

Alternative therapies in the treatment of headache in childhood, adolescence and adulthood

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Summary

In recent years, it has become common practice, in the treatment of headache, to use alternative methods, both alone and in association with drug therapies. Alternative therapies would appear to be more indicated in certain subjects: patients opposed to pharmacological treatments, those showing low tolerance of drugs or with a history of drug abuse, and those presenting medical contraindications or poor response to certain drugs.

Numerous studies of alternative therapies have been published and here we review the literature data on the topic, considering in particular the accuracy of the various study methods in evaluating the effectiveness of the different therapies and their specificity for the different forms of headache. Specialists involved in the assessment and care of headache patients should strive to increase their knowledge of alternative therapies, so as to be better equipped to guide patients towards safe, economical and potentially effective treatments, rather than useless, costly or dangerous ones.

KEY WORDS: acupuncture, alternative therapies, chiropractic manipulation, headache, homeopathy, phytotherapy.

Introduction

This study offers an overview of so-called alternative or unconventional therapies and of their use in the treatment of headache.

It is by no means easy to define what is meant by the expression alternative therapies, as these cover a broad spectrum of practices and beliefs. They might be considered medical practices that do not conform with official medical standards, but seem to have some scientific basis, or are in any case very widely used.

A study by Eisenberg et al. (1), which considered the prevalence and costs of unconventional medicine in the United States, estimated that 425 million visits were made to providers of alternative therapies in 1990, and that around 13.7 billion dollars were spent on these treatments. The authors interviewed, by telephone, 1539 adults, enquiring expressly about their recourse to unconventional therapies for some of the most frequent medical conditions they reported (rachialgia, anxiety, allergies, headache, arthrosis, insomnia, arterial hypertension, digestive disorders, depression). In this study, 27% of headache sufferers reported using alternative treatments, which only rachialgia (36%) and anxiety (28%) patients were found to use more. In a more recent study, the same authors (2) revealed that the percentage of adult patients using alternative therapies increased over the subsequent years, rising from 34% in 1990 to 42% in 1997. This increase over the years in the use of alternative medicine is also reflected in the general paediatric population of the United States, in which recourse to unconventional therapies rose from 11% to 20% in the period 1994-1999 (3).

In a study by von Peter et al. (4), 73 adult headache patients were administered a standardised questionnaire with the aims of determining the extent of their recourse to unconventional therapies for headache and of deepening the patients' knowledge and expectations of these treatments. The results reveal that 98% of the subjects were familiar with at least one of the so-called alternative therapies, the most well-known seeming to be acupuncture, phytotherapy, and physical and dietary-nutritional therapies. Eighty-four per cent of the patients reported using these therapies, while 88% of those interviewed viewed them as potentially effective headache remedies. The explanations most frequently given for failure to have recourse to unconventional treatments were: lack of adequate information and recommendations on the part of medical professionals, lack of time, high costs and lack of insurance cover.

In view of the considerable extent to which unconventional therapies are used in the treatment of various pathologies, including headache, it would appear important for physicians to increase their knowledge of these therapies, so as to be able to guide patients towards the safer and potentially more effective ones, thereby realising the "synergistic" model hypothesised by Andrew Weil (5), in which unconventional therapies are intended not to replace traditional medicine, but to complement it.

In spite of this highly frequent recourse to alternative therapies, the results relating to their effectiveness in the treatment of various conditions are still controversial, partly because clinical trials of unconventional therapies often present major methodological weaknesses. Linde et al. (6) evaluated the methodological accuracy of 207 randomised trials, contained in five previously published systematic reviews on acupuncture, homeopathy and phytotherapy. The authors found that the accuracy of the studies varied greatly, and that they had major methodological flaws, relating above all to the patient sampling criteria and follow-up methods used, and to the variability of the study designs and therapies investigated.

We examine, with reference to clinical trials that have assessed their effectiveness, the main alternative therapies used in the treatment of headache.

