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ALTERNATIVE THERAPIES IN WOMEN'S HEALTH

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Dietary Supplements for Migraine: Magnesium and Riboflavin

By Adriane Fugh-Berman, MD

MIGRAINES ARE TWICE AS COMMON IN WOMEN THAN MEN. SEVERAL trials indicate that two dietary supplements—magnesium and riboflavin—have excellent safety profiles and may be promising in the prophylaxis of migraines.

Magnesium

Magnesium is an essential mineral necessary for the function of many enzymes; it is essential for all reactions using ATP and is vital to each step involved in DNA replication and transcription and mRNA translation.[1] It's the fourth most common cation in the body.

Few women obtain adequate magnesium from the diet. Estimates from NHANES III (1988-91) indicate that magnesium intake was lower than the RDI in males and females ages 12-60 in all racial and ethnic groups of adults (with the single exception of non-Hispanic white males).[2] Magnesium deficiency is quite common, at least among inpatients: 65% of those in intensive care, up to 12% on general wards, and 30% of hospitalized alcoholics have hypomagnesemia.[1]

Role in Headaches of Vascular Origin

Prevention of migraine with oral magnesium supplementation has been shown effective in two of three double-blind trials of migraine. One open-pilot study showed significant relief of acute migraine pain with intravenous magnesium.

Prevention of Menstrual Migraine

In one trial of 24 women with menstrual migraine,[3] women received magnesium (360 mg magnesium pyrrolidine carboxylic acid tid—equivalent to 360 mg magnesium ion daily) or placebo from the 15th day of their cycle until menses. During this phase of the trial, both groups reported reduction in pain total index (a measure of both frequency and intensity of attacks). Women receiving magnesium had significantly less pain than the placebo group, and the number of days with headache decreased only in the magnesium

INSIDE

group. After two months the trial became an open-label trial in which magnesium was given to all patients for an additional two months. Significant decreases in pain total index were seen in both groups between the second and fourth months.

It does not appear that subjects in this trial were routinely asked about side effects, but it is noted that two of the four dropouts were due to side effects; one patient in the magnesium group reported diarrhea and one in the placebo group reported continuous headache.

Prevention of Migraine

In the second positive study, 81 migraine patients aged 18-65, with a mean migraine frequency rate of 3.6/month, received either magnesium (24 mmol or 600 mg trimagnesium dicitrate qd) or placebo for 12 weeks.[4] In weeks 9-12 frequency of migraine attacks was reduced by 41.6% in the magnesium group, compared with 15.8% in the placebo group. The number of days with migraine was also significantly decreased in the magnesium group; there was no significant change in the duration or intensity of migraine attacks, nor in drug consumption during an attack. Diarrhea was reported in 18.6% and gastric irritation in 4.7% of patients receiving magnesium.

A third placebo-controlled, double-blind trial of 69 subjects with migraine showed no benefit of magnesium over placebo on migraine.[5] Patients were treated with magnesium 10 mmol bid (equivalent to a daily dose of 500 mg) or placebo for 12 weeks, and the endpoints were reduction of migraine intensity or duration by at least 50%.

This trial, originally designed to enroll 150 patients, was stopped after interim analysis of 69 patients showed no benefit of magnesium. An equivalent number of patients experienced reduction of migraine intensity or duration (28.6% of those receiving magnesium and 29.4% of those receiving placebo). Mild adverse effects were experienced by 45.7% of those receiving magnesium and 23.5% of those on placebo; diarrhea or soft stool was the most common complaint in the magnesium group.

It would have been preferable for the investigators to allow this trial to progress to completion. It is quite possible that this trial had an unusually high number of placebo responders, and that the situation would have straightened itself out with increased enrollment. Trials are usually stopped at interim analysis only when there is such a large difference in either benefit or risk between the groups that it is deemed unethical to continue in the face of what is known at that point. It's peculiar to stop a trial at interim analysis simply because the treatment isn't winning, and results are not statistically significant.

