

Non-pharmacological approach to migraine prophylaxis: part II

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Abstract Acupuncture has been used to both prevent and treat diseases for over 3,000 years. Recently, a Cochrane review on its use in migraine concluded that acupuncture is effective and should be considered as a prophylactic measure for patients with frequent or insufficiently controlled migraine attacks. In contrast, there is no clear evidence to support or refute the use of homeopathy in the management of migraine. Among vitamins and other supplements, riboflavin and coenzyme Q10 significantly decreased the frequency of migraine attacks. Alpha lipoic acid also reduced migraine frequency, albeit not significantly as compared to placebo. The prophylactic efficacy of magnesium, particularly for children and menstrually related migraine, has recently been substantiated. Among the herbal remedies, butterbur significantly decreases attack frequency, whereas the efficacy of feverfew was not confirmed in a Cochrane review, probably because of the 400% variations in the dosage of its active principle. Finally, ginkgolide B has proved significantly effective in controlling migraine with aura and pediatric migraine in uncontrolled studies that need a confirmation.

Keywords Acupuncture · Complementary therapies · Dietary supplements · Migraine · Phytotherapy

Acupuncture

Acupuncture is one of the main treatment modalities of traditional Chinese medicine that has been used for over 3,000 years for the prevention and treatment of diseases and is currently one of the most widely used complementary therapies in many countries [1].

Acupuncture for migraine prophylaxis has a long history of encouraging results. In 2001, a systematic Cochrane review on idiopathic headache judged it effective in this respect, whereas the evidence for its efficacy in the management itself was marred by methodological or reporting shortcomings in the majority of the studies [2].

Several large and strictly controlled trials have since been undertaken. In 2009, an updated Cochrane review of 22 randomised controlled trials [3] compared the efficacy of acupuncture in migraine prophylaxis with that of three control interventions:

- acupuncture versus no prophylactic treatment or routine care only.

Six trials showed that patients receiving acupuncture had higher response rates and fewer headaches as compared to those receiving no treatment other than therapies of acute migraine attacks or routine care.

- acupuncture versus “sham”(placebo) acupuncture.

Fourteen trials compared “true” acupuncture (insertion of needles at acupuncture points, pain points or trigger points) to “sham” acupuncture (intervention mimicking “true” acupuncture, but deviating in at least one aspect considered important by acupuncture theory, such as skin penetration or correct point location). Both treatments resulted in fewer headaches, but there was no difference between their effects. In this respect, however, the validity

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of “sham” acupuncture and the best way of inducing its placebo effect are still open questions.

– acupuncture versus pharmacological prophylaxis.

Four trials compared acupuncture to proven prophylactic drug treatments. Acupuncture was generally associated with better outcomes and fewer adverse effects.

The authors concluded that “acupuncture should be considered as a treatment option for migraine patients needing prophylactic treatment due to frequent or insufficiently controlled migraine attacks, particularly in patients refusing prophylactic drug treatment or experiencing adverse effects from such treatments”.

Homeopathy

There is no clear evidence to support or refute the use of homeopathy in the management of migraine. It has, indeed, proved ineffective in the few controlled studies published so far [4].

Vitamins and other supplements

Substances involved in the Krebs cycle have been investigated for migraine prophylaxis because mitochondrial disorders are thought to be associated with migraine.

Daily use of 400 mg riboflavin (vitamin B₂) for 3 months resulted in a 50% reduction in attacks in 59% of patients receiving it when compared with 15% of those taking placebo [5].

In another randomized controlled trial coenzyme Q10 (100 mg, t.i.d.) significantly decreased attack frequency, headache days and days with nausea [6]. Coenzyme Q10 supplementation may be particularly effective in the treatment of pediatric migraine [7].

In a double-blind, placebo-controlled trial, alpha lipoic acid (600 mg daily for 3 months) reduced monthly attack frequency, although not significantly as compared to placebo. However, within-group analyses showed a significant reduction in attack frequency, headache days and headache severity in patient treated with alpha lipoic acid, but not in the placebo group [8].

A recent review of the numerous studies of magnesium in migraine prophylaxis has confirmed its efficacy, particularly in some conditions such as pediatric migraine or menstrually related migraine associated with the premenstrual syndrome.

For children suffering from tension-type headache, significant results have been obtained with magnesium pidolate salts as preventive treatment after a pretty long follow-up period [9].

The recommended dose is 400 mg daily [10]. The unwanted side-effects are gastrointestinal (primarily diarrhea). There is no evidence of any short- or long-term safety issues for individuals taking magnesium in the absence of serious renal disease.

Herbal remedies

Butterbur (*Petasites hybridus*) is a perennial waterside plant member of the Compositae family whose root extract seems to have anti-migraine properties. A review of two randomized, placebo-controlled studies found that a dose of 75 mg b.i.d. resulted in a greater decrease in the frequency in migraine attacks, and a greater number of responders (improvement >50%) after treatment over 3–4 months when compared with 50 mg b.i.d. and the placebo [11].

No serious adverse events have appeared in clinical studies [12]. Nonetheless, some parts of this plant are hepatotoxic and carcinogenic, and pharmacovigilance reports a hepatobiliary toxicity. However, the German Health Authority (Commission E) certifies brand name Petadolex[®] as non-toxic, even if the long-term safety data are limited.

The dried leaves of feverfew (*Tanacetum parthenium*) have been evaluated as herbal preparation in several placebo-controlled trials with conflicting results. A Cochrane review resulted in a negative meta-analysis of all the controlled studies of feverfew [13]. Inconsistencies in the results of those studies were probably related to variations of as much as 400% in the dosage of the active ingredient (parthenolide). Moreover, since feverfew also contains melatonin and other compounds, uncertainty exists with regard to its major active ingredient. In a following multicenter, double-blind, placebo-controlled study, a stable CO₂ feverfew extract highly enriched with parthenolide (6.25 mg t.i.d. for 16 weeks) significantly reduced migraine attack frequency [14].

Feverfew’s unwanted side-effects include sore mouth and tongue (including oral ulcers), swollen lips, loss of taste, abdominal pain, and gastrointestinal disturbances.

Ginkgolide B, a constituent extracted from *Ginkgo biloba* tree leaves, modulates the action of glutamate in the CNS, and is a potent inhibitor of the platelet-activating factor. Its efficacy was assessed in an open trial in which a combination product (60 mg *G. biloba* terpenes phyto-some, 11 mg coenzyme Q10, 8.7 mg vitamin B₂; Migrasoll[®]) was administered twice daily for 4 months in patients suffering from migraine with aura [15]. The number of migraine auras and their duration were significantly decreased by this compound. In a very recent trial, the same compound has also been found significantly effective in pediatric migraine [16].

Conclusion

Overall, there is a promising evidence that a “natural approach” to migraine prophylaxis is possible, even if a further confirmation with rigorous randomized controlled trials is mandatory for the majority of non-pharmacological approaches. Only acupuncture has now reached a consistent level of evidence that can justify its use in routine care.

Conflict of interest statement The authors declare that they have no conflict of interest related to the publication of this article.

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