

Combination of Feverfew, Magnesium, and Riboflavin for Migraine Prevention

Reviewed: Maizels M, Blumenfeld A, Burchette R. A combination of riboflavin, magnesium and feverfew for migraine prophylaxis: a randomized trial. *Headache*. 2004;44(9):885-890.

An advertisement in a Canadian trade publication proclaims: "Doctors discover new hope for MIGRAINE sufferers!" The product being promoted, MigraHealth™ (Health Assure, Sunrise, Florida), is a combination of "magnesium, vitamin B2 (riboflavin), and a proprietary feverfew extract, formulated by leading headache experts and neurologists." In the ad it is touted as "Triple Therapy" and the ad suggests that deficiencies in magnesium and riboflavin can trigger migraine attacks.¹

Both magnesium and riboflavin, with excellent safety profiles, have shown promise as migraine prophylactics in controlled trials (see below). Further, an uncontrolled trial found that an intravenous infusion of magnesium sulfate caused prompt and sustained relief in roughly 50% of patients experiencing acute migraine: a significant correlation was noted between response and serum ionized magnesium levels.² While the mechanism of action of magnesium in migraine is not clearly understood, the metal ion is known to have strong vasodilating effects which may interrupt a vasoconstrictive phase of the migraine process; magnesium also inhibits platelet aggregation in a dose-dependent manner.³

This study reported the results of a randomized, double-blind, placebo-controlled trial (RCT) of a combination formulation, the daily dose of which provided 400 mg riboflavin, 300 mg magnesium, and 100 mg of a proprietary feverfew extract; the "placebo" contained 25 mg riboflavin. This product has the same combination of ingredients as the advertised MigraHealth™ and gives no indication as to the manner of preparation of the feverfew extract. (It is interesting to note that of the three trials of extracts of feverfew leaf, two employed supercritical CO₂ extracts^{4,5} and were successful, whereas an extract produced from protracted extraction [19 days] with 90% ethanol was unsuccessful in migraine prophylaxis.⁶)

The results of this recent RCT are intriguing since the "placebo" response exceeded that reported for any other placebo in trials of migraine prophylaxis, suggesting that 25 mg riboflavin was an active comparator. Of the 49 patients who completed the 3-month trial, there was no significant difference noted between verum (the feverfew combination) and "placebo" groups. For the primary



Feverfew *Tanacetum parthenium*. Photo © 2005 stevenfoster.com

outcome measure, a 50% or greater reduction in migraines was achieved by 10 (42%) and 11 (44%) subjects, respectively. There was also no significant difference between the 2 groups respecting the secondary outcome measures of 50% or greater reduction in migraine days or change in mean number of migraines, migraine index, or triptan doses, being 33% and 40%, respectively. There is a clear indication from these observations that 400 mg riboflavin daily is no better than 25 mg, and that magnesium and this feverfew extract made no perceptible contribution to the anti-migraine effect of the tested formulation. The single positive RCT so far conducted with riboflavin involved a daily dose of 400 mg.⁷ This further suggests that the feverfew extract may not have been properly prepared, since there was no enhancement of prophylactic effect by addition of the extract.

Regarding magnesium, oral supplementation has been found effective in 2 of 3 RCTs. In a trial of 24 women with menstrual migraine,⁸ subjects received magnesium pyrrolidone carboxylic acid 3 times daily (equivalent to 360 mg magnesium ion daily) or placebo from the 15th day of their cycle until menses. The women taking the magnesium supplement experienced significantly less pain and reduced number of days with headache than the placebo group. In the second positive study, 81 patients, aged 18 to 65 years, received either magnesium (600 mg trimagnesium dicitrate daily) or placebo for 12 weeks.⁹ The frequency of migraine attacks was reduced by 42% and 16%, respectively, while the number of days with migraine was significantly reduced only in the treated group. The third trial of 69 subjects showed no benefit from a daily dose of 500 mg magnesium over placebo for 12 weeks.¹⁰

Based on the trials summarized above, it seems possible that the amount of magnesium in the feverfew combination product (360 mg/day) was not sufficiently large to exert a prophylactic effect. The reason for the failure of the third magnesium trial¹⁰ (500 mg/day) is not apparent.

ACHS.edu
AUSTRALASIAN COLLEGE OF HEALTH SCIENCES

Australasian College of Health Sciences is a respected and renowned industry leader in natural health education, providing comprehensive career focused programs since 1978. Your success is our reputation.

