DR DOMINIC PAVIOUR

Consultant Neurologist BSc MBBS PhD FRCP

Practice manager: Ms Kjai Kanone – pa@drpaviour.com – T: 02070421850 F: Fax: 020 7042 1851

The London Clinic	Parkside Hospital	HCA Sydney Street
Consulting Rooms	53 Parkside	102 Syndey Street
116 Harley Street	Wimbledon	Chelsea
London	London	London
W1G 7JL	SW19 5NX	SW3 6NR
02079354448	02089718026	02077308298

Introduction

In recent years there has been a growing interest and demand from the public for 'natural' treatments such as vitamins and supplements in trying to control migraine headaches. A variety of natural supplements, vitamins and herbal preparations have been promoted as having efficacy (being helpful) for migraine prophylaxis (prevention).
Among the most commonly recommended vitamins and supplements are magnesium, riboflavin, and Coenzyme Q10 (CoQ10) while the most common herbal preparations are feverfew and butterbur.
Each of these compounds has a theoretical mechanism or reason for the effect on migraine, and has had at least one placebo-controlled trial that has demonstrated efficacy.

Understanding research trials

During a placebo-controlled study patients are given the specific substance to be evaluated (e.g. magnesium or riboflavin) while in parallel another group of patients is treated with placebo treatment which appears identical to the patient, but is specifically designed to have no real effect such as dummy pills. Placebo is regularly used in controlled trials as a substance that is objectively without specific activity for the condition being treated, so that all the effects recorded can be attributed to the substance used.
Prior to involvement in the study each patient is interviewed and an adequate headache history is ascertained including age at migraine onset, headache attack frequency, severity, duration, presence or absence of aura, associated symptoms (nausea, vomiting, photophobia, phonophobia), and family history of migraine.

Principles of pharmacologic treatment of migraine

Following diagnosis of migraine, the next step is developing a successful treatment plan. The goals are to reduce attack frequency, severity and duration to improve the patient's quality of life. Unfortunately migraine cannot be cured at present. It is a chronic health condition that needs to be managed. Migraine management will be likely to include both medication and lifestyle changes such as sleeping and eating on time and exercising regularly. Whilst there is a range of acute and preventative medications available for the treatment of migraine headaches, it is well recognised that those living with migraine can benefit from lifestyle changes in order to reduce the frequency and severity of their headaches.

I want to receive a treatment for migraine but I would like to try something more 'natural', what are the options available?

Magnesium

Adult human bodies contain about 24 grams of magnesium. Magnesium plays a vital role in multiple physiologic processes and therefore it is a vital component in a healthy diet. It is absorbed through the gastrointestinal tract (gut), with more absorbed when the internal content is lower. Magnesium also appears to facilitate calcium absorption.
Spices, nuts, cereals, coffee, cocoa, tea, and vegetables are rich sources of magnesium. Leafy vegetables, as well as grains and nuts, generally have higher magnesium content than meats and dairy products.
No adverse effects have been associated with taking magnesium as a naturally occurring substance in foods.
However, adverse effects have been seen with excessive magnesium intake as a consequence of the use of various

DR DOMINIC PAVIOUR

Consultant Neurologist BSc MBBS PhD FRCP

Practice manager: Ms Kjai Kanone – pa@drpaviour.com – T: 02070421850 F: Fax: 020 7042 1851

The London Clinic	Parkside Hospital	HCA Sydney Street
Consulting Rooms	53 Parkside	102 Syndey Street
116 Harley Street	Wimbledon	Chelsea
London	London	London
W1G 7JL	SW19 5NX	SW3 6NR
02079354448	02089718026	02077308298

magnesium salts for pharmacological/medicinal purposes. The primary manifestation of excessive ingestion of magnesium from non-food sources is diarrhoea, which is reversible and thus stops when you stop taking the magnesium.
Side effects from increased magnesium intake are not common because the body removes excess amounts.

