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Did You Remember to Take Your Ginkgo?

ABSTRACT & COMMENTARY

Synopsis: *When taken at its recommended dose, ginkgo does not improve the memory of healthy elders.*

Source: Solomon PR, et al. *JAMA.* 2002;288:835-840.

To evaluate the efficacy of ginkgo for memory enhancement, Solomon and colleagues from New England recruited healthy volunteers by way of newspaper advertisements that asked for volunteers for a study of memory improvement. To be included, the volunteer had to be living in the community, be older than age 60, be able to give informed consent, have a companion with whom they had regular contact, be willing to complete a questionnaire, and score greater than 26 on the Mini-Mental State Examination (MMSE). Subjects were excluded if they had a history of psychiatric or neurologic disease, a life-threatening illness within the last 5 years, or ingestion of an antidepressant or other psychoactive medication within the last 60 days. From July 1996 to September 1998, they screened 338 potential participants. After exclusion, 230 were randomized to ginkgo (Ginkoba®) 40 mg 3 times a day with meals (the manufacturer's recommended dose) or to placebo. The randomization was double blinded. The subjects ranged in age from 60 to 82 years. The 2 groups were similar in age (about 69 years), gender (about 45% male), education (about 14 years), and MMSE score (just short of 29 out of 30). All were independent in instrumental activities of daily living. Immediately before starting the study, and again at 6 weeks, they took 14 standardized tests of learning, memory, attention and concentration, expressive language, and mental status along with a self-assessment of memory. Additionally, at the 6-week mark, the companion completed a global evaluation of the subject that provided "an overall impression of change in memory." Compliance with the study design was monitored by biweekly telephone calls and return of the drug envelopes at the end of the study. Analysis was by modified intention-to-treat (those who received at least 1 dose of ginkgo) and the fully evaluable population (those who completed the study and took all the drug). Both analyses failed to show a

VOLUME 24 • NUMBER 18 • SEPTEMBER 29, 2002 • PAGES 137-144

significant difference in any test between the study group and the control group. Both groups performed better at the 6-week evaluation than the initial one, which Solomon et al attribute to a practice effect.

COMMENT BY ALLAN WILKE, MD

Ginkgo biloba (or Maidenhair tree) has been around forever, its roots (pun intended) in prehistoric times. I think that has something to do with its cachet; anything that could have survived unchanged since the Permian period must have something going for it! The word ginkgo is derived from its Chinese name *yin kuo* (silver fruit). It is a staple of Chinese medicine and has been used by millions for hundreds of years. With that kind of record, you would think that any benefit or hazard would be well known by now. The active ingredients are thought to be flavonoid glycosides and ginkgolides (a type of diterpines). It is a potent inhibitor of platelet activating factor and has antioxidant properties. Ginkgo is touted to treat a wide variety of ills, including acute mountain sickness,[1] schizophrenia,[2] female sexual dysfunction,[3] intermittent claudication,[4] dementia,[5] ocular blood flow,[6] equilibrium disorders,[7] premenstrual syndrome,[8] and Alzheimer disease.[9] The aphorism, "if it seems too good to be true, then it probably is not," apparently applies to ginkgo's ability to enhance memory in healthy, nondemented adults.

This study had limitations. Adverse effects were not monitored, although no one dropped out of the study because of adverse effects. In past reports, ginkgo has been regarded as benign with bleeding, mild gastrointestinal upset, dizziness, palpitations, allergic skin rashes, and headache being the most common complaints. There were no power calculations; a larger study might reveal a difference between the study and control groups. Perhaps this was not the right product, and there exists a more efficacious formulation. It will probably be argued that the length of treatment was too short or the dose was not high enough. However, the manufacturer recommends a dose of 120 mg/d and states that, "Our clinical research indicates that with at least 4 weeks of uninterrupted use of Ginkoba®, consumers can begin to enjoy its many benefits-including improvements in mental sharpness and focus." (This and other product statements can be found at www.ginkoba.com.)