Treatment of Acute Migraine

An uncontrolled trial that found that intravenous infusion of magnesium sulfate caused prompt and sustained relief in 21/40 patients with acute migraine. A significant correlation was found between response and serum ionized magnesium levels. Of the 21 patients with serum IMG++ levels above 0.54 mmol/L, 86% had sustained (more than 24-hour) relief of pain and associated symptoms.[6]

Mechanism

The conventional view of migraine is that vascular spasm causes neurological symptoms and subsequent vasodilation causes headache and tenderness. There is debate about the etiology and pathogenesis of migraine. One theory concerns the fact that platelets aggregate during a migraine attack, and subsequently release serotonin (5-hydroxytryptamine or 5HT), a potent vasoconstrictor of cerebral arteries (this is why sumatriptan and other serotonin receptor antagonists are thought to be effective). Although the exact mechanism of magnesium's effects is unclear, it may interrupt the process at the vasoconstriction stage; magnesium has strong vasodilating effects and also inhibits platelet aggregation in a dose-dependent manner.[6]

Adverse Effects

Too much magnesium causes diarrhea, an effect seen in any trial that collected this data. The risk of hypermagnesemia is pronounced in renal patients.

Laboratory Testing

Serum magnesium levels, however, will not be helpful

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in determining which migraine patients will respond to supplementation; studies are mixed as to whether serum magnesium levels are decreased in migraine patients.

Intracellular levels of magnesium are probably more important than serum levels; it is not uncommon for intracellular levels of magnesium to be decreased while serum levels are normal. In one study of 40 patients with acute migraine attacks,[7] 50% had ionized magnesium levels below 0.54 mmol/L (normal adult IMg++ levels are 0.54-0.65 mmol/L). The authors suggest that total magnesium levels are less important than ionized magnesium.

Differences Among Magnesium Preparations

Various magnesium formulations are available. Although it has been claimed that chelated magnesium diglycinate is better absorbed then other preparations, there is no convincing evidence that this type is superior to magnesium oxide, magnesium chloride, or magnesium gluconate. Inorganic forms (magnesium oxide, magnesium chloride) may be more likely to cause diarrhea than organic forms (magnesium citrate, magnesium aspartate), but diarrhea can occur with any preparation.

Riboflavin (B_2)

Riboflavin, a water-soluble B vitamin, is an enzyme cofactor necessary to the production of ATP. Although gross riboflavin deficiency is very rare in Western countries, marginal deficiency is relatively frequent, especially among the elderly and adolescents.

A randomized, placebo-controlled, three-month trial in 55 patients with migraine found that high-dose riboflavin (400 mg/d) was superior to placebo in reducing attack frequency and headache days.[8] The proportion of patients who improved by at least 50% was 59% in the riboflavin group and 15% in the placebo group. Two of three patients who reported mild adverse effects (polyuria and diarrhea) were in the treatment group.

A previous open-label pilot study by the same investigators compared 26 patients who received 400 mg riboflavin daily for three months with 23 patients who received both riboflavin and low-dose (75 mg) aspirin.[9] Mean global improvement was 68.2% and there were no significant differences between the groups. One patient in the riboflavin with aspirin group withdrew due to gastric intolerance; otherwise no adverse effects were reported.

The dose of riboflavin used in these trials is quite high, especially given that the RDI for females 11-50 is 1.3 mg. However, riboflavin is extraordinarily benign. In dogs, 2 g/kg po causes no ill effects. Researchers have established a lethal dose for rats only by giving doses inconsistent with reason; the LD50 (a lethal dose for 50% of rats tested) is 560 g/kg, intraperitoneally.[10] It seems safe to assume that pouring half of a rat's body weight of anything into its peritoneum would kill it.

Conclusions

Magnesium may be effective for preventing both menstrual and non-menstrual migraine. High doses of riboflavin also may be helpful in migraine prophylaxis. Although clinical trial evidence is limited, both nutrients have low toxicity profiles and may be worth trying in patients with migraine. ❖

