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MIGRAINE

1271 HIGH STREET, AUBURN, CA 95603 • PHONE (530) 823-7092 • ORDER LINE (800) 359-6091
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June 2015

Volume 11: Issue 2

INTRODUCTION

Migraine headache is one of the most common pain syndromes affecting approximately 15% of the American population. The word migraine derives from the Greek word for “pain on one side of the head.”

A typical migraine affects one half of the head, lasts from 2 to 72 hours, and is pulsating. Those with a migraine may experience nausea, vomiting, and enhanced sensitivity to light, sound, or smell. Physical activity tends to make the pain worse. Migraines are much more common in women than in men, although boys have more migraines than girls prior to puberty.

This newsletter provides an update on some of the most recent findings related to the condition.

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MAGNESIUM

Dr. Burton Altura developed a very sensitive ion-selective electrode which makes it possible to detect magnesium deficiency, physiologically a very difficult task. This technology was used by Alexander Mauskop who found that up to half of patients with an acute migraine attack had low ionized magnesium levels.

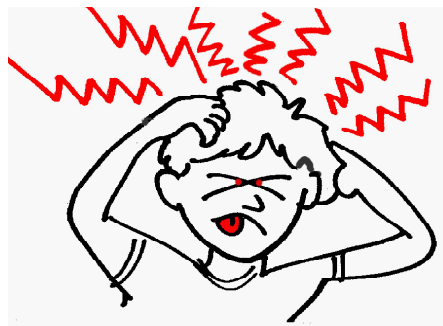
Mauskop found that 85% of these patients responded when infused with a magnesium sulfate solution. Head-

aches in responders resolved within minutes. By contrast, only 15% of patients with normal ionized magnesium levels responded to infusions of the mineral.

The infusion created a feeling of heat in most of the patients. One experienced nausea and two felt light headed. None of the side-effects were unduly severe.

Mauskop does not believe that oral magnesium supplementation will be very effective for an acute attack as it is not likely to cause a rapid rise in blood levels of the mineral. Taken as a preventative, magnesium supplementation may be an effective measure for the half of migraine sufferers who are magnesium deficient. In view of the many benefits of adequate magnesium intake regular supplementation by migraine sufferers should not be a problem.

Unfortunately, magnesium is a difficult mineral to absorb and migraine sufferers may have more difficulty in absorbing the mineral than the average person.



Dr. Arthur Furst, Ph.D., who pioneered the idea of chelation began his work with magnesium because of the difficulty of absorbing this mineral. The word chelate comes from a Greek word meaning “claw.” The technology involves grabbing onto a mineral with another substance with the idea of improving absorption.

Most chelating agents are not very effective at improving mineral absorption. The problem lies in the stomach. The hydrochloric acid in the stomach can break apart most mineral bonds. Minerals bound to amino acids are most resistant to degradation by the stomach acid.

Dr. Furst developed a process of wrapping minerals like magnesium with two amino acids to totally neutralize the two positive charges on a mineral. This increases absorption and utilization of minerals anywhere from two-fold to six-fold. Mauskop prefers a chelated form of the mineral for enhanced absorption.

Calcium and magnesium compete with one another for absorption. Supplementation with calcium alone can induce a magnesium deficiency, while use of magnesium alone may impair calcium absorption. Most suggest a supplement that includes two parts calcium to one part magnesium. Some recommend a one to one ratio where serious magnesium deficiency exists.

Magnesium regulates a wide va-



riety of enzymes and neurotransmitters. It is intimately involved with the NMDA receptor which is involved with pain transmission in the body. The NMDA receptor becomes active when calcium moves through it causing the transmission of pain. It is difficult for calcium to move through the receptor if magnesium sits inside it. If magnesium is low the receptor is easily opened up for calcium flow.

Magnesium is also necessary for muscle relaxation. Blood vessels in animal experiments go into spasm if magnesium levels are low, but adding magnesium results in relaxation of the blood vessels.

Mauskop's work was subjected to a randomized trial by Dora. Dora did not test for low magnesium status. 13 of 15 patients in the group receiving magnesium experienced relief from pain and 2 experienced a diminishing of the pain. Only 4 of the patients in the placebo group saw a partial improvement. The placebo group was subsequently given magnesium and the attack ended in 14 of the 15 while the intensity decreased in one patient.

Swanson found eleven different pathways by which magnesium could reduce the risk of migraine.

More than half of the United States population is magnesium deficient. Assessment of deficiency can be difficult. In 2005, I had the opportunity to meet Mildred Seelig, a world famous magnesium researcher. Her research suggests that magnesium deficiency is very common. She felt routine calcium-magnesium supplementation should consist of 2 parts calcium to one part magnesium.

Seelig has a discussion of assess-

ment of magnesium status, consequences of deficiency, and supplementation in her excellent book, *The Magnesium Factor*.

A paper by Killilea and Ames suggests that magnesium deficiency speeds the aging process of cells which they believe could explain how magnesium deficiency could contribute to age-related diseases.

Chlorophyll, which is responsible for the green color of plants, is a magnesium molecule. Increasing intake of dark greens, whole grains, and fish improves magnesium status.

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VITAMIN B12

Deficiency of vitamin B12 and elevated levels of homocysteine have been suggested as causative or contributory factors to migraine. Hydroxycobalamin, a form of vitamin B12, was used in a trial by Van der Kuy and associates in a migraine trial. This form of vitamin B12 is an efficient antagonist to nitric oxide which may be involved in migraine. Kuy reported that 53% of the 19 patients tested had a decrease in frequency of

migraine attack of about 50%.

One of the supports for the fact that vitamin B12 may be helpful for migraine is the association of the condition with a genetic variation called MTHFR. The variation is associated with accumulation of homocysteine which can often be reduced by nutrients such as vitamins B6, B12 and folic acid. One six month trial of these vitamins found that they reduced migraine disability considerably.