What should you advise your patients who ask if they should purchase Ginkoba®? As with any decision, they should weigh the benefits and risks. Ginkgo has a number of potential benefits as mentioned above, although short-term memory enhancement does not appear to be one of them. My local Rite Aid Pharmacy sells a 72-tablet (24-day supply—curiously, a few days short of the recommended 4 weeks) for $18.99. A 4-week trial, assuming the bleeding, GI upset, headache, etc. are tolerable, seems innocuous enough and not terribly expensive. If your patient has any bleeding tendencies, including use of warfarin or aspirin, you should caution against its use, and, of course, use by a pregnant patient should be avoided. ■

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A New Use for an Old Drug

ABSTRACT & COMMENTARY

Synopsis: *Nortriptyline significantly increased smoking cessation rates compared with placebo.*

Source: da Costa CL, et al. *Chest.* 2002;122:403-408.

This was a straightforward, randomized, prospective, placebo-controlled study. One hundred forty-four patients recruited from a "Smokers' Support Group" in a cancer hospital in Sao Paulo, Brazil, completed the study. After screening, patients were randomized to receive either Nortriptyline (Pamelor) or placebo daily for 6 weeks. The dose was begun at 1 tablet, and increased to 3 tablets by the end of the study period (75 mg/d of nortriptyline). It is important to note that patients also received weekly group support therapy conducted by a psychiatrist. Smoking cessation was defined as stopping smoking for at least a week at the end of the treatment period. Phone calls 3 months and 6 months after termination of the study were also done to determine continued abstinence rates.

At the end of 6 weeks, 32% of those who received placebo and 68% of those who received nortriptyline reported stopping smoking. At 6 months, 20.6% of the nortriptyline and 5.3% of the placebo group reported continued abstinence. There were no differences in rates of side effects, the most common of which were dry mouth, constipation, and anxiety. Of possible univariate predictors of cessation, including age, years smoking, age of smoking onset, cigarettes/d, previous quit attempts, and Fagerstrom score, only Fagerstrom score (> 7) predicted reduced likelihood of quitting.

COMMENT BY BARBARA A. PHILLIPS, MD, MSPH

Nortriptyline has been around a long time, and is a safe and inexpensive drug. As pointed out in the accompanying editorial,[1] this study is the third double-blind placebo-controlled study in the peer-reviewed literature to demonstrate that nortriptyline enhances smoking cessation efforts.[2,3] The quit rates demonstrated here are similar to those reported in the 2 previous reports. Another antidepressant, buproprion, has also been shown to approximately double long-term cessation rates compared to placebo,[4,5] but other antidepressants have not,[6] so the effect seen with nortriptyline and buproprion is probably not simply related to the antidepressant effect.

Smoking cessation is big business. A month's worth of buproprion (Zyban) as marketed for smoking cessation is about $120, and nicotine replacement can range from $55 (for the patch) to $400 (for inhalers) a month. A month's worth of nortriptyline costs about $6. Since most well-studied pharmacologic treatment of nicotine addiction just about doubles the long-term quit rate (from 10-20%), and because patients should and do keep trying, addition of a cheaper tool in our armamentarium against the leading cause of preventable illness in this country is welcome.

Drugs are probably not the "magic bullet" against nicotine addiction, however. An article in *JAMA*[7] reminds us that nicotine replacement therapy, when sold over the counter, appears to lose its long-term effectiveness. Perhaps good old physician advice is an important part of the treatment. ■

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How do Different Insulinotropic Drugs Differ in their Effects on Fasting and Postprandial Insulin Secretion?

ABSTRACT & COMMENTARY

Synopsis: *Glipizide and repaglinide are both effective in lowering the postprandial blood glucose.*

Source: Cozma LS, et al. *Diabetes Care.* 2002;25:1271-1276.

Cozma and colleagues note that "recent prospective studies have attempted to assess the effects of fasting and postprandial hyperglycemia independent of each other." There is increasing evidence that

postprandial glucose levels may contribute more to diabetic complications than fasting levels of glucose.

Cozma et al, therefore, attempted to compare the effects of repaglinide, glipizide, and glibenclamide on insulin secretion and postprandial glucose after a single 500-kcal test meal.

Twelve type 2 diabetics with early diabetes (A1c of 6.1%) and 12 matched control subjects were enrolled in this randomized, double-blind, crossover trial. Subjects received placebo, 2 mg repaglinide, 5 mg glipizide, and 5 mg glibenclamide in a random fashion during the trial. Administration of each drug was followed by a single standard 500-kcal test meal.