Acupuncture

Acupuncture, part of a whole complex of naturalistic theories compatible with Confucianism and Taoism, is a technique that has been used in Chinese traditional medicine for around 3000 years (7). Since the 1970s, the use of acupuncture for the treatment of pain (mainly in settings unrelated to the philosophies originally associated with it) has increased in the western world, and at least 500 randomised and controlled clinical studies have evaluated its effectiveness, often yielding conflicting results. In support of the effectiveness of this technique in the treatment of pain, there seems to exist considerable experimental evidence of measurable and repeatable physiological effects. The analgesic effect would appear to depend on the stimulation of small-diameter nerve fibres with a high excitability threshold and the consequent activation, via neuronal circuits at spinal, brainstem and hypothalamic level, of the system of endogenous opioids, an effect that naloxone, an endorphin-antagonist, appears in a dose-dependent fashion, to cancel out (8,9). Stimulation of the expression of neuropeptides has been hypothesised as another possible mechanism of action (10,11), as has activation of descending antinociceptive systems and deactivation of numerous limbic areas involved in pain control (12,13).

In 1998, acupuncture was recognised by the traditional medical establishment (14); as far as the treatment of headache is concerned, the NIH conference ended by affirming that acupuncture could prove to be a useful complementary or alternative therapy, but that its effectiveness needs to be demonstrated further. Manias et al. (15), published a critical review of 27 clinical trials that had evaluated the effectiveness of acupuncture in the treatment of primary headache. Twenty-three of the 27 studies concluded that acupuncture is an effective technique. However, the authors of the review underlined the difficulty in comparing these studies, a difficulty that is due to the extreme variability of their designs, sample sizes, patient selection criteria and follow-up durations. They also drew attention to the fact that many of the studies presented serious methodological weaknesses, relating above all to the type of placebo used. The best would appear to be "minimal" acupuncture, which differs from "true" acupuncture only in the site of needle place-

ment. In the context of a crossover design, however, the use of this placebo raises a further problem, i.e., the need to allow enough time to elapse between the two procedures, since the analgesic effect of "true" acupuncture can last for months. The authors' conclusion is that further clinical research is needed in order to confirm the effectiveness of acupuncture and to clarify its indications in the treatment of headache. A more recent review (16) analysed 26 clinical studies with a total of 1151 patients, in order to determine the effectiveness of "true" acupuncture in relation both to "minimal" acupuncture and to other types of primary headache treatment. Sixteen of the studies considered migraine patients, six focused on tension-type headache patients, and four on subjects affected by various headache forms. In eight of the 16 studies that compared "true" and "minimal" acupuncture in the treatment of migraine and tension-type headache, the greater effectiveness of "true" acupuncture was found to be statistically significant; four of the studies showed a trend in favour of "true" acupuncture, while in the remaining two trials, no differences emerged between the two types of intervention. On the other hand, the 10 trials that compared acupuncture with other types of treatment gave conflicting results.

Another study (17) examined the differences in the effectiveness of acupuncture for the treatment of chronic headache between 24 randomised and 35 non randomised clinical trials. Even though the randomised studies presented, on average, a lower acupuncture response rate than the non randomised ones, the latter seemed to confirm the results of the randomised trials as regards the effectiveness of the treatment, without, what is more, providing any further indications as regards possible adverse and long-term effects. Only one study has considered the role of acupuncture as an alternative treatment for headache in children and adolescents (18). The authors of this study investigated the effectiveness of acupuncture in a group of 22 migraine patients, 7-15 years of age, randomly divided into two groups: one submitted to "true" acupuncture (needles inserted in the dermis) and the other to placebo acupuncture (needles inserted in the stratum corneum). Opioid activity in blood plasma was assayed in all the patients both before and after treatment. The group of subjects undergoing "true" acupuncture recorded a significant reduction in the frequency and intensity of their migraine attacks and a significant increase in β -endorphin levels in the plasma versus the placebo acupuncture group. The authors conclude that acupuncture may be an effective alternative treatment for childhood migraine. Indeed, this treatment is safe, free from adverse effects and can, if necessary, be repeated. However, it can only be practised on patients who are old enough to cooperate and its effectiveness needs to be confirmed through further studies.

