatment of migraine on onset only (usually with painkillers) resulted in 41 in 100 people having the frequency of headaches at least halved, compared to 17 in 100 people given usual care only.

Reviewing all the data, acupuncture should be considered as both a prophylactic and treatment option for people with migraine as a complementary or alternative treatment, particularly in drug-refractory patients. However, more high-quality research is needed to further understand the mechanisms and effectiveness of acupuncture in managing migraines.

CONCLUSIONS
Both CBT and mindfulness are safe, accessible methods with proven benefits in pain management and life quality in migraine patients. Aerobic training is essential in the prevention and treatment of many illnesses and proper intensity can be helpful with migraines, while yoga is a great lower-intensity alternative. Biofeedback, although effective, uses special equipment, which makes it a more expensive and time-consuming method. Acupuncture shows promising results in reducing the frequency and length of a migraine attack with fewer side effects in comparison with medication usage. Butterbur is efficient in treating and preventing migraine episodes but can only be consumed in the form of certified products due to its controversial hepatotoxic properties. All the methods above may be a great alternative or support in migraine management.

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