References

1. Weisinger JR, Bellorin-Font E. Magnesium and phosphorus. *Lancet* 1998;352:391-396.
2. Shils ME. Magnesium. In: Shils ME, et al., eds. *Modern Nutrition in Health and Disease*, 9th ed. Baltimore, MD: Lippincott, Williams & Wilkins; 1999:177.
3. Facchinetti F, et al. Magnesium prophylaxis of menstrual migraine: Effects on intracellular magnesium. *Headache* 1991;31:298-301.
4. Peikert A, et al. Prophylaxis of migraine with oral magnesium: Results from a prospective, multi-center, placebo-controlled and double-blind randomized study. *Cephalalgia* 1996;16:257-263.
5. Pfaffenrath V, et al. Magnesium in the prophylaxis of migraine—a double-blind, placebo-controlled study. *Cephalalgia* 1996;16:436-440.
6. Mauskop A, et al. Intravenous magnesium sulphate relieves migraine attacks in patients with low serum ionized magnesium levels: A pilot study. *Clin Sci (Colch)* 1995;89:633-636.
7. Mauskop A, Altura BM. Magnesium for migraine: Rationale for use and therapeutic potential. *CNS Drugs* 1998;9:185-190.
8. Schoenen J, et al. Effectiveness of high-dose riboflavin in migraine prophylaxis. *Neurology* 1998;50:466-470.
9. Schoenen J, et al. High-dose riboflavin as a prophylactic treatment of migraine: Results of an open pilot study. *Cephalalgia* 1994;14:328-329.
10. Linder MC. *Nutritional Biochemistry and Metabolism*. 2nd ed. Norwalk, CT: Appleton and Lange; 1991:117.

Alternative Cancer Therapies: Prevalence and Clinical Trials

Part 1 of a Series

By Adriane Fugh-Berman, MD

SURVEYS ON UNCONVENTIONAL THERAPIES CONSISTENTly find that these therapies are used most often at two ends of the disease spectrum. The most common use is for chronic, bothersome, non-life-threatening conditions

(low back pain, anxiety, headaches). At the other end of the spectrum is its use for life-threatening conditions (including cancer and AIDS) for which conventional medicine may be perceived as insufficient.

This article discusses the prevalence of complementary and alternative medicine use among cancer patients and clinical trials on three alternative cancer therapies: hydrazine sulfate, Livingston-Wheeler therapy, and high-dose vitamin C. Additional therapies and the use of complementary therapies as adjuncts to conventional care will be discussed in a future article.

Prevalence of Use

A telephone survey conducted in 1990[1] found that 24% of patients with "cancer or tumors" used alternative therapies, making cancer one of the top five reasons for using alternative medicine. However, the recent update of this study did not include information on the use of alternative therapies among cancer patients.[2] Most cancer patients using alternative therapies are also receiving conventional treatment. (*See Table 1 for use of unconventional therapies by cancer patients in different countries.*)

An American Cancer Society telephone survey, which queried 5,000 individuals, found that "questionable" cancer methods were used 9% of the time, with a positive correlation between higher income and higher education and questionable therapy use.[3] Interestingly, an article published in 1984 found that 60% of those providing alternative therapies were MDs, PhDs, or both.[4] The other 40% were health care professionals. In 35% of cases, the patients' primary physicians had recommended the treatment method; in 15% of cases the physicians had approved the therapy; in 35% of cases the patients did not tell their primary physicians about the use; and in 2% of cases the therapy was used despite the physicians' opposition.

What do clinical studies of alternative cancer therapies show? There are not many clinical studies; very few of these studies have used survival as an endpoint, and most are problematic.

Table 1

Use of unconventional therapies by cancer patients in different countries

United States	54%
Germany	65%
Austria	59%
Switzerland	52-65%
France	52%

Source: Hauser SP. Unproven methods in cancer treatment. *Curr Opin Oncol* 1993;5:646-654.

Livingston-Wheeler Therapy

One study compared 78 cancer patients who received Livingston-Wheeler therapy (immune-enhancing vaccines, a vegetarian diet, coffee enemas, and injections of the antituberculosis vaccine bCG) with a control group that only received conventional care[5] (some Livingston-Wheeler patients also received concurrent conventional therapy). There was no difference in survival between the two groups, and quality-of-life measures were better among the conventionally treated patients.

Vitamin C

A controlled, double-blind study compared 60 patients who took 10 g of vitamin C daily with 63 patients who took a placebo.[6] There was no difference between the two groups in symptoms, weight, or survival. These were terminal patients with an average survival time of seven weeks. A common criticism of this study is that vitamin C treatment was undertaken too late to do these patients any good.

Hydrazine Sulfate

Hydrazine sulfate, an industrial chemical, is used as an unconventional anti-neoplastic agent and an anti-wasting agent; it is not generally perceived as effective therapy in the United States.