Homeopathy

Homeopathy is one of the most widely used and widely accepted alternative therapies. In the UK, for example, many hospitals use NHS approved homeopathic treatments. However, in spite of being so widespread, homeopathy continues to be much debated, particularly in

relation to two points: its founding principle (i.e., that like cures like) and its use of minute doses. Furthermore, it has to be considered that homeopathic treatments are highly personalised, with the choice of therapeutic agent depending not on the diagnosis the patient has been given, but on the symptoms he or she presents. For migraine, for example, which is a complex of symptoms that can occur in combinations that differ from patient to patient, there exists no set remedy that can be prescribed, even though the most frequent are: Belladonna, Bryonia, Iris versicolor, Kali bichromatum, Lachesis, Natrum muriaticum, Nux vomica, Sanguinaria, Sepia, Silica and Sulphur (19). The methodological implications of this are considerable as clinical studies investigating the effectiveness of homeopathy cannot, given that homeopathic treatments always involve a variety of therapeutic agents, focus on a single remedy. In one recent study of homeopathic prophylaxis (20), for example, 11 different remedies were used. This four-month, randomised, double-blind, placebo-controlled trial, conducted on 63 adults affected by migraine with or without aura, failed to demonstrate any prophylactic benefit of homeopathic treatment versus placebo. In another randomised, double-blind, placebo-controlled study (21) a classic homeopathic treatment was found to be effective in 98 adult chronic headache (migraine and tension-type headache) patients. The authors of this study underlined that, from a homeopathic point of view, considering these two headache forms as a single group does not constitute a methodological problem, since the choice of treatment does not depend on the specific type of headache presented by the patient. However, in this study, too, no significant differences emerged, over the three-month treatment, between the effectiveness of homeopathic therapy and placebo on a series of parameters (days with headache, duration and intensity of attacks). In 2000, the same authors published a further study (22) in which they reported the results of a one-year follow up in the same group of chronic headache patients. This study was prompted by the consideration that the three months considered in the previous trial might not, in fact, have been long enough to allow the homeopathic treatment process full expression. However, the results of this study showed that the effects obtained at three months did not differ significantly from those found at 12 months in the patients who continued the homeopathic therapy for a year.

We thus found that there currently exists no evidence-based proof of the effectiveness of homeopathic treatments in headache, and that no relative study of paediatric subjects has been published in the indexed journals.

Nutritional factors

The possibility of adopting a dietary approach in the treatment of headache has often been raised, but few scientific studies have considered the question. In susceptible subjects, foods containing tiramine can trigger migraine attacks, as can additives and sweeteners. Some patients claim to benefit from the elimination of starchy foods, sugars and milk products from their diets. Although these claims have not been investigated scien-

tifically, there is no real reason to discourage patients inclined to try these approaches, given that they are both safe and economical. Vegetarian-type diets, on the other hand, can result in a deficiency of B12, which can aggravate headache and provoke other disorders (23).

Magnesium is an element that plays an important role in migraine pathogenesis. Numerous studies have reported low magnesium levels in the plasma and tissue cells of migraineurs (24-26). Magnesium deficiencies reduce the migraine threshold through various mechanisms: vasoconstriction, reduction of the affinity of serotonergic receptors and activation of N-methylaspartate receptors. Mauskop et al. (27) administered, via intravenous infusion, 1 gram of magnesium sulphate to 40 migraine patients during acute migraine attacks and obtained a significant reduction of pain in 87% of them. Intravenously administered magnesium has also been found to be effective in the treatment of cluster headache attacks; in a study of 22 patients, 41% experienced a significant reduction of the pain, a good result given that cluster headache has been found to be refractive to various therapies (28).

Two double-blind, placebo-controlled studies have evaluated the effectiveness of magnesium in the prophylaxis of migraine in adults. In a study by Peikert et al. (29), magnesium was found to be superior to placebo, while Pfaffenrath et al. (30) did not find significant differences between the two. However, it should be pointed out that this second study used a magnesium salt that is not easily absorbed (aspartate hydrochloride trihydrate) and that diarrhoea occurred in 45% of the treated subjects (as opposed to 18.6% in the study by Peikert et al., which used trimagnesium dicitrate). A double-blind, placebo-controlled study of magnesium efficacy in migraine prophylaxis conducted by Wang et al. (31) considered, instead, a group of 118 juvenile subjects. The authors reported that the patients receiving magnesium oxide for 16 weeks showed a significant reduction in the frequency and intensity of their attacks compared with the placebo-treated group.

