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Evidence-based Basics on Nutraceuticals: Herbs, Minerals, Vitamins, and Supplements in Migraine Management

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Is there a place for nutraceuticals in the management of migraine? This document reviews the randomized, controlled trials (RCT) for migraine for various minerals, herbs, vitamins and supplements, and gives therapeutic recommendations for the interested clinician.

Rationale for Use

There are two basic potential mechanisms for the usually tried supplements for migraine prevention, 1) to reduce migraine brain neuronal hyperexcitability, or 2) to improve energy metabolism. Low ionized magnesium levels, abnormal neuronal membrane ion channels (channelopathies) with resultant increased excitatory glutamatergic activity, and mitochondrial dysfunction with abnormal energy metabolism are linked to the genesis of migraine. Low magnesium and channelopathies are related; riboflavin or coenzyme Q10 can be used to treat mitochondriopathy; petasites may decrease the meningeal inflammatory mechanisms of migraine pain.

Magnesium

Low magnesium is linked to influx of calcium into neurons, with resultant glutamate release into the synapse. Low magnesium at the synapse causes post-synaptic neuronal excitation. Multiple studies demonstrate low magnesium in migraine patients. Trials with magnesium supplementation for migraine prophylaxis have yielded mixed results, with the positive studies in patients with aura and with perimenstrual migraine. Parenteral magnesium (1 gram IV) can terminate migraine in patients with low ionized magnesium levels, and in those with aura. The recommended dose is 400–600 mg/day of chelated magnesium (taurate, glycinate, oxide, etc) for at least 3 to 4 months. Diarrhea limits oral magnesium supplementation clinically.

Riboflavin (Vitamin B2)

Riboflavin is a cofactor in the Krebs cycle during respiration, and several studies suggest mitochondrial dysfunction in some migraine patients, with abnormal phosphorylation of ADP to ATP. Thus, giving B2 could theoretically improve energy metabolism. There are four RCTs on B2 for migraine prevention. In the first, in adults, 400 mg riboflavin taken daily for 3 months was superior to placebo for reduction of migraine frequency and headache days. Two patients had diarrhea and polyuria. In the second, also in adults, 400 mg of B2 (combined with feverfew and low dose magnesium) was no different than 25 mg of B2, which was selected as a placebo dose.

In both dose groups and both studies, > 40% of patients had ≥ 50% reduction in migraine frequency. Thus, it was unclear whether 25 mg B2 is an active dose, or whether B2 was no more effective than placebo. Two pediatric RCTs were both negative. Thus, 3 of 4 RCTs with B2 weigh against effectiveness.

Coenzyme Q10 (CoQ10)

CoQ10 transfers electrons in the electron transport chain, so it can theoretically treat mitochondriopathy. One RCT of 42 patients found 100 mg TID of CoQ10 for 3 months superior to placebo; 48% of subjects had ≥ 50% reduction in attack frequency. In another study of 1,478 migraine patients from 3-22 years old, low CoQ10 levels occurred in 33%. Repleted CoQ10 with daily supplementation was linked to reduced migraine frequency.

CoQ10 is generally well tolerated. Side effects at high doses are uncommon, including nausea, anorexia, dyspepsia, diarrhea, and rash.

Feverfew

Feverfew is sold as capsules of the dried leaves of the weed plant tanacetum parthenium in the US. A meta-analysis of all of the RCTs up to 1998 concluded that data were of too low quality and too varied in results to be sure whether feverfew works in migraine prevention. Two recent RCTs of a purified stable extract of feverfew, MIG-99, suggest once again that feverfew is ineffective in migraine prevention, or has so low a clinical effect as to be close to useless. A more recent meta-analysis of five RCTs on feverfew found a suggestion of effect for migraine with aura, but otherwise the studies were negative, and concluded that feverfew is no better than placebo. The potential complications of arthralgias, gastrointestinal disturbances, and mouth ulcers, and the wide variety of potency in dried leaves, preclude its recommendation for migraine prevention.

Petasites (Butterbur root)

Petasites hybridus is a very poisonous plant, but a detoxified root extract (Petadolex™) has so far tested safe in post-marketing in Germany. The mechanism of action may be anti-inflammatory. Two RCTs have found efficacy for Petadolex™: a small study of 100 mg/day, and a larger study of 150 mg/day vs. placebo. It is well tolerated; the only side effect of the drug is burping. The recommended dose is 150 mg/day, taken as 50 mg QAM, 100 mg QHS.

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