Hydrazine sulfate has Investigational New Drug status in the United States. It may be obtained legally in Canada with a medical prescription from distributors approved by the Health Protection Branch (roughly equivalent to the U.S. FDA) of Health Canada. Neither private nor public insurance in the United States or Canada covers the cost of this treatment.

One positive and two negative controlled trials of lung cancer patients have been conducted. In the positive trial, 65 patients with stage IIIB or IV non-small-cell lung cancer received either hydrazine sulfate or placebo in conjunction with conventional chemotherapy.[7] Median survival for patients with an initial performance status of 0 (asymptomatic) or 1 (symptomatic but ambulatory) was significantly higher in the hydrazine sulfate treated group but not in those with an initial performance status > 2 (significant time in bed). Subjects on hydrazine sulfate ate more and their levels of albumin improved.

In 243 patients with unresectable, non-small cell lung cancer randomized to hydrazine sulfate or placebo in combination with cisplatin and etoposide, disease progression was worse in the hydrazine sulfate group.[8]

There was no significant difference in the groups in terms of median survival time, quality-of-life assessment, weight change, albumin levels, or toxicity.

Two hundred ninety-one patients with IIIB or IV non-small cell lung cancer were randomized to either hydrazine sulfate or placebo for one month in conjunction with conventional chemotherapy.[9] There were no differences in survival, tumor regression, weight gain, or nutritional status between evaluable members of the two groups (dropout rates were >80% in each group).

In a placebo-controlled trial of 128 patients with metastatic colorectal cancer resistant to 5FU, no statistically significant difference was seen in survival, tumor regression, or quality of life.[10] (Admission to this trial was prematurely halted when interim analysis showed decreased survival in the hydrazine sulfate treated group.)

Side effects of hydrazine sulfate include anorexia, dizziness, drowsiness, excitation, impaired motor function, nausea, vomiting, numbness of the extremities, peripheral neuritis, pruritus, seizures, and, at high doses, liver damage.

Positive effects on tumor regression or survival have occurred only in small or poorly controlled trials. Controlled trials done in Russia, and a number of uncontrolled trials, show positive results.[11] Three of four randomized, controlled trials done in the United States have demonstrated no benefit of hydrazine sulfate as a cancer therapy; only one reported increased survival in end-stage lung cancer patients.

Conclusion

Little clinical trial data are available on alternative cancer therapies. Given the popularity of such treatments, it is vital to do more research in this area. ❖

References

1. Eisenberg DM, et al. Unconventional medicine in the United States. *N Engl J Med* 1993;328:246-252.
2. Eisenberg DM, et al. Trends in alternative medicine use in the United States, 1990-1997: Results of a follow-up national survey. *JAMA* 1998;280:1569-1575.
3. Lerner IJ. The physician and cancer quackery. *N Y State J Med* 1993;93:96-100.
4. Cassileth BR, et al. Contemporary unorthodox treatments in cancer medicine. A study of patients, treatments, and practitioners. *Ann Intern Med* 1984;101:105-112.
5. Cassileth BR, et al. Survival and quality of life among patients receiving unproven as compared with conventional cancer therapy. *N Engl J Med* 1991;324: 1180-1185.
6. Creagan ET, et al. Failure of high-dose vitamin C (ascorbic acid) therapy to benefit patients with advanced cancer. A controlled trial. *N Engl J Med* 1979;301:687-690.
7. Chlebowski RT, et al. Hydrazine sulfate influence on nutritional status and survival in non-small-cell lung cancer. *J Clin Oncol* 1990;8:9-15.
8. Loprinzi CL, et al. Placebo-controlled trial of hydrazine sulfate in patients with newly diagnosed non-small-cell lung cancer. *J Clin Oncol* 1994;12:1126-1129.
9. Kosty MP, et al. Cisplatin, vinblastine, and hydrazine sulfate in advanced, non-small-cell lung cancer: A randomized placebo-controlled, double-blind phase III study of the cancer and leukemia group B. *J Clin Oncol* 1994;12:1113-1120.
10. Loprinzi CL, et al. Randomized placebo-controlled evaluation of hydrazine sulfate in patients with advanced colorectal cancer. *J Clin Oncol* 1994;12: 1121-1125.
11. CBCRI Canadian Breast Cancer Research Initiative. *Hydrazine Sulphate: An information package.* Toronto: CBCRI: 1996. Available from Canadian Breast Cancer Research Initiative, Suite 200, 10 Alcorn Avenue, Toronto, Ontario, Canada M4V 3B1.

