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Nonpharmacologic Management of Migraines

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PART 2 OF A SERIES ON MIGRAINES

THE QUESTION OF WHETHER ACUPUNCTURE IS EFFECTIVE FOR THE treatment of migraine headaches is a complex one. The practice is variable in different countries, among different traditions, and between individual practitioners, as are the certification requirements to perform this procedure. Thus, it is difficult to generalize results of acupuncture practice from one clinical situation to others.

In Germany, a multicenter, randomized controlled trial, the Acupuncture Randomized Trial or (ART), compared acupuncture according to traditional Chinese medicine (TCM) practice (verum) to sham acupuncture (needling in areas of skin for which no TCM acupuncture points are known) and a waiting list control group for the treatment of migraine in 302 patients (88% female). The percentage of responders (persons achieving at least 50% reduction in headache days) was 51% in the verum acupuncture group, 53% in the sham acupuncture group, and 15% in the waiting list controls. Although there were no statistically significant differences between the two acupuncture groups, both acupuncture interventions were significantly more effective than the control treatment.[1]

The German Acupuncture study GERAC, a randomized, multicenter, parallel-group trial, involved 960 migraine patients divided into three arms. One arm received 10 TCM acupuncture sessions over eight weeks, another received 10 sham acupuncture sessions in eight weeks, and in the third arm patients were continuously treated with standard migraine prophylactic medications (beta blockers, calcium channel blockers, or anticonvulsives). After 26 weeks, 47% of the verum treatment group were responders, 39% of the sham group were responders, and 40% of the medication group were

responders.[1] Since there were no statistically significant differences between treatment groups, and in part due to the findings of this study, migraine is no longer a reimbursable diagnosis for acupuncture therapy in Germany.[2]

There is controversy regarding the interpretation of these studies, as well as methodological and design problems with blinding of patients and practitioners. Sham acupuncture is viewed by most experts not to be an inert placebo control when compared to verum acupuncture, as light touch or needling employed with this technique can stimulate C-tactile afferent nerves, which can result in analgesic effects. This may be the reason that no differences were found between acupuncture treatments.[3]

Vickers et al, in a primary care practice-based trial of 400 headache patients (predominantly migraine), evaluated the effect of 12 acupuncture sessions over three months vs. standard care (not explicitly defined).[4] After one year, the acupuncture group experienced a statistically significant decline of 34% in headache symptoms compared with the standard care group which had a 16% decline ($P = 0.0002$). Additionally, the acupuncture group used 15% less medication, took 15% fewer sick days, and had 25% fewer visits to their primary care physicians.

Wonderling et al conducted a cost-benefit analysis of this randomized trial and found acupuncture to be cost effective in terms of the significant improvement in quality adjusted life years for the acupuncture vs. placebo patients. As a result of this study, the authors recommended that the National Health Service offer coverage for treatment of migraines with acupuncture.[5]

Mind-body or Behavioral Therapies

The Multidisciplinary U.S. Headache Consortium's recommendations regarding behavioral interventions for migraine are that relaxation training, thermal biofeedback combined with relaxation training, EMG biofeedback, and cognitive behavioral therapy (CBT) may be considered as treatment options for migraine prevention (Grade A evidence) and that behavioral therapy may be combined with preventive drug therapy to achieve enhanced clinical improvement for migraine (Grade B evidence). They also conclude that behavioral treatments may be most suitable for patients who: 1) prefer this approach; 2) cannot tolerate pharmacologic treatment secondary to side effects; 3) are currently or will imminently be pregnant or nursing; or 4) have a long history of frequent or excessive analgesic medication use, which can exacerbate headaches.[6,7] A brief descriptive outline of these mind-body therapies follows.[6]

Relaxation Training. Relaxation techniques appear to increase control over headache-related physiologic responses and, over time, lower sympathetic arousal. Patients may practice a series of graded relaxation techniques that could include diaphragmatic breathing, progressive relaxation of isolated muscle groupings, or relaxing imagery for 20-30 minutes daily. As patients learn to differentiate between tense and relaxed states, they are encouraged to practice the techniques at intervals throughout the day, both as a preventive measure and as an abortive intervention.

