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## Complementary and Integrative Medicine for Episodic Migraine: An Update of Evidence from the Last 3 Years

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### Abstract

**Objective**—The purpose of this review is to evaluate evidence from the last three years on complementary and integrative medicine treatment options for episodic migraine.

**Methods**—Using Pubmed, Embase, and Cochrane databases, research published from 2015–2018 evaluating the modalities of mind/body therapies, supplements, and manual therapies for treatment of migraine were assessed.

**Results**—Although many studies had major methodological challenges that limit interpretation, several studies reported decreased headache frequency, improved quality of life, or less affective responses to pain. The evidence is currently most promising for the mind/body treatment options of mindfulness, yoga, and tai chi. Mindfulness meditation may be as effective as pharmacological treatment for medication overuse headache after the offending medication is withdrawn. While older research has shown magnesium, riboflavin, feverfew, and butterbur to be helpful in migraine treatment, new research is promising to suggest potential benefit with melatonin, Vitamin D, higher dosages of Vitamin B6 (80mg)/folic acid 5mg combinations, and the combination of Magnesium 112.5mg/CoQ10 100 mg/feverfew 100 mg. Omega 3's have limited evidence of efficacy in migraine. Butterbur needs to be free of Pyrrolizidine alkaloids (PA) to ensure safety given their hepatotoxicity. Physical therapy (PT) continues to have strong evidence of support, and acupuncture is superior to sham acupuncture and placebo. Side effects and risks reported were minimal and well-tolerated overall, with the exception of the life-threatening risk of cervical artery dissection with high-velocity chiropractic manipulation and hepatotoxicity with the PAs in butterbur. Several studies are ongoing to further evaluate mindfulness, melatonin, PT, exercise, chiropractic manipulation, and acupuncture. The American Academy of Neurology (AAN) and American Headache Society (AHS) are currently updating the guidelines for integrative treatment options for migraine, so additional recommendations may be available soon.

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Conflicts:

The authors declare that they have no conflicts of interest.

**Conclusion**—In conclusion, many complementary and integrative treatment options may be helpful for patients with migraines, and understanding potential efficacy, benefits, and risks can help providers discuss these modalities with their patients. Such a conversation can empower patients, build the therapeutic relationship, and increase self-efficacy, thus improving outcomes and patient-centered care.

### Keywords

Complementary and Integrative Medicine; Complementary and Alternative Medicine; Migraine; Mindfulness; Supplements; Acupuncture

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## Introduction

Up to 50% of those with severe headaches/migraines use complementary and alternative medicine (CAM) and Integrative medicine treatment options.(1,2) This review will evaluate evidence from the last three years on mind/body therapies, supplements, and manual therapies for treatment of migraine. Only a few studies specifically evaluated treatment for episodic migraine, so all migraine studies will be reported.

## MIND/BODY

The mind/body interventions of mindfulness meditation, meditation, yoga, and tai chi are reviewed. Space reasons excluded the analyses of guided imagery, biofeedback, hypnosis, qi gong, deep breathing exercises, mindfulness-based cognitive therapy, and progressive muscular relaxation. Other reviews may discuss modalities not included here. (3–5) In the PubMed, Embase, & Cochrane databases, studies published from 2015–2018 were evaluated with the search terms of migraine AND: mindfulness, yoga, tai chi, integrative medicine, and meditation.

### Meditation

Only two studies evaluated meditation specifically for episodic migraines and both focused on “spiritual meditation.” In the first, 74 participants (mostly undergraduates) with 2–15 migraines/month were asked to practice 20 minutes/day for 2 weeks of “relaxation” (R), “standardized mindfulness” (STM), or “spiritualized meditation” (SPM) taught at an introductory education session.(6) Instructors used scripts to teach patients to “relax your body and calm your mind” (R), “focus on your breath and... become more engaged in this present moment” (STM), or focus on “feeling that you are closer to something within and around you, something more fundamental or sacred” (SPM). Before and after the intervention, participants completed a cold-pressor task and were asked to rate the stressfulness and painfulness of the experience. Reported stress was lower in those who had learned standardized mindfulness compared to relaxation, although mindfulness was higher in those from the SPM group versus the STM group. No differences were found for time in water or perceived pain. This study was limited by its lack of randomization, its short training session and duration of treatment, and the lack of headache frequency, severity, or duration measures assessed. In the second study, 92 participants with at least 2 migraines/month verified by the ID Migraine screener were randomized to one of four types of

