Magnesium for Migraine Prevention

The ideal medication for prevention and treatment of migraine would have no side effects, no risk, would be safe in pregnancy, as well as being highly effective while remaining inexpensive. Of course, no such medication exists, but magnesium comes closer than many interventions on all these fronts.

Magnesium oxide is frequently used in pill form to prevent migraine, usually at a dose of 400-500 mg per day. Acutely, it can be dosed in pill form at the same dosage, or given intravenously as magnesium sulfate at 1-2 gm. The most frequent side effect is diarrhea, which can be helpful in those prone to constipation. The diarrhea and abdominal cramping that is sometimes experienced is dose responsive, such that a lower dose or decreasing the frequency of intake usually takes care of the problem.

Magnesium oxide in doses up to 400 mg is pregnancy category A, which means it can be used safely in pregnancy. Magnesium sulfate, typically given intravenously, now carries a warning related to bone thinning seen in the developing fetus when used longer than 5-7 days in a row. This was discovered in the context of high doses being given to pregnant women to prevent preterm labor.

The strongest evidence for magnesium's effectiveness is in patients who have, or have had, aura with their migraines. It is believed magnesium may prevent the wave of brain signaling, called cortical spreading depression, which produces the visual and sensory changes that are the common forms of aura. Other mechanisms of magnesium action include improved platelet function and decreased release or blocking of pain transmitting chemicals in the brain such as Substance P and glutamate. Magnesium may also prevent narrowing of brain blood vessels caused by the neurotransmitter serotonin.

Daily oral magnesium has also been shown to be effective in preventing menstrually related migraine, especially in those with premenstrual migraine. This means that preventive use can be targeted at those with aura and/or those with menstrually related migraine.

It is difficult to measure magnesium levels accurately, as levels in the blood stream may represent only 2% of total body stores, with the rest of magnesium stored in the bones or within cells. Most importantly, simple magnesium blood levels do not give an accurate measure of magnesium levels in the brain. This has led to uncertainty concerning whether correcting a low magnesium level is necessary in treatment, or whether magnesium effectiveness is even related to low blood levels in the first place.
Measurement of ionized magnesium or red blood cell magnesium levels is thought to possibly be more accurate, but these laboratory tests but are more difficult and expensive to obtain.

Because magnesium may not be accurately measured, low magnesium in the brain can be difficult to prove. Those prone to low magnesium include people with heart disease, diabetes, alcoholism, and those on diuretics for blood pressure. There is some evidence that migraineurs may have lower levels of brain magnesium either from decreased absorption of it in food, a genetic tendency to low brain magnesium, or from excreting it from the body to a greater degree than non-migraineurs. Studies of migraineurs have found low levels of brain and spinal fluid magnesium in between migraine attacks.

In 2012, the American Headache Society and the American Academy of Neurology reviewed the studies on medications used for migraine prevention and gave magnesium a Level B rating, that is, it is probably effective and should be considered for patients requiring migraine preventive therapy. Because of its safety profile and the lack of serious side effects, magnesium is often chosen as a preventive strategy either alone, or with other preventive medications.

Magnesium has also been studied for the acute, as-needed treatment of severe, difficult-to-treat migraine. Magnesium sulfate given intravenously was found to be most effective in those with a history of migraine with aura. In those without a history of aura, no difference was seen in immediate pain relief or nausea relief by magnesium, but there was less light and noise sensitivity after the infusion.

Magnesium oxide, in tablet form, is very inexpensive, does not require a prescription, and may be considered as very reasonable prevention in those who have a history of aura, menstrually related migraine, no health insurance, or who may become pregnant. Because of the excellent safety profile of magnesium, any patient who has frequent migraines and is considering a preventive strategy to reduce the frequency or severity of their headaches may want to consider this option and discuss it with their physician.