Interaction with other drugs

Some antibiotics, called aminoglycosides, can affect the muscles. Magnesium can also affect the muscles, so taking these antibiotics and magnesium might cause muscle problems.
Magnesium might decrease how much antibiotic the body absorbs. Taking magnesium along with some antibiotics might decrease the effectiveness of some antibiotics. To avoid this interaction these antibiotics should be taken at least 2 hours before, or 4 to 6 hours after, magnesium supplements.
Magnesium might decrease blood pressure. Taking magnesium with medication for high blood pressure might cause your blood pressure to go too low, also known as hypotension.
Magnesium seems to help relax muscles. Taking magnesium along with muscle relaxants can increase the risk of side effects of muscle relaxants.

Use for migraine

Studies have shown that migraineurs have low brain magnesium during migraine attacks (1) and may also suffer from magnesium deficiency (2, 3). Furthermore, magnesium deficiency may play a particularly important role in menstrual migraine (4). Two controlled trials have shown that oral magnesium supplementation (taking in by mouth) is effective in headache prevention (5, 6). A third study (7) was negative, but this result has been attributed to the use of a poorly absorbed magnesium salt, as diarrhoea occurred in almost half of patients in the treatment group. In general, the published trials yielded mixed results, with favourable effects reported for acute treatment of patients with aura and possibly also menstrual migraine prevention. Magnesium's efficacy may depend on a "high dose" supplementation (over 600mg) for a minimum of 3 to 4 months to achieve any benefit from preventative therapy.

Feverfew

Feverfew (Tanacetum parthenium) is an herb that is available as an off-the-shelf remedy. Its yellow-green leaves and yellow flowers resemble those of chamomile (Matricaria chamomilla), with which it is sometimes confused.
The herb feverfew has had a long history of use in traditional and folk medicine. Recently it has become a popular prophylactic treatment for migraine headaches and its extracts have been claimed to relieve menstrual pain, asthma, dermatitis, and arthritis. Traditionally, the herb has been used as an antipyretic (fever reducer), from which its common name is derived.

Human safety data

If you have any health problems that may be treated with feverfew, consult your doctor before use. Caution is advised if you have diabetes, alcohol dependence or liver disease. Liquid preparations of this product may contain sugar and/or alcohol, and feverfew is not recommended for use in children under 2 years of age. Because of the potential risk to the infant, breast-feeding while using this product is not recommended, and feverfew is contraindicated during pregnancy.

Potential side effects

Most adverse effects of treatment with feverfew are mild, although some patients have experienced increased heart rate. Feverfew possibly may interact with anticoagulants. A small percentage of people may experience mild stomach upset from feverfew, although this is rare. Chewing fresh feverfew leaves may lead to minor mouth ulcerations occasionally, an effect not observed with capsule users.

Dr Dominic Paviour PhD FRCP
Consultant Neurologist
info@drpaviour.com

DR DOMINIC PAVIOUR

Consultant Neurologist BSc MBBS PhD FRCP

Practice manager: Ms Kjai Kanone – pa@drpaviour.com – T: 02070421850 F: Fax: 020 7042 1851

The London Clinic	Parkside Hospital	HCA Sydney Street
Consulting Rooms	53 Parkside	102 Syndey Street
116 Harley Street	Wimbledon	Chelsea
London	London	London
W1G 7JL	SW19 5NX	SW3 6NR
02079354448	02089718026	02077308298

Interaction with other drugs

It is advised to avoid use of feverfew when taking anticoagulant drugs. Feverfew is contraindicated to those allergic to other members of the family Compositae (Asteraceae) such as chamomile, ragweed, or yarrow.

Use for migraine

Seventeen migraine patients who already used feverfew daily as migraine prophylaxis enrolled in a controlled trial in which 8 patients continued to receive feverfew while 9 stopped taking their feverfew and received placebo treatment instead (i.e. untreated patients) (8). Those who received placebo had a significant increase in the frequency and severity of headache (an average of 3.13 headaches every 6 months when taking placebo vs. only 1.69 headaches every 6 months when taking feverfew), nausea, and vomiting, whereas there was no change in the group receiving feverfew. In a larger study of 72 patients, feverfew was associated with a 24% reduction in the mean number and severity of attacks although the duration of the individual attacks was unaltered (9).