meditations.(7) Each group was instructed to spend 20 minutes/day for 30 days focused on a mantra, such as “God is Peace” (Spiritual Meditation), “I am content” (Internal Secular Meditation), “Grass is Green” (External Secular Meditation), or instructed to practice Progressive Muscular Relaxation (PMR). Participants kept a daily headache log for 30 days. Frequency of headaches decreased in the Spiritual meditation group. Medication usage decreased in all groups, with a significantly sharper decline in the “Spiritual Meditation” group. No differences were seen in headache severity ratings across groups. The authors hypothesized that decreased analgesic use, without decreased pain ratings, suggested increased pain tolerance. This study’s limitations included no clinical assessment to evaluate the diagnosis of migraine for participants, most of whom were undergraduates, limiting generalizability. A major limitation is the lack of clarity of how baseline measures (including headache frequency) were assessed.

Several studies published in the last three years have evaluated treatment of headache with Mindfulness Based Stress Reduction (MBSR), a standardized 8 weekly program developed by Dr. Jon Kabat-Zinn. A 2015 study assessed MBSR plus medication treatment to medication treatment alone in 37 adults with 15+ days/month with “chronic headache” (migraine or tension-type).(8) The MBSR group had less pain intensity and improved quality of life after the intervention compared to the control group, assessed pre/post intervention with a headache report (monthly headache pain intensity, duration, and frequency) and Short Form (SF)-36 instrument. This study was limited by the small sample size, lack of follow-up, participants’ varying use of medications, and the lack of a daily headache diary to assess headache outcomes. In 2018, an online MBSR program was compared to medical treatment as usual in 30 patients with migraine or tension-type headache, with use of four instruments pre/post intervention to assess pain intensity (McGill Short Form Questionnaire), disability (Migraine Disability Assessment MIDAS), distress (Depression, Anxiety, and Stress Scale DASS-21), and mindfulness (Mindfulness Inventory). The MBSR intervention did not affect sensory pain sensation ( $p<0.44$ ) but did impact emotional dimension of pain ( $p<0.0001$ ), disability ( $p<0.0001$ ), mindfulness ( $P<0.001$ ) and distress ( $p<0.0001$ ). The main limitation of this study was the lack of daily headache measures as only pre/post survey assessments were done.

A non-randomized mindfulness intervention was conducted in 44 adults with chronic migraine-medication overuse (MOH) headache.(9–12) After completing a 5-day structured outpatient day hospital medication withdrawal program, participants selected either a prophylactic medication regimen or mindfulness training (delivered in 30 minute small weekly groups for 6 sessions).(9) Daily headache diaries were maintained for 12 months. Participants completed Headache Impact Test (HIT)-6, MIDAS, State-Trait Anxiety Index (STAI), and Beck Depression Inventory instruments at baseline, 3, 6, and 12 months later. Headache frequency decreased in both groups (by 6–8 days per month), as did use of medication and MIDAS scores.(12) HIT-6 improved for the medication group only and STAI did not improve for either group. Similar statistically significant improvements in noradrenaline, epinephrine, and dopamine were reported in both groups at 12 months (11) and non-statistically significant decreases in all inflammatory biomarkers.(10) This study showed that a mindfulness intervention may have equal benefit to the current standard pharmacological treatment of refractory MOH. However, this study limited by its non-

randomized, non-blinded approach, although the authors label it as an “effectiveness” (rather than an efficacy) trial.