CME Questions

1. A study of Livingston-Wheeler therapy found that, compared to a group receiving conventional treatment for cancer, patients in the Livingston-Wheeler group had:
a. improved survival.
b. decreased survival.
c. improvement in quality-of-life measures.
d. decline in quality-of-life measures.

2. A cup of green tea contains:
a. 10-20 mg polyphenols.
b. 20-50 mg polyphenols.
c. 50-100 mg polyphenols.
d. 100-200 mg polyphenols.

3. A recent trial of a low-energy diet combined with hydroxycitrate or placebo found that:
a. both groups lost weight.
b. the hydroxycitrate group lost significantly more weight.
c. the placebo group lost significantly more weight.
d. neither group lost weight.

4. According to the NHANES survey, magnesium intake among women in the United States is:
a. low.
b. adequate.
c. high.
d. variable by race and ethnicity.

5. Magnesium has the following effects:
a. vasodilation.
b. decreases platelet aggregation.
c. can cause diarrhea.
d. all of the above.

With Comments from Adriane Fugh-Berman, MD

NuStart™ Women's Breast Health Formula

Label Information

"Stimulates the major cleansing pathways in the body and helps eliminate pollutants and other foreign elements"

"Patented calcium D-glucarate with soy"

"A portion of the NuStart™ proceeds goes to support cancer research" [a picture of a pink ribbon is next to this statement]

"Breast health is the number one concern of women. To date, quality nutritional supplements that address these concerns have been limited. NuStart's Breast Health Formula contains the patented compound Glucarate, which has been shown to enhance the major cleansing pathways in the body. Glucarate nutritionally supports glucuronidation, the process by which the body rids itself of pollutants and foreign elements not conducive to breast health."

"Consult a physician before using if pregnant or nursing."

Suggested Use

As a dietary supplement, take two (2) capsules per day, preferably with a meal.

Supplement Facts

	Amount per serving	*% daily value*
Calcium (as Calcium D-Glucarate)	24 mg	2%
Selenium (as selenomethionine) From SelenoMax™)	100 mcg	140%
Calcium D-Glucarate	200 mg	*
Green Tea Extract (*Camellia sinensis*) (standardized to 48% polyphenols) (leaf)	200 mg	*
Rosemary extract (*Rosmarinus officialis*) (standardized to 6% Rosemaric acid) (folia)	200 mg	*
Soy extract (standardized to 3% isoflavones)	400 mg	*
Citrus bioflavonoids (*Citrus aurantium*) (standardized to 25% bioflavonoids) (peel)	100 mg	*
Boron Aspartate	3 mg	*

*Daily value not established

Other ingredients: White rice powder

(NuStart™ Breast Health Formula is a trademark of Great American Nutrition®.) Great American Nutrition®, Salt Lake City, Utah 84104 (another fine brand of Weider Nutrition International)

Price: $13.49/60 capsules

Analysis of Ingredients

Calcium, 24 mg: This may be the amount of elemental calcium in the "Calcium D-Glucarate 200 mg" that appears further down on the label. This is not very clear; 24 mg is an infinitesimal dose, given that the RDI for women ranges from 800-1200 mg daily.

Selenium (as selenomethionine), 100 mcg: This is a safe supplemental dose of selenium.

Green tea extract (*Camellia sinensis*), 200 mg: This amounts to 96 mg polyphenols from tea. A cup of green tea contains 50-100 mg polyphenols[1] so this is equivalent to a cup or two of tea.

Rosemary extract (*Rosmarinus officinalis*), 200 mg: A reasonable dose of rosemary would be difficult to calculate.

Soy extract (standardized to 3% isoflavones), 400 mg: This is equivalent to 12 mg isoflavones, a very low dose. In Asia, consumption of isoflavones ranges from 25-200 mg/d.[2]

Citrus bioflavonoids (*Citrus aurantium*), 100 mg: This is the bitter orange, also called Seville orange. Although bioflavonoids are important nutrients, doses have not been established.