Coenzyme Q10 (CoQ10)

Coenzyme Q10 (CoQ10) is often described as a vitamin, or a vitamin-like substance. CoQ10 is involved in the creation of the important substance in the body known as adenosine triphosphate (ATP). ATP serves as the cell's major energy source and drives a number of biological processes including muscle contraction and the production of protein. CoQ10 also works as an antioxidant.

Some food sources, such as meat and fish, contain CoQ10 but the amounts in food are naturally less than can be obtained from supplements. Primary dietary sources of CoQ10 include oily fish (such as salmon and tuna), organ meats (such as liver), and whole grains. Most individuals obtain sufficient amounts of CoQ10 through a balanced diet, but supplementation may be useful for individuals with particular health conditions.

If you use or are planning to use CoQ10 for any specific health condition, you may want to let your doctor know. It appears to be safe, and when taken by healthy volunteers in a trial at different doses over 4 weeks did not cause safety concerns or adverse events. Other safety assessments have been favourable, but it seems sensible to avoid supplementation in pregnancy.

No toxicity has been reported with supplements up to 600 mg for every kg of body weight. Minor side effects that may occur with supplementation (but are unusual) include a burning sensation in the mouth, loss of appetite, nausea and diarrhoea. In large studies the incidence of gastrointestinal side-effects is less than 1%.

Interaction with other drugs

Cholesterol-lowering drugs such as lovastatin block the natural synthesis of CoQ10, so supplementation of 100 mg/day is recommended while taking these drugs.

Use for migraine

Thirty-two patients diagnosed as having migraine with or without aura were treated with CoQ10 at a dose of 150 mg per day in a controlled experiment (10). No adverse events were associated with CoQ10 therapy in any of the trial participants. As a result of the treatment, 61.3% of the patients treated had a greater than 50% reduction in number of days with migraine headache. Only two participants showed no improvement with CoQ10 therapy in their migraine headache intensity compared with baseline (ie when the trial started). The average number of days with migraine headache during the baseline non-treatment phase was 7.34 and this decreased to 2.95 days by the end of the trial. The reduction in migraine frequency after 1 month of treatment was 13% and this improved to 55% by the end of 3 months of therapy. From this open-label (called “open” as participants were aware of whether they were taking CoQ10 or not) investigation, CoQ10 appears to be a good migraine preventive. The data presented in this trial suggest that CoQ10 starts to work within 4 weeks but usually takes 5 to 12 weeks to yield a significant reduction in days with

Dr Dominic Paviour PhD FRCP
Consultant Neurologist
info@drpaviour.com

DR DOMINIC PAVIOUR

Consultant Neurologist BSc MBBS PhD FRCP

Practice manager: Ms Kjai Kanone – pa@drpaviour.com – T: 02070421850 F: Fax: 020 7042 1851

The London Clinic	Parkside Hospital	HCA Sydney Street
Consulting Rooms	53 Parkside	102 Syndey Street
116 Harley Street	Wimbledon	Chelsea
London	London	London
W1G 7JL	SW19 5NX	SW3 6NR
02079354448	02089718026	02077308298

migraine. An important finding from this study is that taking CoQ10 appears to be associated with no significant adverse events and is extremely well-tolerated. In another study (11) migraine attack frequency after 4 months of treatment was reduced at least 50% in 48% of patients as compared to 14% for placebo. CoQ10 supplementation may be particularly effective in the treatment of childhood migraine (12).