Several additional studies have assessed mechanisms of mindfulness in headache. One recent cross-sectional study compared stress coping skills (with the Stress Coping Questionnaire) and cortical activity (assessed with contingent negative variation measures) in healthy controls versus meditators (one+ year of experience of twice/week meditation, yoga, mindfulness, tai chi, etc.) versus migraineurs (with <15 days/month headaches).(13) Migraineurs used negative stress coping skills more frequently than the other two groups, especially rumination (which was lowest in meditators). In addition, frequent rumination correlated with high contingent negative variation (CNV) amplitudes, suggesting cortical and stress processing was worse in migraineurs compared to healthy controls and meditators. In another cross-sectional study, an online survey of 217 migraineurs found that baseline mindfulness levels negatively correlated with and predicted negative affect, pain catastrophizing, fear of pain, pain hypervigilance, and headache duration ( $p<0.05$ ).<sup>(14)</sup> Mindfulness was not correlated with headache pain intensity or frequency and did not moderate the relationship between pain intensity and pain catastrophizing. The authors hypothesize that mindfulness may be a key component of the Fear-Avoidance model of chronic pain. Although limited by their cross-sectional nature, these two studies provide insight into potential mechanisms of mindfulness in migraineurs. A third mechanistic study assessed heart rate variability in healthy controls ( $n=39$ ) and headache patients (migraine and tension-type,  $n=36$ ) at baseline, during a stress-inducing situation, and after the stressful procedure during a recording of either instructions to practice mindfulness meditation or a recording describing mindfulness meditation.<sup>(15)</sup> Overall, headache patients perceived the same stress-inducing situation as more stressful than healthy controls. In addition, heart rate variability did not recover in headache patients as in healthy controls after the stress-inducing situation, but the mindfulness instruction recording did help heart rate variability recovery for headache patients (and healthy controls). The authors concluded that in headache patients, mindfulness may improve imbalances in autonomic system dysregulation and promote effective recovery from a stressful event.

In 2018, two meta-analyses assessed the recent and past research of mindfulness for headaches.<sup>(16,17)</sup> The first analysis of ten studies of primary headache disorders ( $n=315$ ) found that mindfulness meditation significantly improved pain intensity and headache frequency.<sup>(16)</sup> The second meta-analysis was limited to five studies specifically of MBSR for chronic headache ( $n=185$ ); all five were included in the larger meta-analysis.<sup>(17)</sup> In this more focused analysis, MBSR did not improve headache frequency, duration, or intensity. The authors felt that the results were imprecise due to small sample sizes and risk of bias; they recommended larger studies with more rigor.

## Yoga

Prior to 2015, there were a few studies demonstrating benefit of yoga in migraineurs<sup>(18–20)</sup> and two additional studies in 2018 suggest that yoga may be beneficial.<sup>(21,22)</sup> In 60 migraineurs (with 5+ migraines in prior 3 months), an intensive Ayurvedic treatment regimen (traditional Panchakarma, a biopurificatory process x 13 days) followed by yoga

daily up to 90 days was compared to a control condition (symptomatic use of NSAIDs).(21) The yoga/Ayurvedic group improved from day 1 to day 90 on the Comprehensive Headache-related Quality of Life Questionnaire and a visual analogue scale (1–10) of headache intensity ( $p<0.001$ ). Another study in 32 female migraineurs assessed medication plus a 12-week yoga treatment program (3 sessions/week x 75min each) to a control group who received medication only.(22) Headache frequency, severity, and impact decreased in yoga vs. control groups (assessed via questionnaire). Plasma nitric oxide levels did not differ significantly between groups before or after the study. Both studies were significantly limited by the lack of daily headache logs to assess headache measures, using only questionnaires pre/post treatments.

### Tai Chi

No studies have been published in the last few years assessing tai chi for migraine. However, an abstract was presented at both the 2018 American Heart Association conference (published in *Circulation*) and at the 2017 International Headache Society meeting (published in *Cephalalgia*) of a tai chi intervention in 82 Chinese women with episodic migraine.(23,24) Participants were randomized to either Tai Chi (modified 32-short form Yang-style training 1 hour/day 5 days/week for 12 weeks) or a wait-list control group, with assessments at baseline and 3 and 6 months later. Women in the tai chi group had fewer migraine days compared to controls ( $-3.6$  migraine days,  $p<0.001$ ). Participants in the tai chi group also lost weight and their systolic blood pressure decreased compared to controls. Among the tai chi group, the BP change was significantly correlated to the change in migraine days ( $p<0.05$ ).