Schoenen et al. (32), on the other hand, demonstrated the effectiveness of riboflavin (vit. B2) in migraine prophylaxis in a randomised, double-blind, placebo-controlled study of 55 adult patients. The maximum effect was reached after three months of treatment with the vitamin (400 mg/day). Riboflavin is the precursor of flavin mononucleotide and flavin adenine dinucleotide, both of which are involved in electron transport in the respiratory chain. The rationale for using this drug is the hypothesis that a deficit of mitochondrial energy metabolism has a role in the pathogenesis of migraine (33, 34).

Phytotherapy

Herbs have been used as remedies for a number of centuries and feverfew (*Tanacetum parthenium*) is undoubtedly the plant that has been most studied in connection with the treatment of headache. Feverfew is known in herbal medicine for its anti-inflammatory, antipyretic and lenitive properties in the treatment of burns (35). The main active compound of feverfew is sesquiterpene lactone parthenolide, which has been demonstrated, *in vitro*, to inhibit serotonin release from platelets (36). This mechanism of action constitutes the rationale for the use

of feverfew in migraine prophylaxis. Vogler et al. (37) conducted a systematic review of the literature, analysing five randomised, double-blind, placebo-controlled studies that had evaluated the effectiveness of feverfew (daily doses ranging from 50 mg to 143 mg) as a preventive treatment for adult migraine. Studies by Johnson et al. (38) and Murphy et al. (39) demonstrated a significant reduction in the frequency of attacks and accompanying phenomena in feverfew-treated patients vs controls on placebo. Palevitch et al. (40) also reported a significant reduction in pain intensity and accompanying symptoms in feverfew-treated patients, while a further two studies (41,42) failed to find significant differences compared with placebo. The authors concluded that the effectiveness of feverfew in migraine prophylaxis remains to be proven. The randomized, double-blind, multicentre, controlled trial by Pfaffenrath et al. (43) provided data on the safety and tolerability of a new stable extract (MIG-99) reproducibly manufactured with supercritical CO₂ from feverfew in the prophylaxis of migraine with and without aura. MIG-99 compared with placebo failed to show a significant migraine prophylactic effect in general and was shown to be effective only in a small predefined subgroup of patients at an intermediate dosage. On the other hand the incidence of adverse events was similar for the active treatment groups and the placebo group and no dose-related effect was observed in any safety parameter. Because of the low number of patients these findings should be verified in a larger sample.

A study by Grossmann et al. (44) demonstrated a significant reduction in migraine attacks with a prophylactic treatment with a special CO₂ extract from the rhizome of *Petasites hybridus* compared to placebo, without adverse events. Because of the combination of high efficacy and excellent tolerance the authors emphasised the value of *Petasites hybridus* in the prophylactic treatment of migraine.

Aromatherapy

The fact that certain intense smells can trigger migraine attacks in predisposed subjects suggests a role for the olfactory system in mediating headache. Conversely aromatherapy is used in the treatment of headache. In a randomised, double-blind, placebo-controlled study of 32 healthy volunteers, Göbel et al. (45) evaluated the effect, on certain neurophysiological and algometric parameters, of local applications (on the temples and forehead) of peppermint and eucalyptus oil extracts. The peppermint preparation was found to raise the pain threshold and to have a muscle-relaxing effect, while the eucalyptus, despite producing a relaxing effect, did not significantly modify the pain threshold. According to the authors, these results provide a basis for the use of this substance in the treatment of tension-type headache.

Physical therapies

Within the context of these alternative approaches, we should also consider the various manoeuvres that are instinctively performed by headache patients in an attempt to relieve their pain. These are self-administered