Riboflavin

Riboflavin, also known as vitamin B2, is found in small amounts in many foods. It is needed for converting food to energy, and like CoQ10 also works as an antioxidant by mopping up the damaging free radicals.
Lean meats, eggs, legumes, nuts, green leafy vegetables, dairy products, and milk provide riboflavin in the diet. Breads and cereals are often fortified with riboflavin. Because riboflavin is destroyed by light, foods with riboflavin should not be stored in exposed glass containers. Riboflavin is stable when heated but will leach into cooking water, and the pasteurisation process causes milk to lose about 20% of its riboflavin content. Alkalis, such as baking soda, also destroy riboflavin.

Human safety data

No toxic symptoms have been reported at doses of up to 400 mg per day for at least 3 months, other than occasional minor side effects that were not clearly attributable to the compound. Because riboflavin is a water-soluble vitamin, excess amounts are excreted, and harmless yellow discoloration of urine occurs at high doses. While apparently non-toxic at any dose in adults, and while foetal toxicity is unproven, riboflavin supplementation in pregnancy is not always recommended so please check with your health visitor.

Potential side effects

In general the limited capacity of adults to absorb riboflavin taken by mouth limits its potential for harm. Possible reactions to very high doses (over 400 mg) include itching, numbness (insensitivity), burning/prickling sensations, and yellow discolouration of the urine. Individuals who have inadequate food intake are at risk of deficiency, particularly children in developing countries. It is thought that riboflavin also aids the body in absorbing iron, since it is common for iron deficiency to accompany a deficiency in riboflavin.

Interaction with other drugs

Riboflavin is necessary for the activation of vitamin B6. Sulfa drugs, anti-malarial drugs, oestrogen and alcohol may interfere with riboflavin metabolism. High doses of riboflavin can reduce the effectiveness of the anticancer drug methotrexate, whilst some antibiotics and phenothiazine drugs may increase riboflavin excretion. Riboflavin must be activated in the liver which may be inhibited by major tranquilizers and some antidepressants.

Use for migraine

In the only study involving riboflavin alone, Schoenen and others studied 55 migraine patients and reported that 59% of the participants who took 400 mg/day riboflavin for 3 months experienced at least 50% reduction in migraine attacks compared with 15% for placebo (13). Statistically significant reductions in both migraine frequency and number of headache days were reported. Adverse events reported from studies investigating riboflavin have been limited to diarrhoea and polyuria (passing of large volumes of urine), both occurring in extremely low numbers.

Dr Dominic Paviour PhD FRCP
Consultant Neurologist
info@drpaviour.com

DR DOMINIC PAVIOUR

Consultant Neurologist BSc MBBS PhD FRCP

Practice manager: Ms Kjai Kanone – pa@drpaviour.com – T: 02070421850 F: Fax: 020 7042 1851

The London Clinic	Parkside Hospital	HCA Sydney Street
Consulting Rooms	53 Parkside	102 Syndey Street
116 Harley Street	Wimbledon	Chelsea
London	London	London
W1G 7JL	SW19 5NX	SW3 6NR
02079354448	02089718026	02077308298

Butterbur (Petasites hybridus)

Butterbur is a perennial shrub, found throughout Europe as well as parts of Asia and North America. It is usually found in wet, marshy ground, in damp forests, and adjacent to rivers or streams. The common name is attributed to the large leaves being used to wrap butter during warm weather.

Human safety data

For many centuries the butterbur was used as an herbal remedy for conditions like pain, fever and spasms. Today, butterbur is mainly used for migraine prevention, but also for treating headaches and asthma. The butterbur plant also contains liver-toxic pyrrolizidine alkaloids, which are removed by a special patented treatment and only marketed under the name Petadolex®.

Potential side effects

Studies have reported safety and good tolerability of commercially available butterbur products that are free of potentially carcinogenic pyrrolizidine alkaloid constituents, when used short-term, orally and in recommended doses. Raw, unprocessed butterbur plant should not be eaten due to the potential for liver damage of pyrrolizidine alkaloids with long-term use. This includes any teas, capsules of raw herb, or unprocessed tinctures or extracts. Use should be limited to commercially available products free of pyrrolizidine alkaloids, and is not recommended in women who are pregnant or breastfeeding due to a lack of safety studies.