Boron aspartate, 3 mg: This is a safe supplemental dose of boron; recommended doses have not been established.

Comments

This labeling—and the prominently displayed picture of the pink ribbon, symbol of the breast cancer movement—is clearly intended to imply that this formulation prevents breast cancer. There is scant evidence to support this claim with any of the ingredients in the listed doses.

The trumpeting of "patented calcium D-glucarate" to "nutritionally support glucuronidation" is apparently a reference to glucuronide conjugation, a biotransformation process that inactivates many drugs. It is not clear what the manufacturers are trying to claim here.

Although there is evidence supporting a link between intake of the antioxidant selenium and reduced risk of

gastrointestinal, lung, and prostate cancers, data to date have not supported a role for selenium in reducing breast cancer risk.[3]

Epidemiologic studies on green tea are equivocal but there is some evidence to support a reduction in gastrointestinal (not breast) cancers among tea drinkers.[4] Polyphenolic flavonoids in tea decrease the risk of lung, gastrointestinal, and skin cancers in animals; evidence of chemoprevention of mammary tumors is not conclusive. A recent study found that tea partially blocked the promotion of DMBA-induced mammary tumors in rats fed a high-fat diet.[5] No consistent effect was seen in rats fed a normal diet. There are no clinical trials of green tea extract and breast (or any other) cancer risk.

Rosemary contains some interesting compounds, some of which have reduced chemically-induced mammary carcinogenesis in rats.[6] There are no clinical trials of rosemary extract and breast (or any other) cancer risk. Both the botanical name, *Rosmarinus officinalis L.*, and rosmarinic acid are misspelled on the label.

While a high intake of soy isoflavones reduces endogenous estrogen levels in premenopausal women (see *Alternative Therapies in Women's Health*, January 1999, pp.12-14), this dose is too low to have any effect.

Some flavonoids in citrus may have cancer protective effects. However, it is the terpene D-limonene (found in citrus oils), not a bioflavonoid, for which there are animal data showing a beneficial effect on mammary cancers at a very high dietary intake.[7] In any case there are no human data on D-limonene or citrus bioflavonoids and breast cancer risk. There is no evidence for an anticancer effect of boron.

Conclusion

Although this supplement does not claim specifically to prevent breast cancer, that is clearly implied on the label. Not one of its ingredients has been tested for treatment or prevention of breast cancer in a clinical trial. The manufacturers have apparently overinterpreted data about health benefits based on preliminary clues from animal research and epidemiological research. ❖

References

1. Luo M, et al. Inhibition of LDL oxidation by green tea extract. *Lancet* 1997;349:360-361.
2. Knight DC, Eden JA. A review of the clinical effects of phytoestrogens. *Obstet Gynecol* 1996;87:897-904.
3. Giovannucci E. Selenium and risk of prostate cancer. *Lancet* 1998;352:755-756.
4. Dreosti IE. Bioactive ingredients: Antioxidants and polyphenols in tea. *Nutr Rev* 1996;54:S51-S58.
5. Rogers AE, et al. Black tea and mammary gland carcinogenesis by 7,12-DMBA in rats fed control or high fat diets. *Carcinogenesis* 1998;19:1269-1273.
6. Singletary K, et al. Inhibition by rosemary and carnosol of 7,12-DMBA-induced rat mammary tumorigenesis and in vivo DMBA-DNA adduct formation. *Cancer Lett* 1996;104:43-48.
7. Haag JD, et al. Limonene-induced regression of mammary carcinomas. *Cancer Res* 1992;52:4021-4026.

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Clinical Abstracts

With Comments from Adriane Fugh-Berman, MD

Acupuncture Point Stimulation Turns Breech Babies

Source: Cardini F, Weixin H. Moxibustion for correction of breech presentation: A randomized controlled trial. *JAMA* 1998;280:1580-1584.

Design and Setting: Randomized, controlled, open clinical trial in outpatient obstetrics departments of three hospitals in the People's Republic of China.

Subjects: 260 primigravidas in the 33rd week of gestation with ultrasound diagnoses of breech presentation.

Treatment: Heat stimulation of acupuncture point BL 67 (Zhiyin, beside the outer corner of the fifth toenail) by moxibustion (smoldering mugwort, an herb). The control group received routine care. All subjects were offered external cephalic version after two weeks.