### Risks/Side Effects

No major side effects or risks were reported in the mind/body studies described. Although typically considered safe and without harm, many studies excluded patients with severe psychiatric co-morbidities; rare case reports of mind/body treatments triggering psychosis have been reported. Musculoskeletal side effects can occur with yoga and Tai chi. The major challenges that limit the use of many of the mind/body treatment options include time, energy, effort, cost, and finding a skilled teacher/instructor.

## SUPPLEMENTS

This current review assessed studies of supplements from the last three years for migraine treatment using the search terms of riboflavin (Vitamin B2), coenzyme Q10 (CoQ10), magnesium, feverfew, butterbur, melatonin, vitamins D, E, C, B6, folic acid, omega-3, boswellia, ginger, guarana, white willow, griffonia, and turmeric.

The American Headache Society (AHS)/American Academy of Neurology (AAN) 2012 Guidelines assessed efficacy for supplements for migraine prevention and provided the following grades of evidence: feverfew (Level B-probably effective), magnesium (Level B), riboflavin (Level B), and CoQ10 (Level C-possibly effective)(25). Based on two randomized controlled trials, butterbur was classified as having Level A evidence. However, concerns over hepatotoxicity with butterbur resulted in these entire guidelines being retired and new

ones are now pending. No new studies have been published in the last three years assessing efficacy for any one of these supplements with AAN/AHS efficacy ratings. This review will assess one study that evaluated the safety of butterbur, a few studies that have assessed combination supplements, and several supplements without prior evidence rating.

### **Butterbur (*Petasites hybridus*)**

Butterbur contains pyrrolizidine alkaloids (PA), which are hepatotoxic. PA toxins have been removed from certain butterbur preparations to ensure safety. A recent analysis by the National Center for Natural Products Research analyzed 21 commercial butterbur products in the US for petasins (active ingredient in butterbur) and PAs (the toxin) (26). They found 7/21 products to be safe and effective, with petasin present and no detectable PAs. However, 6/21 products had no detectable amounts of petasin and 7/21 had toxic PA levels. The NIH recommends only using butterbur if the product is labeled and certified as PA-free.

### **Combination Treatments (Magnesium, CoQ10 and either riboflavin or feverfew)**

In a randomized, double-blind placebo-controlled study (n=130) a supplement containing magnesium 600mg, CoQ10 150mg, and riboflavin 400 mg, along with a multitude of vitamins/trace elements (Migravent® in Germany, Dolovent® in USA) was compared to placebo in patients with migraines (diagnosed by neurologist using ICHD criteria) (27). After 3 months of treatment, use of the supplement did not significantly reduce migraine days vs. placebo (-1.8 vs. 1.0, p= 0.23). Improvements were seen in the secondary end-points of maximal pain intensity (p= 0.03), HIT-6 (p= 0.01), and patient's perception of efficacy (p= 0.01) Side effects were mild (diarrhea and chromaturia, n=8). An observational unblinded study without a control group (n=75) assessed a combination supplement of Magnesium 112.5mg, CoQ10 100 mg, and feverfew 100 mg daily for 3 months in episodic migraineurs (28). Those on the supplement had a reduction in number of migraine days (-3.5 days ± 2.9; p < 0.0001), photophobia, phonophobia, and nausea, depression and anxiety, and improved quality of life (p < 0.0001).

### **Combination Treatments (Vitamin B6, Folic Acid +/- Vitamin B12)**

A randomized double blind placebo controlled study (n=300 with migraine with aura) found a combination supplement of Vitamin B6 25mg, Folic Acid 1mg, and Vitamin B12 400 µg for 6 months did not improve migraine frequency, severity, disability or reduce plasma homocysteine levels (29). However, a randomized double-blind placebo controlled study (n=95) with higher dosages of B6 and folic acid (80mg and 5mg folic, respectively) reduced headache frequency (-3.35 ± 0.09 vs -2.73 ± 0.05; p < 0.001), headache severity (-2.71 ± 0.08 vs -2.19 ± 0.05; p < 0.001), and "headache diary results" of headache duration x frequency (-74.15 ± 0.2 vs -72.73 ± 0.1; p < 0.001) versus placebo (30). In a recent Iranian study (n=66, migraine with aura), 80 mg of Vitamin B6 alone did not improve headache frequency but did reduce headache duration (-8.30 ± 12.60 vs -1.70 ± 9.60; p= 0.030), severity (-2.20 ± 1.70 vs -1 ± 1.50; p= 0.007) and headache diary results (-89.70 ± 134.60 vs -6.10 ± 155.50; p= 0.04) (31).