Interaction with other drugs

Long-term health effects and interaction with other drugs have not been studied so we don't know if there are any side effects from long term use.

Use for migraine

According to the first trial published by Lipton in 2004 (14) and conducted in the USA and Germany with 245 migraine patients with and without aura, the participants found relief from migraine symptoms with butterbur. The participants were treated for 4 months twice daily with either placebo or 50 mg or 75 mg commercial butterbur. Maximum response was achieved after 3 months resulting in an attack reduction of 58% with a 2x75 mg/day dosing. This was statistically significant compared to the placebo response of 28%. The percentage of patients responding to the therapy was 71% after treatment with butterbur. Two randomized, placebo-controlled migraine prevention trials with a total of 289 patients demonstrated the safety and efficacy of the butterbur root extract in adults (15, 16), prompting an exploration of the prevention of migraine in children also.

Use for migraine in children

Between April 1998 and July 2002, a total of 112 patients entered an open-label trial (17), consisting of 29 children between the ages of 6 and 9 years and 79 adolescents between the ages of 10 and 17 years. The attack reduction in the total sample population was 63%. About 86% (18 out of 21) of the younger and 74% (43 out of 58) of the older patients responded. Prophylactic (preventative) treatment with butterbur extract also reduced the duration of migraine attacks from about 10 hours on average before the study to about 7 hours during treatment. However, approximately 25% of patients still experienced a prolonged attack under treatment. About 82% (71 out of 87) of all patients reported substantial improvement of their migraine compared to the situation prior to the study. None of the patients reported worsening of migraine, but one patient each per age group reported that they had stopped the treatment early due to lack of efficacy. About 92% (78 out of 85) of all patients felt as well as or even better than before the study. Only one migraine patient in both age groups felt much worse because of the treatment.

Dr Dominic Paviour PhD FRCP
Consultant Neurologist
info@drpaviour.com

DR DOMINIC PAVIOUR

Consultant Neurologist BSc MBBS PhD FRCP

Practice manager: Ms Kjai Kanone – pa@drpaviour.com – T: 02070421850 F: Fax: 020 7042 1851

The London Clinic	Parkside Hospital	HCA Sydney Street
Consulting Rooms	53 Parkside	102 Syndey Street
116 Harley Street	Wimbledon	Chelsea
London	London	London
W1G 7JL	SW19 5NX	SW3 6NR
02079354448	02089718026	02077308298

I am pregnant / breastfeeding and experiencing migraine; I feel that it would be better for me and my baby to use a 'natural' remedy, is there any scientific data to help me decide?

Pregnancy and lactation are situations that warrant special consideration in the treatment of the migraine. Although migraines generally improve during pregnancy, headaches may worsen or remain the same in some women. An increase in headaches during the first trimester is not uncommon, due to wide fluctuations in oestrogen levels.

Women of reproductive age should be counselled about the risks of acute and preventative migraine medications. Owing to the limitations on pharmacologic treatment of migraine during pregnancy and lactation non-drug approaches such as regular exercise and lifestyle changes are the first issues to consider (18). Maintaining hydration is also crucial, especially for those in whom nausea and vomiting are prominent. These women should avoid herbal remedies, including feverfew and butterbur as there may be unidentified risks for the unborn baby (18).

For women who continue to have frequent headaches during pregnancy and lactation, magnesium supplementation is an option, both in acute and preventative treatment. For acute migraine treatment, the dose is much lower than with some other health conditions.