All 3 drugs were equally effective on the total prandial insulin secretion. However, clear differences were noted in the early insulin secretion; both repaglinide and glipizide increased secretion in nondiabetic subjects by 61% and 34%, respectively, compared with placebo. In diabetic patients, the difference compared to placebo was 37% and 47%, respectively. The difference between glipizide and glibenclamide reached significance in both groups; whereas repaglinide was more effective only in nondiabetics. All 3 drugs were effective in decreasing total glucose in both diabetics and nondiabetics. In the nondiabetic subjects, however, repaglinide was significantly more effective than glibenclamide. The differences disappeared in the diabetic subjects, probably as a result of increased prevalence of insulin resistance in this group.

Repaglinide and glipizide—but not glibenclamide—significantly enhanced the early insulin secretion in both diabetic and nondiabetic subjects with preserved beta cell function after a single meal.

COMMENT BY RALPH R. HALL, MD, FACP

Another way to state the purpose of this study is: How do the 3 insulinotropic agents used in this study effect the early and late phases of insulin release from the pancreas and how might this effect the postprandial blood glucose level? The importance of the postprandial blood glucose is that it seems to be more closely correlated with arteriosclerotic vascular disease than fasting blood glucose levels,[1] and that the nonfasting blood glucose level is a better marker for diabetic control than the fasting glucose level.[2]

We now have a variety of new insulins and insulinotropic agents to use and it is important to know which one will get the results we desire. However, a question raised by the accompanying editorial is are they worth the extra costs compared with the earlier agents?[3] You and your patient will be the best judges of this question.

As the Cohen and Ramlo-Halsted note, large randomized trials "have shown approximate equivalence for the efficacy between repaglinide and sulfonylureas and slightly lower efficacy for nateglinide in terms of A1c lowering."[3]

To make the best informed decisions about which drug to use we need to do a better job of stratifying our patients in terms of the stage of their type 2 diabetes and perhaps move to insulin therapy earlier in the course of the disease.

We still have to realize that there are no data that prove tight control will reduce the incidence of macrovascular disease.[4] However, there is strong evidence for lowering the A1c to prevent microvascular complications.

If any of these therapies worked as well as weight loss and exercise and for so little cost, there would be large headlines extolling their virtues in *The Wall Street Journal*! ■

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Brief Update

Meningitis and Cochlear Implants

Source: FDA Public Health Notification, July 24, 2002. (www.accessdata.fda.gov.scripts/medwatch)

THE FDA ISSUED A PUBLIC HEALTH ADVISORY IN LATE July regarding a possible association between cochlear implants and bacterial meningitis. Cochlear implants are a novel new technology that allows activation of auditory nerve fibers via electrodes implanted in the inner ear. An estimated 60,000 individuals worldwide have been implanted with the devices. Unfortunately, at least 25 adults and children with the implants, varying in age from 21 months to 63 years, have developed meningitis. Nine persons have died. Infections in several patients were due to pneumococcus (none of these persons were vaccinated to this organism). The basis for the increased risk of infection is not clear, but probably is not a result of contamination of the device. Rather, it is believed that many people who are candidates for the device have sub-chronic or chronic otitis, or congenital

abnormalities that predispose them to middle ear infections—and subsequent meningitis. The device may additionally serve as a nidus of infection in the inner ear.

The FDA is seeking information regarding possible additional cases (Office of Surveillance and Biometrics, e-mail: phann@cdrh.fda.gov). In the meantime, it has been suggested that patients receiving cochlear implants receive prophylactic antibiotics or treatment for middle ear infection prior to surgery. The immunization status of candidates should be evaluated and consideration should be given to vaccination against *S pneumoniae* and *Haemophilus influenzae*. ■

This Brief Update was written by Carol Kemper, MD. Dr. Kemper is Clinical Associate Professor of Medicine, Stanford University, Division of Infectious Diseases, Santa Clara Valley Medical Center, Palo Alto, Calif.

Highlights from the 8th Annual International Alzheimer's Disease Meeting

CONFERENCE COVERAGE

Synopsis: *New information on statins, mild cognitive impairment, and acetylcholinesterase inhibitors was presented.*

Source: *Neurobiol Aging.* 2002;23(1 Suppl):S1-S606.

More than 2000 dementia-related studies were presented at the 8th International Conference on Alzheimer's Disease and Related Disorders (ICADRD), held in Stockholm, Sweden, July 20-25, 2002. Several items of potential interest to neurologists bear mention.

If there were such a title, cholesterol would probably have been voted "Molecule of the Year" at the 2002 ICADRD meeting, based on the sheer number of presentations concerning the cholesterol-lowering statins as a potential means of treating Alzheimer's disease (AD).