## Melatonin

A randomized double-blind placebo controlled study (n=178) compared melatonin 3 mg, amitriptyline 25 mg, and placebo 1:1:1 (32). After three months, migraine headache days per month were fewer in the melatonin and amitriptyline groups as compared to placebo ( $p < 0.05$ ). Responder rate (defined as  $>50\%$  improvement) was higher in the melatonin group versus placebo ( $p < 0.01$ ) and amitriptyline ( $p < 0.05$ ). Weight loss was seen in the melatonin group, versus weight gain in the placebo and amitriptyline groups. A small open-label study (n=49; migraine=37, chronic tension-type headache=12) without a control group found 6 months of treatment with melatonin 4 mg (Circadian®-prolonged release) resulted in fewer migraine days ( $p < 0.001$ ) and less disability (HIT-6  $p < 0.001$ ) (33). In pediatric (5–15yo) migraineurs (n=80) both melatonin 0.3mg/kg (max 6mg) and amitriptyline 1 mg/kg/day (max 50 mg) for three months reduced headache frequency, severity, duration, and disability, but greater clinical effect and more side effects were seen with amitriptyline. (34).

## Vitamin D

Older studies have conflicting results assessing vitamin D's role in headache management and a challenge of these studies is the lack of consensus of adequate Vitamin D levels. (35–38). A recent study of vitamin D levels in children found migraineurs had lower levels compared to controls ( $17.3 \pm 9.0$  vs.  $25.8 \pm 12.8$  ng/ml,  $p < 0.001$ ) (39). Another study showed a possible correlation between higher serum vitamin D levels ( $> 57$  nmol/l) and lower incidence of severe headache/migraine in patients taking a statin(40). A 2015 randomized double-blind placebo controlled study (n=65) of 10 weekly vitamin D supplement treatments (50,000IU) versus placebo did not find a difference in headache frequency ( $p=0.06$ ) or CRP levels, but did report a decrease in “headache diary results” (headache duration x frequency) ( $p=0.04$ ). (41) However, a 2018 randomized placebo-controlled double-blinded study found that vitamin D 100  $\mu$ g daily versus placebo for 24 weeks resulted in a reduction in migraine days ( $p=0.047$ ). Baseline participant vitamin D levels were within the optimal level (75–125 nmol/L; e.g., they did not have low levels at the beginning of the study prior to study participation). While serum 25(OH)D levels improved, levels of 1,25(OH)<sub>2</sub>D did not increase.(42)

## Ginger

An interesting study recently added Ginger Extract 400mg (known for its anti-emetic properties) versus placebo to standard migraine abortive treatment with IV Ketoprofen 100mg in the Emergency department (n= 60). They found that the addition of ginger decreased headache intensity at one hour ( $p= 0.04$ ), 1.5 hours ( $p=0.01$ ) and two hours ( $p=0.04$ ) and increased pain freedom at two hours (56.7 vs 33.3.;  $p= 0.03$ ). (43)

## Omega 3 $\omega$ -3

Although touted for anti-inflammatory effect, a recent systematic review and meta-analysis of 11 RCTs assessing omega-3 fatty acids' impact on migraine found no effect on frequency ( $p=0.4$ ) or severity, ( $p=0.66$ ) but a reduction in migraine duration ( $-3.44$  hours,  $p=0.003$ ). (44) However, since the systematic review was published, a new double-blind, randomized placebo-controlled study of 41 chronic migraineurs showed that 1.5 grams per day of

omega-3 polyunsaturated fatty acids, OPFA  $\omega$ -3 (400mg of eicosapentaenoic acid EPA and 350mg of docosahexaenoic acid DHA) in addition to 10mg amitriptyline was superior to control (10mg amitriptyline plus placebo).(45) Two-thirds of those receiving the Omega-3's had 80% reduction of headache frequency, while only 1/3 of such improvement in the control group ( $p=0.036$ ). Caution is advised as high dosing of omega-3 (over 3 grams/day) can lead to a weakened immune system and increased risk of bleeding.(45)

### **Ginkgolide B**

Older studies have looked at Ginkgolide B for migraine prevention and have shown potential positive results; no recent studies looking at Ginkgolide B were found(46,47).

