

Migraine Protocol Evidence

Here at Nervana, we have an IV Migraine Protocol and a Nutraceutical Protocol. Here are the reasons we suggest what we suggest!

Studies/Pharmaceutical rationales:

- When added to standard acute migraine therapy, parenteral treatment with dexamethasone reduces the rate of early headache recurrence. Supporting evidence comes from a meta-analysis of seven randomized trials conducted in emergency departments or headache clinics. All patients (n = 738) received standard abortive migraine headache treatment, and were also randomly assigned to treatment with either a single dose of dexamethasone (intravenous or intramuscular, 10 to 24 mg) or placebo. In the pooled results, dexamethasone was significantly more effective than placebo for reducing migraine recurrence from 24 to 72 hours after treatment (relative risk 0.74, 95% CI 0.6-0.9). Dexamethasone provided no additional benefit for immediate relief of headache. There were no significant differences regarding adverse events between the dexamethasone and placebo groups. Oral Prednisone was not shown to be beneficial.
- Selective serotonin receptor (5-HT₃) antagonists block serotonin both peripherally on vagal nerve terminals in the gastrointestinal (GI) system and centrally in the chemoreceptor trigger zone in the area postrema of the fourth ventricle, resulting in powerful antiemetic effects.
- Magnesium – There is evidence supporting magnesium supplementation for migraine prevention in adults. Several small randomized controlled trials using variable formulations of oral magnesium produced mixed results, with three trials finding a statistically significant benefit for magnesium and one trial finding no benefit. Magnesium is typically used at 400 to 600 mg daily for migraine prevention. Diarrhea and gastrointestinal discomfort were the most common side effects of magnesium supplementation in these trials. Known as “the relaxation mineral”, magnesium may help with lowering stress and anxiety.
 - Studies examining the use of intravenous magnesium in the treatment of acute migraine have been conflicting. A study on 40 patients with acute migraine attacks showed an 85% correlation between levels of serum ionized magnesium (measured during an attack) and clinical response to 1g of intravenous magnesium sulphate ([Mauskop et al., 1995](#)). Although the study was neither double-blinded nor placebo-controlled, both researchers and subjects were blinded to ionized magnesium levels. A further study on various headache types found 1g of magnesium sulphate to provide rapid relief in patients with low serum ionized magnesium levels ([Mauskop et al., 1996](#)).
 - A single-blind placebo-controlled, randomized trial involved 30 patients with migraines who were randomized to receive either magnesium sulphate 1g or placebo ([Demirkaya et al., 2001](#)). After 30 minutes, patients in the placebo group who had ongoing pain, nausea or vomiting were given magnesium sulphate 1g. Treatment was superior to placebo in terms of both response rate (100% for magnesium sulphate vs 7% for placebo) and pain-free rate (87% for magnesium sulphate vs 0% for placebo) and those treated did not experience headache recurrence within 24 hours. 87% complained of flushing or a burning sensation in the face and neck.
 - A double-blind placebo-controlled, randomized study evaluated the efficacy of magnesium sulphate 1g on the pain and associated symptoms of migraine with and without aura ([Bigal et al., 2002](#)). In subjects with migraine without aura, although there was a significant decrease in the intensity of photophobia and phonophobia, no significant differences were observed in pain relief

or nausea. However subjects with migraine with aura had significant improvement in pain and all associated symptoms.

- An emergency room-based double-blind placebo- controlled, randomized study of 44 subjects with acute migraines tested a combination of magnesium sulphate 2g and metoclopramide 20mg versus metoclopramide 20mg alone at 15 minute intervals for up to 3 doses, or until pain relief occurred ([Corbo et al., 2001](#)). Pain intensity was recorded using a standard visual analogue scale (VAS). Although both groups experienced more than 50mm improvement in the VAS score, improvement was smaller in the magnesium group, both comparing VAS score improvements and evaluating normal functional status. The authors suggested that magnesium may diminish the efficacy of metoclopramide in decreasing migraine pain.
 - A study involving 22 patients with cluster headaches who were treated with magnesium sulphate 1g found that 41% of patients reported 'meaningful relief' (defined as complete cessation of attacks or relief for more than 3 days) after treatment ([Mauskop et al., 1995](#)).
 - Magnesium is central to numerous physiological functions, and the role it plays in the various aspects of migraine pathogenesis is well described. Although some studies have shown an association between migraines and magnesium deficiency, it is difficult to assess this with routine blood testing and serum magnesium levels are a poor reflection of body stores of the cation. Therefore, treatment should be based on clinical suspicion, with both oral and intravenous magnesium available as simple, safe, inexpensive and well-tolerated options for the management of migraines. . It may also be used for the treatment of acute migraines, or as a monthly prophylactic infusion, often administered premenstrually.
- Melatonin – Small, short-term randomized controlled trials evaluating melatonin for episodic migraine prevention have provided conflicting results. One such trial found that melatonin 2 mg (extended release) was not more effective than placebo for reducing headache frequency, while another trial reported that melatonin 3 mg (immediate release) was more effective than placebo, and equally as effective as amitriptyline, for reducing headache frequency. Studies to date have found that magnesium supplementation maintains healthy blood pressure levels. Calcium is essential to the contraction of muscles, while magnesium aids muscle relaxation. Insufficient magnesium levels can contribute to constriction of the muscles in blood vessels and trigger changes in blood pressure levels which can also lead to symptoms of headaches/migraines.
 - Vitamin D – In a randomized controlled trial of 57 adults with episodic migraine, in which participants continued their pre-study abortive and prophylactic migraine medications, treatment with simvastatin (20 mg twice daily) plus vitamin D3 (1000 international units twice daily) was superior to placebo over a 24-week intervention period for reduction in the number of days with migraine headache and some secondary outcome measures.
 - Co-Q10 : Supports neurological health. Neurons are characterized by high rates of metabolic activity and the need to respond quickly to energy demanding fluctuations in the brain. Mitochondrial alterations, leading to reduced ATP production, can promote neuronal dysfunction and degeneration via increased production of reactive oxygen species in the central nervous system. As an effective carrier with strong antioxidant properties, CoQ10 has been shown to promote neurological health.