Two years ago, 2 retrospective epidemiologic studies suggested that use of statins might reduce the risk of AD as much as 40-79%.[1,2] Two new epidemiologic studies presented at the ICADRD lend further support to this idea. A retrospective study from Boston University carried out on 2378 individuals from Alzheimer-affected families, including 547 African Americans, found reduced risk of AD among statin users regardless of their APOE genotype, race, or the brand of statin prescribed. Another study examined 4740 residents of Cache County, Utah, older than 65 years and found that statin use was associated with a reduced prevalence of dementia but had no statistically significant effect on AD incidence. In addition, use of statins that penetrated the blood brain barrier was associated with less risk reduction than use of agents that did not enter the brain, such as atorvastatin (Lipitor®). This is the first substantive study to find that statin use inversely correlated with the prevalence, but not incidence, of AD, and the first to indicate possible differences among available statins in lowering risk of AD. Other presentations at the ICADRD provided evidence that cholesterol can influence the pathophysiology of AD and suggested mechanisms whereby statins might exert their protective effects. While these developments are encouraging, prospective verification of AD risk reduction by statins has yet to be carried out. However tempting this may seem, it is premature to consider prescribing statins for the sole purpose of preventing or treating dementia until prospective tests are completed.

Another topic that received considerable attention at the ICADRD meeting was the identification of prognostically relevant subgroups among patients with mild cognitive impairment (MCI). Patients with MCI have memory or other cognitive impairments that are greater than most people their age, but are not sufficiently impaired functionally to be considered demented. MCI patients are at increased risk for development of dementia, with an estimated 10-15% progressing to diseases such as AD each year. Several studies have now indicated that the MCI population is heterogeneous, and not all patients with MCI have the same level of risk for developing AD. The emerging consensus is that most patients with MCI will go on to develop dementia within 10 years, but not all will develop AD. It is now recognized that subgroups of MCI patients can be distinguished that have the highest likelihood of developing AD. Unfortunately, there is still a great deal of variability across studies in defining these MCI subtypes. "Amnestic MCI" and "MCI-AD" are 2 such characterizations of MCI patients that attempt to identify a greater likelihood of developing AD based on the characteristics of the cognitive impairments. Definitional issues and the difficulties involved in testing for the relatively subtle cognitive deficits associated with MCI are likely to limit the clinical application of the MCI construct for the time being. Once these issues have been overcome in the future, identification of MCI and its subtypes is likely to become an important part of the strategies used for the early detection and prevention of AD.

Acetylcholinesterase inhibitors were the subject of some discussion at the ICADRD conference. Head-to-head comparisons of the available agents revealed distinc-

tions among donepezil, rivastigmine, and galantamine in terms of their ease of use and tolerability, but less clear differences in their efficacy. Broadened use of these agents in treating other forms of dementia can be anticipated based on the results of studies using galantamine and donepezil in patients with vascular dementia and mixed dementias. The results reported at the ICADRD suggested short-term (6 month) symptomatic benefits in treating patients with vascular dementia. The long-term benefits have yet to be determined, and as yet, none of the cholinesterase inhibitors have received FDA approval for this indication.

Acetylcholinesterase inhibitors are the mainstay of therapy for AD throughout the world, but several new classes of medicines are under development. Among the latter group, the selective NMDA antagonist Memantine shows promise, both in terms of its efficacy in treating severe dementia and its track record of tolerability. Memantine has been approved for treatment of dementia in Germany for over a decade, and it is currently in Phase 3 clinical trials in the United States. The glutaminergic mechanism of action of memantine is distinct from that of other currently approved treatments. At least one study presented at the ICADRD suggested that memantine can be safely administered in combination with acetylcholinesterase inhibitors. Barring unexpected results in ongoing clinical trials, memantine appears to have reasonable prospects for future approval in the United States as a symptomatic treatment for AD. ■

This article was written by Norman R. Relkin, MD, PhD. Dr. Relkin is Associate Professor of Clinical Neurology and Neuroscience, New York Presbyterian Hospital-Cornell Campus, New York, NY.