Biofeedback. The biofeedback methods of thermal hand-warming (feedback of skin temperature from an externally attached finger probe), electromyographic (EMG) feedback (feedback of electrical activity from scalp, neck, and upper body musculature), and electroencephalographic (EEG) biofeedback or neurofeedback (feedback of cortical brain wave frequencies monitored on a computer screen) all have in common subconsciously controlled body functions such as skin temperature, skeletal muscle tension, or brain wave frequency, respectively, that patients learn to impact by means of feedback with a monitoring device. The goal for patients, whether using self-regulation skills or a home biofeedback training device, is to practice for 20 minutes daily and incorporate it into their daily routine.

Cognitive Behavioral Training. Based upon the concept of stress as a common trigger factor for migraine *(see Table)*, it logically follows that stress

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management training may be an effective treatment approach. CBT addresses both intellectual and affective precipitants, and teaches patients to reframe stress-generating thoughts and behavior, thus rendering them less vulnerable to stress-related headaches.

Lipton et al suggest that certain patients with cognitive impairment, comorbid psychiatric disorders, and more severe headaches may need multimodal intervention, which may include mind-body therapies, depending upon their ability to participate.[8]

Holroyd et al compared results reported in 25 preventive drug (propranolol) therapy trials and in 35 thermal biofeedback/relaxation trials that included more than 2,400 patients. Both propranolol and thermal biofeedback training yielded a 55% reduction in migraine activity while the placebo (pill) yielded only a 12% reduction in migraine activity.[1] Subsequently, Holroyd et al compared the effectiveness of limited contact thermal biofeedback training alone and with propranolol (60-180 mg/d). Propranolol significantly enhanced the effectiveness of thermal biofeedback training on measures of migraine activity, analgesic use, and quality of life.[9]

Nestoriuc and Martin examined the efficacy of biofeedback techniques for the treatment of migraines in a meta-analysis of 55 studies. The frequency and duration of migraine attacks were significantly reduced compared to waiting list controls. Additionally, biofeedback reduced the associated symptoms of depression and anxiety, and these treatment effects remained stable over an average follow-up interval of 17 months.[10]

Kaushik et al, in a comparative study of propranolol prophylaxis vs. biofeedback-assisted diaphragmatic breathing and systemic relaxation in 192 migraine patients, found that both propranolol and biofeedback groups experienced significant clinical improvements without significant intergroup differences at six months. However, during the one year post-treatment follow-up period, the biofeedback group as a whole experienced less recurrence of migraine headaches (9.37%) compared to the propranolol group, which had a recurrence rate of 38.54%.[11]

Table

Common migraine triggers for migraineurs

- Stress
- Menses
- Excess sensory stimuli (bright lights, loud noises, strong odors)
- Chronobiologic changes (sleep, meals, exercise)
- Alcohol
- Caffeine withdrawal
- Aspartame (diet soda)
- Tyramine (cheese, wine, broad beans, and sauerkraut)
- Nitrites (hot dogs, cured meats)
- Monosodium glutamate (MSG, frozen, canned, and processed foods, condiments)
- Chocolate

Adapted from: Millichamp JG, et al. The diet factor in pediatric and adolescent migraine. *Pediatr Neurol* 2003;28:9-15.

Adverse Effects: All Therapies

The adverse events (AEs) reported in clinical studies of feverfew were generally mild and similar in both treatment and placebo groups.[12-14] Mouth ulceration is a rare AE observed in the clinical trials of Johnson et al. Such inflammation of the mucous membrane of the mouth and tongue, accompanied by swelling of the lips and taste loss, is probably a contact phenomenon, and is unlikely to be significant with encapsulated feverfew preparations.[15,16] With a history of use as a folk remedy for abortions, feverfew should not be used in pregnant females. Its safety has also not been established in young children or lactating women. Because feverfew interferes with platelet aggregation, physicians should carefully consider alternative agents in persons on anticoagulation therapy.[17,18]

Magnesium supplements can frequently cause diarrhea; taking magnesium with food can reduce this side effect. Individuals with renal impairment should not be given supplemental magnesium as they are unable to excrete it and can build up toxic levels. ConsumerLab purchased many leading magnesium supplements sold in the United States and tested them to determine whether they: 1) possessed the claimed amount of magnesium; 2) could disintegrate properly in the digestive tract in order to be absorbed; and 3) were free of unacceptable levels of lead. Results of the Consumer Labs analysis can be viewed at www.consumerlab.com/results/magnesium.asp.[19]

The safety of CoQ10 has not been evaluated for pregnant or breastfeeding women and therefore should not be used in these patients.