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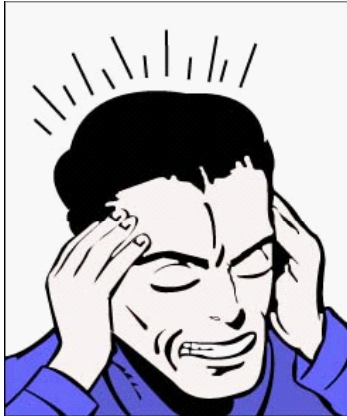
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COENZYME Q10 AND RIBOFLAVIN

One theory of migraine is that it is associated with faulty functioning of the mitochondria where energy is produced in the cell. Based on this theory Rozen and associates supplemented migraine sufferers with 150 mg per day of Coenzyme Q10. After 3 months there was a 50% reduction in the number of days with migraine headache.

Another nutrient involved in the





production of energy by the mitochondria is vitamin B2 or riboflavin. Schoenen and associates compared a 400 mg dose of riboflavin with a placebo. The number of patients who improved by at least 50% was 59% in the riboflavin group and 15% in the placebo group. Maximum efficacy of vitamin B2 is reached only after two to three months of intake of the vitamin. Side effects were minimal with about 1 percent of patients experiencing gastric intolerance. Schoenen suggested that magnesium and vitamin B3 could also improve functioning of the mitochondria. I have seen recurrent headaches disappear with regular supplementation with vitamin B complex and chelated calcium-magnesium.

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ESSENTIAL FATTY ACIDS

In one 6 month trial migraine patients were given a combination of nutrients including alpha-linolenic acid (linseed oil), gamma linolenic acid (evening primrose oil), vitamins B3 B6, C, E and beta-carotene. The study looked at 128 patients and 86% saw a reduction in severity, frequency and duration of migraine, while 22%

became free of migraine. More than 90% of the patients had reduction of nausea and vomiting.

The vitamins used in this study are essential as coenzymes in fat metabolism while the antioxidants were utilized to stabilize the fats being supplemented which are prone to oxidation.

A key component of this program developed by Wolfgang Wagner was maintaining a diet high in carbohydrate and low in protein. The ratio was 5 or 6 parts carbohydrate to one part protein. This high carbohydrate intake optimizes serotonin function.

Wagner utilized linseed oil as a source of omega-3 fatty acids, but fish oils have also been used. In one placebo controlled trial by McCarren patients on fish oil were either headache free or had only mild headaches 49% of the 6 week trial, while the placebo group was free of severe headache only 19% of the time. Wagner's shotgun approach makes sense as nutrients have synergistic effects and the use of a variety of beneficial nutrients is likely to be more effective than a single nutrient.

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MAST CELLS AND MIGRAINE

Most people are unfamiliar with the mast cells. Mast cells are part of the immune system. They contain many granules of histamine and heparin.

Mast cells were first described by Paul Ehrlich in a 1878 doctoral thesis. He named the cells from the German word Mast which means "fattening" as he was of the belief that the large granules in the cells nourished sur-

rounding cells.

The granules in the mast cells contain heparin and histamine. Heparin is an anticoagulant. Heparin is used medically for anticoagulation, especially on test tubes and renal dialysis machines. Strangely, heparin is released at sites of tissue injury and does not appear to act as an anticoagulant, but as a defense against invading bacteria.

Histamine regulates the sleep-wake cycle and the release of hydrochloric acid in the stomach. Histamine is also involved in local immune inflammatory responses. Histamine acts as a neurotransmitter in the brain. Histamine is released in the process of allergic responses and may play a role in migraine.

Mast cells are very similar to white blood cells and can be activated by immune mechanisms. They are involved with anaphylactic shock and allergy responses. Uncontrolled accumulation and activation of mast cells is associated with rheumatoid arthritis, atherosclerosis, multiple sclerosis, asthma, and allergic rhinitis.

Research by Levy and associates published in 2007 was the first to demonstrate activity of mast cells and activation of a pain pathway which underlies migraine headache. This research has begun pharmaceutical firms on a hunt for drugs that can block this biochemical pathway.

Natural alternatives exist. The vitamin E complex has been shown to modulate the activity of the mast cells. Tocotrienols in particular have the ability to inhibit release of histamine. This vitamin can actually alter gene expression of mast cells and is





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worth a trial in mast cell associated disorders including migraine. Akhteh goes so far as to say, “vitamin E has a stabilizing effect of the hyperactivity of mast cells.”

Vitamin D3 has also been shown to inhibit the release of histamine by the mast cells in both human and animal cells.

Flavonoids are also being examined as potential agents to down-regulate the activity of mast cells. One research paper concluded, “The pharmacological actions of these flavonoids (fisetin, kaempferol, myricetin, quercetin, and rutin) suggest their potential activity for treatment of allergic inflammatory diseases through the down-regulation of mast cell activation.”

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MELATONIN

Perez and associates studied the use of melatonin in 32 migraine patients. The patients were given 3 mg. of melatonin 30 minutes before bedtime. Twenty-five of the patients had at least a 50% reduction in incidence of migraine. Of these patients, 25% had complete remission while 21.8% of patients had a greater than 75% reduction and 31.3% had a 50-75 % reduction after 3 months.

Since melatonin is produced during sleep when the room is dark, paying attention to sleep hygiene might also be expected to improve migraine.

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CONCLUSION

There is a good deal of evidence that a number of the nutrients discussed in this paper interact with one another. For example, magnesium, riboflavin, and coenzyme Q10 all im-

prove mitochondrial function. It is entirely possible that using a combination of nutrients will produce greater improvement than the attempt to use isolated nutrients following the pharmaceutical model.

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