## **MANUAL THERAPY**

“Manual therapy” encompasses a multitude of interventions to enhance mobilization, reduce pathologic restrictions, and provide neuromodulation via a physical treatment. The manual modalities reviewed here include physical therapy (PT), massage, osteopathic manipulative treatment, chiropractic spinal manipulation, exercise therapy, acupuncture, reflexology, and daith piercings. Many modalities often focus on the craniocervical area due to the frequency of suboccipital and pericranial muscle pain in migraine.

### **Physical Therapy (PT)**

The PT modalities assessed include: diaphragm respiratory training, cervical mobilization and traction, massage therapy and myofascial release, digital compression on muscle trigger points, and passive stretching. A 2016 RCT ( $n=50$ ) found PT (eight 50 minute standardized sessions over 4 weeks) plus medication versus medication alone in migraineurs with cervical pain resulted in non-statistically significant improvements in migraine frequency ( $p>0.05$ ) and pain intensity and pain perception.(48) A 2018 study randomized migraineurs ( $n=46$ ) to four sessions of either myofascial trigger point therapy and stretching (control) or control treatment plus suboccipital soft tissue inhibition (experimental group). (49) Although headache measures were not directly assessed, both groups had less headache related disability, measured with HIT-6 and MIDAS, with the experimental group having greater treatment effect ( $p<0.05$ ). Side effects or adverse events were not reported in either study.

### **Osteopathic Manipulative Treatment (OMT) and Chiropractic Therapy**

These modalities rely on the principle of realignment of somatic dysfunction to promote better healing. Techniques include myofascial release, balanced ligamentous tension, and balanced membranous tension. A three armed RCT ( $n=105$ ) of OMT (8 sessions over 6 months) + medication treatment, sham + medication treatment, or medication only in migraineurs found OMT improved migraine days/month, medication usage, and HIT-6 scores ( $p<0.001$ ) compared to sham and control (50). In a retrospective chart review, 11 migraineurs with co-morbid mood disorders treated with OMT had improvements in headache disability, depression, and anxiety.(51) A recent RCT compared chiropractic spinal manipulation (with a high-velocity, low-amplitude technique) vs. sham push maneuver vs. medication treatment.(52) All three groups reported fewer monthly migraine days, yet only the intervention and sham groups had continued improvement at 3, 6, and 12 month follow-



ups (without statistically significant difference between the two). The authors concluded that the effect of the chiropractic manipulation may be due to placebo response.

High velocity techniques have a risk of cervical dissection. A debate exists as to whether the association is actually causal, as many with neck pain (and possibly already with existing dissections) seek chiropractic care. A 2017 retrospective hospital chart review of cervical artery dissections over 4 years revealed that of 141 dissections, 12 patients (with 16 dissections) had documented chiropractic manipulation immediately prior to onset of symptoms (all with strokes, with one resulting in death). (53) A 2018 case report of a 32-year-old woman who died from a vertebral dissection and brainstem stroke immediately following chiropractic manipulation demonstrates the gravity of this concern. (54)

### Exercise Therapy

Physical exertion can trigger migraines for some patients, and the diagnostic criteria for migraine includes routine physical activity (like climbing stairs) exacerbating headaches. However, many believe that regular exercise may be beneficial for migraines. A 2016 review of nine studies showed “at least modestly beneficial outcomes for migraine” from aerobic exercise, with the underlying mechanisms unclear.(55) A 2018 RCT (n=52) compared aerobic exercise (45 min for 3 days/week for 3 months) vs. control (continued usual activities) in adults with migraines and concurrent tension type headache and neck pain. Migraine frequency did not differ between groups, although the exercise group reported reduced migraine frequency, pain intensity, duration of migraine, and migraine disability. Aerobic exercise did not induce changes in quantitative sensory measures, suggesting exercise may exert its effect on migraine via non-nociceptive pathways such as increased well-being.(56)