Call Today 800.487.8839

DANTES Affiliated • GI & VA Approved • Accredited Member DETC

A fundamental problem in the trial of combination products is that trials of such products are often conducted without the activity of all constituents having been established individually. It appears that the specific feverfew extract employed in this recent trial had not been clinically tested to determine its efficacy. So far there have been three positive trials recorded that use encapsulated dried feverfew leaf of a parthenolide-dominant sesquiterpene lactone chemotype; however, it is quite evident that parthenolide is not a direct appreciable anti-migraine principle,¹¹ though conspicuously still regarded in some quarters as the main feverfew active in that respect. 🌿

– Dennis V.C. Awang, PhD, FCIC
MediPlant Consulting Inc., White Rock, Canada

References

1. Advertisement Supplement, *The Vancouver Sun*, November 6, 2004.
2. Mauskop A, Altura BT, Cracco RQ, Attura BM. Intravenous magnesium soleplate relieves migraine attacks in patients with low serum ionized magnesium levels: a pilot study. *Clin Sci (Lond)*. 1995; 89(6):663-666.
3. Fugh-Berman A. Dietary supplements for migraine: magnesium and riboflavin. *Alternative Therapies in Women's Health*. 1999;1(3):17-19.
4. Pfaffenrath V, Diener HC, Fischer M, Friede M, Henneicke-von Zepelin HH. The efficacy and safety of *Tanacetum parthenium* (feverfew) in migraine prophylaxis – a double-blind, multicentre, randomized placebo-controlled dose-response study. *Cephalalgia*. 2002;22:523-532.
5. Diener HC, Pfaffenrath J, Schnitker J, Friede M, Henneicke-von Zepelin H-H. Efficacy and safety of 6.25 mg tid feverfew-CO₂-extract (MIG-99) in migraine prevention – A randomized, double-

- blind, multicentre, placebo-controlled study. *Cephalalgia*. In press.
6. de Weerd CJ, Bootsma HPR, Hendriks H. Randomized double-blind placebo-controlled trial of a feverfew preparation. *Phytotherapy*. 1996;3(3):225-230.
7. Schoenen J, Jacquy J, Lenaerts M. Effectiveness of high-dose riboflavin in migraine prophylaxis. *Neurology*. 1998;50:466-470.
8. Facchinetti F, Sances G, Norella P, Gennazzani AR, Nappi G. Magnesium prophylaxis of menstrual migraine. Effects on intracellular magnesium. *Headache*. 1991;31:298-301.
9. Peikert A, Wilimzig C, Kohne-Volland R. Prophylaxis of migraine with oral magnesium. Results from a prospective, multi-center, placebo-controlled and double-blind randomized study. *Cephalalgia*. 1996;16:257-263.
10. Pfaffenrath V, Wesseley P, Meyer C, Isler HR, Evers S, Grottemeyer KH, et al. Magnesium in the prophylaxis of migraine – a double-blind, placebo-controlled study. *Cephalalgia*. 1996;6:436-440.
11. Awang DVC. Prescribing therapeutic feverfew [*Tanacetum parthenium* (L.) Schultz Bip., syn. *Chrysanthemum parthenium* (L.) Bernh.]. *Integrative Medicine*. 1998;1(1):11-13.

HerbClip™

The preceding Research Reviews are drawn from more than 2,500 HerbClip critical reviews available online to members of ABC at the Academic level and above. The full HerbClip Educational Mailing Service is distributed bimonthly and includes 12 critical reviews along with many of the original articles drawn from a variety of professional and mainstream sources. To receive the full service, contact Wayne Silverman, PhD, at 512/926-4900 ext. 120, or via email at <wayne@herbalgram.org>.



.....
S T E V E N F O S T E R G R O U P , I N C .



Featured in HerbalGram for over a decade, the photographs of Steven Foster are available for licensing for editorial or commercial projects.

Specializing in medicinal and aromatic plants,
our stock photo files include more than 70,000 images,
including most major herbs sold as dietary supplements.



CONTACT

Steven Foster Group, Inc.
Steven Foster, President
P.O. Box 57, Brixey, MO 65618
417/261-2663 fax 417/841-4843
email: sfoster@stevenfoster.com www.stevenfoster.com

C O M E T O T H E S O U R C E
.....



Copyright of HerbalGram is the property of American Botanical Council and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.