procedures that have not been recommended by a physician or other health professional, but are routinely used by some patients. Zanchin et al. (46) investigated recourse to some of these manoeuvres (compression, the application of heat or cold, massage of different areas of the head) in a sample of 400 patients affected by primary headaches (migraine with and without aura, tension-type headache and cluster headache). Of the patients recruited, 65% used at least one of the manoeuvres mentioned: 30% used compression, 27% the application of cold, 25% massages, and 8% the application of heat. Furthermore, a statistically significant relationship emerged between type of headache and type of manoeuvre adopted: cold and compression of the forehead or temples in migraine without aura, compression of the temples in migraine with aura, and nape or temple massage in tension-type headache. Ultimately, however, the effectiveness of these measures in reducing pain was found to be low: they were found to be satisfactory pain control methods by only 8% of the subjects, and more often than not gave only temporary relief. Despite this, they were still used routinely (in every attack) by 46% of the patients studied. The authors conclude that use of these manoeuvres in headache becomes fundamentally a ritual, the practising of which does not necessarily correlate with the benefit obtained. A study by Puustjarvi et al. (47) evaluated the effects of massage in patients with chronic tension-type headache. The authors reported a reduction in the pain, still present after six months, following a series of ten one-hour massage sessions conducted over a period of two weeks. However, in spite of the effectiveness of this type of approach (the treatment procedure was, incidentally, poorly described), most of the patients found it to be too much of a commitment. In a more recent study, Quinn et al. (48) reported that nape and shoulder massage could, potentially, be an effective non pharmacological treatment for reducing the frequency and duration of chronic tension-type headache attacks.

Another physical approach that is quite widespread in the treatment of headache is that of chiropractic manipulation. While recognising the potential benefits of chiropractic techniques, it is important to remember that in over a hundred reported cases they have been linked with severe complications, mainly stroke. Given that there exists no definite proof of the effectiveness of chiropractic manipulation, it would seem wise to discourage headache patients from having recourse to it (23).

Concluding remarks

On the basis of this review of the literature on the use of so-called alternative therapies in the treatment of headache, we can affirm that scientific proof of their effectiveness is often lacking. However some treatments are known to have a good scientific basis, such as the use of magnesium, feverfew and riboflavin. The fact that some of the studies considered were found to present major methodological weaknesses means that further studies, conducted according to the principles of evidence-based medicine, are certainly needed in order to provide definitive evaluations. That said, we should, given the extensive use of alternative therapies, strive

to learn more about them, and not ignore the fact that a considerable proportion of the world's population uses different therapeutic methods from those familiar in the west. It is also important that physicians, when encountering patients who use or intend to use alternative therapies, are able to draw on their own knowledge in order to guide these patients, discouraging them from using potentially harmful ones (e.g., chiropractic manipulation, dietary restrictions) and possibly pointing them in the direction of safer ones, whose therapeutic effects have been demonstrated (e.g., acupuncture, magnesium, riboflavin). Furthermore, in subjects whose headache is not adequately controlled using acute treatment or prophylactic drugs, there is a need to understand better and possibly to integrate the use of non pharmacological and/or alternative treatments. There can be no doubt that this considerable recourse to alternative therapies reflects some of the limits of modern medicine: indeed, treatments are never effective in 100% of cases and patients are often unhappy with their relationship with their doctor. In the case of adult migraine, for example, the advent of the triptans has certainly revolutionised treatment, and allowed millions of people to achieve a better quality of life. But we have to remember that 30% of patients do not respond to these drugs, and that some patients experience unpleasant adverse effects, which in some can be severe. It is not surprising therefore that many of these patients, disappointed in traditional medicine, turn to unconventional therapies. It is also important to consider the fact that headache patients often do not consult their physician, but have recourse directly to alternative therapies, which are frequently more economical, seem safer (although this is not always the case), and whose practitioners often adopt a holistic approach to the care of the patient (23). Finally, in the case of juvenile patients, there are specific elements that favour recourse to unconventional therapies: i) parents are often uncertain and fearful of submitting their children to treatment with traditional drugs; ii) adolescents can use recourse to alternative therapies as a way of affirming their independence; iii) as far as headache is concerned, there are fewer drugs available to treat children than adults. To conclude, given the high response to placebo in headache sufferers (30-40%) (23) we feel (and this applies particularly to children) that patients should not be prevented from using alternative treatments, providing they are actively liked by the patient, and on condition that the treatment in question is not costly or harmful. On the contrary expensive treatments with no evidence-based proof of efficacy should not be encouraged. However, it is to be hoped that other studies will be conducted, in accordance with the criteria of evidence-based medicine, in order to clarify the indications, effectiveness and limits of alternative methods of treating headache in the different age groups.

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