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Pharmacology Update

Risedronate (Actonel)—A New Weekly Option for Osteoporosis

By William T. Elliott, MD, FACP, and James Chan, PharmD, PhD

RISEDRONATE HAS BEEN APPROVED IN A 35 MG ONCE weekly formulation for the treatment of osteoporosis. The drug is currently available as a 5 mg once daily product, but because the drug requires special precautions when it is taken, the once-a-week form may be more convenient. Alendronate (Fosamax), the other currently available oral bisphosphonate, is also available in a once a day and once a week formulation. Risedronate is marketed as Actonel by Proctor & Gamble and Aventis Pharmaceuticals.

Indications

Risedronate is indicated for the treatment and prevention of osteoporosis in postmenopausal women.

Dosage

Risedronate 35 mg is taken once weekly. It should be taken 30 minutes before the first food or drink of the day other than water. The patient should swallow the tablet with a full glass (6-8 oz) of water while in an upright position. The patient should not lie down for 30 minutes after taking the drug. Calcium, aluminum, or magnesium containing products should not be taken at the same time.[1]

Calcium and vitamin D supplementation is recommended in patients whose dietary intake is inadequate.

Risedronate is supplied as a 35-mg tablet for once-weekly dosing.

Potential Advantages

Risedronate may have better gastrointestinal (GI) tolerance than alendronate.[2,3] Patients who have not tolerated alendronate because of upper GI side effects may tolerate risedronate. In a small, randomized, double-blind study (n = 66) patients who have discontinued alendronate due to upper GI side effects were given risedronate (5 mg daily) or placebo. Discontinuation due to upper GI side effects and the incidence of upper GI events in patients were comparable.[4] A pooled analysis of 9 clinical trials concluded that risedronate 5 mg daily was not associated with a greater frequency of adverse GI events compared to placebo even among patients at high risk.[5] The newly approved strength of risedronate permits once-weekly dosing and may reduce esophageal exposure.

Potential Disadvantages

The oral bioavailability of risedronate and bisphosphonates in general is low (about 1-3%). In addition, bioavailability is reduced by food, cations (such as calcium, aluminum, and magnesium), and liquids other than water. The most common side effects are mild-to-moderate GI events. To reduce upper GI side effects and reduce drug cation interaction, risedronate should

be taken at least 30 minutes before the first food or drink. In addition, the patients should not lie down for 30 minutes after taking the drug. Products containing calcium, aluminum, or magnesium cations should be taken at a different time of the day.[1]

Comments

Risedronate is a pyridinyl bisphosphate recently approved for once-weekly dosing. The new dose (35 mg) was shown to be equivalent to 5 mg per day in terms of the increase on bone mineral density in lumbar spine after 1 year.[1] The efficacy of daily administered risedronate for the treatment of postmenopausal osteoporosis in women has been established in large studies in Europe, Australia, and North America.[1,6,7] It was also shown to be effective in increasing bone mineral density as preventive treatment of osteoporosis.[8] The antifracture efficacy is considered to be comparable to alendronate.[9] Alendronate and risedronate both reduce the risk of vertebral and nonvertebral fractures. The wholesale cost for risedronate 35 mg is about $52 for 4 weeks compared to about $55 for alendronate 70 mg for 4 weeks.

Clinical Implications

Bisphosphonates are effective in reducing the risk of vertebral and nonvertebral fractures but do not have any extra skeletal benefits. These drugs may be preferred in patients at high risk of nonvertebral fractures. Once-weekly risedronate provides another convenient alternative to alendronate and may be better tolerated in those who have not tolerated alendronate. ■

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CME Questions

17. When taken by healthy older adults, ginkgo improved:
a. learning.
b. memory.
c. attention and concentration.
d. expressive language.
e. the manufacturer's bottom line.

18. Which of the following statements about pharmacologic treatment of nicotine addiction is true?
a. All antidepressants tested so far improve smoking cessation rates compared with placebo.
b. Nicotine replacement treatment is cheaper than nortriptyline.
c. Pharmacologic treatment of nicotine addiction roughly quadruples quit rates at one year compared with placebo.
d. Over-the-counter smoking cessation aids appear to be as effective in the long run as are prescription drugs.
e. Nortriptyline appears to enhance smoking cessation rates with no more side effects than placebo.

19. Which one of the following statements is *false*?
a. Repaglinide is slightly more effective in lowering the A1c than nateglinide
b. We do not have conclusive evidence that lowering the A1c will decrease the incidence of cardiovascular disease.
c. The fasting blood glucose level has a far greater effect on the incidence of cardiovascular disease than the postprandial blood glucose level.
d. The nonfasting blood glucose may be a better marker of control than the fasting level of blood glucose.