Dose/Route/Duration: One treatment daily for seven days, followed by an additional seven days of treatment if breech presentation persisted.

Outcome Measures: Fetal movement counted by the mother during one hour each day for a week; number of cephalic presentations at 35 weeks and at delivery.

Results: The intervention group experienced a mean of 48.45 fetal movements

vs. 35.35 in the control group. By the 35th week, 98/130 fetuses (75.4%) in the intervention group were cephalic vs. 62/130 fetuses (47.7%) in the control group. Although 24 subjects in the control group (19 successfully) and one in the moxibustion group (unsuccessfully) received external cephalic version, at birth 98/130 fetuses (75.4%) in the moxibustion group were cephalic, compared to 81/130 fetuses (62.3%) in the control group.

Funding: Centro di Orientamento Educativo, Milan, Italy (a non-governmental, non-profit organization for cooperation) and the Commission des Communauts Europtennes, Brussels, Belgium.

Comments: Several trials have claimed some success with moxibustion version, but this is the first large, randomized, decently designed prospective study to test this intervention. The results support the use of the technique.

There are very few conditions that can be treated by acupuncture point stimulation at a single point; nausea and vomiting (see *Alternative Therapies in Women's Health*, January 1999, pp. 9-11) and the turning of breech babies are exceptions.

A particularly nice thing about this intervention is its low cost and simplicity. The first application of moxa was done in the clinic, but after an instruction session the woman or her partner performed the rest of the treatments at home.

It is very unlikely that a trial performed in another country would affect clinical practice in the United States, but this trial should definitely be repeated. If the results are replicated, it would have the potential to prevent many cesareans and could be an easy intervention to incorporate into clinical practice. ❖

Herb Garcinia Ineffective for Weight Loss

Source: Heymsfield SB, et al. *Garcinia cambogia* (hydroxycitric acid) as a potential antiobesity agent: A randomized controlled trial. *JAMA* 1998;280: 1596-1600.

Design and setting: Twelve-week randomized, double-blind, placebo-controlled trial in an outpatient weight control research unit in New York.

Subjects: 135 overweight men and women ages 18-65; mean BMI 32 kg/m^2.

Treatment: Hydroxycitric acid (purported active ingredient in *Garcinia cambogia*) vs. placebo. Both groups were prescribed a high-fiber, low-energy diet (5040 kJ/d with 20% fat, 50% carbohydrate, and 30% protein).

Dose/Route/Duration: Two 500 mg caplets po tid taken 30 minutes before meals for 12 weeks. Total daily dose was 3000 mg herb containing 1500 mg hydroxycitric acid.

Outcome Measures: Body weight change and fat mass change.

Results: Patients in both groups lost weight, but there were no significant differences between the two groups. Reported adverse events were minor and not significantly different between the two groups.

Funding: NIH grants RR00645 and P30DK26687 and contract with Thompson Medical Company, manufacturer of products that include *Garcinia*.

Comments: Hydroxycitrate inhibits fatty acid synthesis, so there is a theoretical basis for possible efficacy, but this study demonstrates that *Garcinia* adds no benefit to a conventional weight loss plan. The authors note that their trial is longer than seven previous trials (all of which were four to eight weeks long, and five of which claimed a positive result for *Garcinia*). Additional comments on previous trials included the fact that five trials were not published in peer-reviewed journals and that five trials administered *Garcinia* with other potentially active ingredients, including chromium, caffeine, and L-carnitine.

This trial may be better than previously published trials, but limitations still exist, including lack of monitoring of diet compliance. Of most concern is the fact that only 62% of the subjects completed the trial. Although the dropouts appeared evenly divided between the two groups, inadequate information is provided about drop-outs—for 36 patients (27%) it is noted only that they were "lost to follow-up." In a long-term trial this may be more acceptable but that's a lot of patients to disappear in a three-month trial.

All trials performed to date appear to have included a low-calorie diet; this is perhaps not an ideal circumstance in which to test a product that decreases lipid synthesis. It would be interesting to study if *Garcinia* has any effect when given to people who have not changed their diets. ❖

In Future Issues:

Chocolate Addiction

Massage for Lymphedema

Magnetic Therapy and Depression

Dangers of Asian Medicines