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- **How it works** Studies show that migraine sufferers have lower brain and blood levels of micronutrients (riboflavin, magnesium and coenzyme Q10) than nonmigraineurs (Hershey, 1999; Hershey, 2007; Mauskop, 1998). A deficit of these nutrients could play a role in how well nerves can function. The common effect of these micronutrients on mitochondrial dysfunction may explain why they are ineffective for some people who likely do not suffer from this etiology of their migraine disease and only partially reduce symptoms in other people in this complex disease. **Magnesium** - Needed in various biological processes that occur with migraine (vasoconstriction, platelet inhibition, secretion of serotonin). Magnesium is also needed as a co-factor for proper functioning of the ATP-synthase, which produces ATP. Furthermore, magnesium is the physiological antagonist at the NMDA-channel which is involved in the regulation of neuronal excitability. **Riboflavin** - A precursor for flavin-mononucleotide (FMN) and flavin-adenine-dinucleotide (FAD). Both are essential components of complex I and complex II responsible for electron-transport in the mitochondrial membrane. Like CoQ10, it also works as an antioxidant by mopping up the damaging free radicals.

Memantine - May reduce migraine symptoms by blocking a glutamate receptor in the brain (glutamate N-methyl-D-aspartate receptor antagonist). Like serotonin, glutamate is a chemical that helps to send messages between nerve cells. **Melatonin** - Linked to a variety of mechanisms related to the pathophysiology of headaches such as its anti-inflammatory effects, toxic free radical scavenging, reduction of pro-inflammatory cytokine up-regulation, inhibition of nitric oxide synthase activity and dopamine release, GABA and opioid analgesia potentiation, glutamate neurotoxicity protection, neurovascular regulation, and serotonin modulation. Melatonin's chemical structure is also very similar to indomethacin, a common NSAID. (Peres, 2005)**Coenzyme Q10** - A vitamin-like compound that can be synthesized by the body from phenylalanine and tyrosine. Coenzyme Q10 is needed for all cellular processes requiring energy. Coenzyme Q10 is an electron-carrier, transferring electrons from complex I/complex II to cytochrome C. **Feverfew** - A study of 17 migraine patients, those on feverfew had half as many headaches. (Johnson, 1985) In a second study of 72 patients those who took feverfew had a 24% reduction in the mean number and severity of attacks although the duration of the individual attacks was unaltered. (Murphy, 1988)**Butterbur (Petasites hybridus) 50 or 75 mg** - This herbal remedy has been used for migraine and other uses for centuries. More recently, two studies (Diener, 2004; Lipton, 2002) demonstrated efficiency and safety of butterbur in adults. Another study (Lipton, 2004) showed that patients who used 75 mg butterbur twice daily for 4 months enjoyed 58% migraine attack reduction versus 28% in placebo group. **Possible side effects. Magnesium**Risk of side effect increases with higher doses. If any of these symptoms were to occur, a lower dose may still be well tolerated and effective.

- Diarrhea (remember Milk of Magnesium)
- Gastrointestinal discomfort
- Constipation

- **Riboflavin** Minimal because the absorption of oral riboflavin is limited.SEPAt high doses it will produce:
  - A harmless yellow discoloration of urine.
  - Itching
  - Numbness (insensitivity)
  - Burning/prickling sensations
- **Melatonin** Excess melatonin can cause
  - Headache
  - Short-term feelings of depression
  - Daytime sleepiness
  - Dizziness
  - Stomach cramps
  - Irritability
  - Hypothermia (reduced body temperature)
  - Stimulate overproduction of the hormone prolactin, which can cause hormonal problems and even kidney and liver issues in men

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- **Coenzyme Q10**
  - Nausea and/or vomiting
  - Diarrhea
  - Heartburn and stomach pain
  - Loss of appetite
  - Itching or rash
  - Insomnia
  - Dizziness
- **Feverfew**
  - Increased heart rate
  - Mild stomach-ache
  - Mouth sores when chewing fresh feverfew leaves
- **Butterbur** The butterbur plant also contains liver-toxic pyrrolizidine alkaloids and potential cancer causing chemicals, which are removed by a special patented treatment and only marketed under the name Petadolex®. No part of the Petasites plant should be ingested other than the commercial products.[SEP]The United Kingdom Medicines and Healthcare products Regulatory Agency (MHRA) announced in 2012 that Butterbur products are linked with liver toxicity and should be removed from the market.[SEP]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.