20. Risedronate 35 mg:
a. is taken once weekly.
b. may have better GI tolerance than alendronate.
c. should not be taken at the same time with products containing calcium, aluminum, or magnesium cations.
d. All of the above
e. None of the above

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We look forward to hearing from you. ■

By Louis Kuritzky, MD

MRC/BHF Heart Protection Study of Antioxidant Vitamin Supplementation in 20,536 High-Risk Individuals

Observational studies have indicated that intake of antioxidant vitamins (AOV), such as vitamins E, C, and beta-carotene, is inversely related to incidence of vascular disease. It has been postulated that this favorable relationship might be mediated, at least in part, through the demonstrated in vitro inhibition of LDL oxidation afforded by AOV. Oxidized LDL is known to be more atherogenic than native LDL. Though the positive potential for AOV benefits is intellectually appealing, want of a randomized, placebo-controlled interventional trial confirming AOV benefit has limited the enthusiasm of the scientific community. The Heart Protection Study Collaborative Group performed such a trial in the largest ever prospective randomized trial of antioxidants (n = 20,536).

Subjects in the trial were at high risk for vascular disease end points, since all had suffered either previous vascular morbidity or were diabetic. The AOV regimen was 600 mg vitamin E, 250 mg vitamin C, and 20 mg beta-carotene daily for 5 years.

There was no significant effect of AOV on any measured end point. To the contrary, there was a small increase in LDL and triglyceride levels in persons receiving AOV compared to placebo recipients. This study concluded that recommendation of AOV supplementation is not justified. ■

Heart Protection Study Collaborative Group. Lancet. 2002;360:23-33.

Prolonged Erections Produced by Dihydrocodeine and Sildenafil

Unless used concomitantly with nitrates, the clinical safety profile of the PDE5 inhibitor sildenafil has been generally very good. Another popular method of erectile dysfunction (ED) treatment, intracavernosal injection, has been associated not uncommonly with the adverse effect of priapism, but this adversity has been noted only in anecdotal case reports with sildenafil. Goldmeier and Lamba report on 2 cases of patients with prolonged erections associated with the combination of dihydrocodeine and sildenafil.

In case 1, a man treated for ED with sildenafil 100 mg had been achieving adequate erections that detumesced appropriately with orgasm. After a minor shoulder injury, for which he was prescribed dihydrocodeine 30 mg, administration of the same sildenafil dose resulted in an erection that persisted 5 hours post-ejaculation. Four days later the patient experienced a 4-hour erection with the same combination. Omission of the dihydrocodeine subsequently restored his previous pattern of appropriate detumescence.

Case 2 describes a patient receiving 100 mg sildenafil for psychogenic ED, who also received dihydrocodeine for soft tissue injury. During the first week of narcotic administration, the patient experienced erections persisting 2-3 hours postejaculation, but this effect disappeared in the next 2 weeks, despite continued concomitant sildenafil-opioid administration. Goldmeier and Lamba state that acute opiate intake heightened cyclic GMP concentrations, resulting in prolonged erections. They suggest that persons receiving sildenafil be cautioned regarding this potential interaction. ■

Goldmeier D, Lamba H. BMJ. 2002; 324:1555.

The Effect of Magnesium Supplementation of Blood Pressure: A Meta-Analysis of Randomized Clinical Trials

Magnesium (MAG) participates in vascular tone and reactivity by its involvement in Na-K transport. Parenteral high-dose MAG has been shown to reduce blood pressure (BP) in eclampsia and glomerulonephritis. Whether dietary intake of magnesium effects BP in healthy populations remains uncertain, since interventional trials have produced conflicting results. Jee and colleagues performed a meta-analysis of interventional MAG supplementation trials (n = 20 trials, with 1220 total subjects) to seek further clarification of the relationship between MAG and blood pressure.

Overall, MAG supplementation reduced BP by 0.6/0.8 mm Hg. There was a dose-response relationship, however, with BP reductions of 4.3/2.3 for each 10-mmol increase/day in MAG dose. This meta-analysis encourages the performance of an adequately powered interventional trial for ultimate confirmation of the potential role of MAG supplementation. ■

Jee SH, et al. Am J Hypertens. 2002; 15:691-696.

In Future Issues: Lung Cancer Screening Using Low-Dose Spiral CT