References

1. Ramadan NM, Halvorson H, Vande-Linde A. Low brain magnesium in migraine. Headache. 1989;29:590–593.
2. Trauinger A, Pfund Z, Koszegi T, et al. Oral magnesium load test in patients with migraine. Headache. 2002;42: 114–119.
3. Mauskop A, Altura BM. Role of magnesium in the pathogenesis and treatment of migraine. Clin Neurosci. 1998; 5:24–27.
4. Mauskop A, Altura BT, Altura BM. Serum ionized magnesium in serum ionized calcium/ionized magnesium ratios in women with menstrual migraine. Headache. 2001;42:242–248.
5. Facchinetti F, Sances G, Borella P, et al. Magnesium prophylaxis of menstrual migraine: effects on intracellular magnesium. Headache. 1991; 31:298–301.
6. Peikert A, Wilimzig C, Kohne-Volland R. Prophylaxis of migraine with oral magnesium: results from a prospective, multicenter, placebo-controlled and double-blind randomized study. Cephalalgia. 1996;16:257–263.
7. Pfaffenrath V, Wessely P, Meyer C, et al. Magnesium in the prophylaxis of migraine—a double-blind placebo-controlled study. Cephalalgia. 1996; 16:436–440.
8. Johnson ES, Kadam NP, Hylands DM, Hylands PJ. Efficacy of feverfew as prophylactic treatment of migraine. BMJ. 1985; 291:569-573.
9. Murphy JJ, Heptinstall S, Mitchell JRA. Randomized, double-blind, placebo-controlled trial of feverfew in migraine prevention. Lancet. 1988; 2:189-192.
10. TD Rozen, ML Oshinsky, CA Gebeline, KC Bradley, WB Young, AL Shechter & SD Silberstein. Open label trial of coenzyme Q10 as a migraine preventive. Cephalalgia, 2002, 22, 137–141.
11. Sandor S, Di Clemente L, Coppola G, et al. Efficacy of coenzyme Q10 in migraine prophylaxis: A randomized controlled trial. Neurology. 2005; 64:713.
12. Hershey AD, Powers SW, Vockell AL, Lecates SL, Ellinor PL, Segers A, Burdine D, Manning P, Kabbouche MA. Coenzyme Q10 deficiency and response to supplementation in pediatric and adolescent migraine. Headache. 2007 Jan; 47(1):73-80.

Dr Dominic Paviour PhD FRCP
Consultant Neurologist
info@drpaviour.com

DR DOMINIC PAVIOUR

Consultant Neurologist BSc MBBS PhD FRCP

Practice manager: Ms Kjai Kanone – pa@drpaviour.com – T: 02070421850 F: Fax: 020 7042 1851

The London Clinic	Parkside Hospital	HCA Sydney Street
Consulting Rooms	53 Parkside	102 Syndey Street
116 Harley Street	Wimbledon	Chelsea
London	London	London
W1G 7JL	SW19 5NX	SW3 6NR
02079354448	02089718026	02077308298

13. Schoenen J, Jacquy J, Lenaerts M. Effectiveness of high-dose riboflavin in migraine prophylaxis. A randomized controlled trial. Neurology. 1998; 50:466-470.
14. Lipton RB, Göbel H, Einhäupl KM, Wilks K, Mauskop A Petasites hybridus root (butterbur) is an effective preventive treatment for migraine. Neurology. 2004 Dec 28;63(12):2240-4.
15. Diener HC, Rahlfs VW, Danesch U. The first placebo-controlled trial of a special butterbur root extract for the prevention of migraine: reanalysis of efficacy criteria. Eur Neurol. 2004;51:89-97.
16. Lipton RB, Göbel H, Wilks K, Mauskop A. Efficacy of Petasites (an extract from Petasites rhizoma) 50 and 75 mg for prophylaxis of migraine: results of a randomized, double-blind, placebo-controlled study. Neurology. 2002;58(suppl 3):A472.
17. Migraine Prevention in Children and Adolescents: Results of an Open Study With a Special Butterbur Root Extract Raymund Pothmann, MD; Ulrich Danesch, PhD (Headache 2005;45:196-203).
18. Loder E. Migraine in pregnancy. Semin Neurol. 2007;27: 425–433.
19. National Research Council. Magnesium (Chapt 6). In: Dietary Reference Intake for Ca, P, Mg, vitamin D, Fluoride. Washington DC: National Academy Press; 1997.

Dr Dominic Paviour PhD FRCP
Consultant Neurologist
info@drpaviour.com