### Acupuncture

A 2016 Cochrane review of acupuncture for episodic migraine, with 22 trials and 4,985 participants (updated from 2009), found acupuncture’s benefits are similar to prophylactic medications and superior to sham.(57) A 50% reduction of migraines was seen in 41% of acupuncture patients vs. 17% with no acupuncture (in studies comparing acupuncture to no acupuncture) and 50% of acupuncture patients vs. 41% receiving sham (in studies comparing true acupuncture to sham acupuncture). (57) A limitation of the studies reviewed was limited length of follow-up. Two additional systematic reviews also concluded that true acupuncture was superior to sham acupuncture for migraine treatment.(58,59) While a 2017 study showed sustained benefit of acupuncture over sham at 16 weeks post-treatment,(60) an RCT of 16 sessions of acupuncture over 20 weeks for migraine found improvements at 3 months that were not maintained for 12 months.(61) A 2018 study using MR Spectroscopy pre/post acupuncture treatment in migraineurs found a significant increase in N-acetylaspartate/creatine in the bilateral thalamus which correlated with a reduction in headache intensity score.(62) This research showed that the biochemical effect of acupuncture may target brain regions important for pain perception (thalamus) and the effect had clinical significance on pain outcomes.

### Massage Therapy

One RCT in the last three years of traditional massage (TM) vs. lymphatic drainage (LD) vs. a wait-list control group WG (n=64) resulted in fewer migraine days per month (-2.4 TM vs. 0.2 WG  $p=0.016$ ; -3.1 LD vs. 0.2 WG,  $p=-0.015$ ) and decreased analgesic intake in the LD group.(63)

### Reflexology

A small study (n=40) of reflexology vs. massage over 10 sessions (2/week x 5 weeks) showed decreases in migraine intensity, frequency, and duration in both groups. A study of reflexology vs. acupuncture vs. electroacupuncture vs. control in chronic migraine (n=84), where all patients also received 100mg topiramate daily, showed all groups had improved headache frequency, with reflexology being “most effective in treatment of autonomic disorders;” only the abstract was available in English.(64) An RCT evaluated the effects of reflexology massage vs. sham placebo vs. control (with no treatment) for abortive treatment of a nitroglycerin-induced migraine. Only the reflexology massage treatment resulted in less intense migraine pain.(65)

### Daith Piercings

Many anecdotal patient reports online have endorsed dramatic improvements with a piercing through the smallest fold of cartilage in the ear (where the outer ridge that runs along the top of the ear connects to the inner ear, just above the ear canal). Proposed mechanisms include targeting an acupuncture pressure point or vagus nerve stimulation (with reduction in cortical excitability). However, the likelihood of a non-acupuncturist targeting the appropriate location is low, and the risk of infection is present.(66) A recent case series presented at the 2018 Migraine Trust International Symposium (67) and a case report (68) suggest benefit, but additional research is needed.

### Summary

Although many complementary and integrative treatment options may have benefits for adults with migraines, most studies have major methodological challenges that limit interpretation, such as small sample sizes, short duration or variability of treatments, limitations of measures or no description of how measures were obtained. Additional limitations include lack of: daily headache diaries, physician confirmed diagnoses, description of intervention techniques, randomization, appropriate control groups, intention-to-treat analyses, and follow-up. Nonetheless, several studies reported decreased headache frequency, improved quality of life or less affective responses to pain. Side effects and risks reported were minimal and well-tolerated overall, with the exception of the life-threatening risk of cervical artery dissection with high-velocity chiropractic manipulation and hepatotoxicity with the PAs in butterbur.

### Mind/Body

In migraineurs, meditation may lower stress in response to stressful events (such as with the cold pressor test or a cognitive stress test) or improve pain tolerance. Rumination and pain catastrophizing may be key components of the Fear Avoidance model of migraine;

mindfulness may be able to effectively target these factors. The mindfulness intervention after withdrawal from MOH showed that mindfulness may be as effective as typical pharmacological treatment in this population. Frequent yoga or tai-chi interventions may also decrease headache impact.

### Supplements

Butterbur may be beneficial for migraine prevention but PA-free products are recommended to avoid hepatotoxicity. The combination supplements of magnesium/CoQ10/riboflavin, magnesium/CoQ10/feverfew and Vitamin B6 (80mg)/folic acid (5mg) may be helpful. Vitamin D deficiency may be more common in migraineurs than controls and some evidence suggests benefit with Vitamin D supplementation on migraine improvement. Supplementation with Omega 3's do not improve migraine frequency. Ginger plus routine NSAID treatment in the emergency setting could help abort headaches. Ultimately, more research is needed for each supplement alone and in combination.

### Manual Therapies

PT appears to have positive benefits on pain perception, frequency, and disability, although PT may not be superior to medication treatment options. The most recent three-armed RCT evaluating chiropractic manipulation in migraine suggests the benefits seen could be due to placebo. The potential life-threatening risk of cervical dissection needs to be discussed and considered before recommending high velocity chiropractic manipulation techniques. Acupuncture has similar benefit as pharmacological treatment and has efficacy over both sham acupuncture and control. Small studies with massage and reflexology suggest potential benefit. Additional research is needed to recommend daith piercings given the risk of infection with the procedure.

### Future Research

Several ongoing studies (as seen on [clinicaltrials.gov](https://clinicaltrials.gov)) will further assess these treatment modalities for migraine. We are currently conducting a study evaluating mindfulness in migraines, another mindfulness study is being conducted by California Pacific Medical Center Research Institute, and a third study is underway at Johns Hopkins assessing MRI outcomes. A protocol for a mindfulness meditation study in children with chronic migraine was published, but full results are pending.<sup>(69)</sup> The AAN/AHS Guidelines for supplement use in migraine prevention are pending and will provide additional guidance on usage. Melatonin for migraine prevention in adolescents and optimal dosing of melatonin is being studied at UCLA and UCSF. An additional study is underway in China assessing neuropsychological outcomes and serum melatonin in medication overuse headache. According to [ClinicalTrials.gov](https://clinicaltrials.gov), additional studies are pending for migraine treatment with PT (Spain), exercise (Canada, Brazil), chiropractic manipulation (US), and acupuncture (US and China).

## Conclusions

Many Complementary and Integrative treatment options may be helpful for migraines. More than 50% of patients often do not tell their provider about their CAM usage (70) and almost 85% of providers may feel they lack the knowledge to inform their patients about complementary medicine.(71) The goal of this paper has been to educate patients and providers about the most recent evidence of Complementary and Integrative treatment options for migraine to increase comfort with discussing these options. The evidence is currently most promising for the mind/body treatment options of mindfulness, yoga, and tai and the manual therapies of physical therapy and acupuncture. While older research has shown magnesium, riboflavin, feverfew, and butterbur to be helpful in migraine treatment, new research is promising to suggest potential benefit with melatonin, Vitamin D, higher dosages of Vitamin B6 (80mg)/folic acid 5mg combinations, and the combination of Magnesium 112.5mg/CoQ10 100 mg/feverfew 100 mg. Omega 3's have limited evidence of efficacy for migraine treatment, as a systematic review of 11 studies was negative, but a more recent RCT showed benefit in chronic migraine of 10mg amitriptyline plus 1.5grams omega-3. Most treatments are well tolerated with limited side effects/risks, although hepatotoxicity with PAs in butterbur and cervical artery dissection/stroke/death with high velocity chiropractic manipulation need to be discussed. Recent studies for these modalities are limited by many major methodological challenges discussed. Future rigorous research is underway for many of these modalities to help address these shortcomings. The predominant limiting factor with many patients for these treatment options includes time, money, and effort. However, one of the major challenges in applying the evidence from research conducted on individual integrative treatment options into clinical practice is that many patients and providers concurrently use or recommend more than one modality through an "integrative approach."(72,73) In addition, many patients often use CAM treatments independent of the research based on persuasive anecdotal or historical bases.(74) As both patients and providers become more educated on both the research-based evidence and on the most common modalities patients practice, an open dialogue can be created to ensure that patients are informed on the safest and most effective treatment options while concurrently playing an active role in the ultimate decision of which modalities to use. Such a conversation can empower patients, build the therapeutic relationship, and increase self-efficacy, thus improving outcomes and patient-centered care.

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