Because the chemical structure of CoQ10 closely resembles vitamin K, it has the potential to antagonize the anticoagulant effect of warfarin, requiring dosage adjustment to achieve therapeutic International Normalized Ratios. Medications such as antidepressants, statins, antipsychotics, and beta blockers decrease the body's natural CoQ10 production; patients using

these agents may require larger doses of CoQ10 than normally recommended. CoQ10 also has the potential to interact with reverse transcriptase inhibitors to exacerbate the neuropathy that can be a side effect of these medications in patients with AIDS. Information about Consumer Lab testing of CoQ10 products can be obtained at www.consumerlab.com/results/CoQ10.asp?#cautions.[20]

Although acupuncture is generally perceived as safe, it is a type of minimally invasive procedure and as such can result in adverse outcomes. Most experts report localized pain and bleeding as the most common complications of acupuncture.[21] There have been rare reports of fatalities due to acupuncture complications published including cardiac tamponade, staphylococcal sepsis, and bilateral tension pneumothoraces. Patients who have been identified to be at increased risk of adverse events associated with acupuncture include those with emphysema and patients on chronic steroids. The complications from acupuncture are associated with inadequate hygiene practices and insufficient training and experience of the practitioner.[22] In well-trained hands acupuncture is quite safe.

Nestoriuc and Martin, in their meta-analysis of 55 studies involving patients treated with behavioral therapies, noted that none of the studies reported adverse effects.[10]

Dosage and Administration

Clinical studies have used 6.25 mg three times daily of the MIG-99 standardized form of feverfew for migraine patients. Because this preparation is not commercially available, it is difficult to know whether available supplements will duplicate the clinical effects seen in the studies.

Although riboflavin is found in small amounts in many vegetables and nuts, much higher supplemental amounts of 400 mg/d have been suggested by clinical studies for the prevention of migraine.[23]

Magnesium supplementation of 360-600 mg/d has been suggested in clinical studies for the prevention of migraines.[24,25]

CoQ10 in a liquid gel capsule formulation and dose of 1-3 mg/kg/d for children and adolescents was successful in normalization of low serum CoQ10 levels and in significantly improving the post-supplementation Ped MIDAS headache disability assessments ($P < 0.001$).[26] For adults, CoQ10 in a daily dose of 300 mg may help prevent migraine headaches, but does not affect the severity or duration of an acute ongoing attack. It can take up to three months to achieve the full migraine-preventing benefits of CoQ10. Products containing CoQ10 dissolved in oil or solubilized in other substances are better absorbed than products containing the dry powder.[20]

If a therapeutic trial of riboflavin, magnesium, or CoQ10 is to be undertaken for migraine prophylaxis, they should each be used for three continuous months. Blood levels of CoQ10 can be routinely assessed due to manufacturing differences in CoQ10 content variability, but this is rarely necessary. It generally takes up to three months of continuous supplementation of either feverfew, riboflavin, magnesium, or CoQ10 to achieve prophylactic benefits.[13,14,19,23-25]

Conclusion

Because migraine headaches reflect a chronic illness, lifestyle changes such as the implementation of regular daily aerobic exercise coupled with a daily dietary fat intake of 20-30 g may decrease the frequency, duration, and intensity of migraines, in addition to promoting improved cardiovascular and general medical health. Consideration should be given to additional supplementation with vitamin B_2, magnesium, and CoQ10, especially in face of low serum levels of the latter as there is good evidence that they all can help prevent migraines. However, patients with significant renal insufficiency should not take supplemental magnesium. Feverfew, CoQ10, and migraine-preventive doses of riboflavin are not indicated for pregnant or lactating patients. Patients on systemic anticoagulation or reverse transcriptase inhibitors for AIDS should discuss CoQ10 with their doctors before initiating therapy, as concerns exist.

Food and food additive triggers can be noted by careful headache diary record keeping and can then be avoided. Mind-body therapies, when initiated and integrated into a patient's lifestyle, have been shown to be as effective as prophylactic pharmacotherapy with additional benefits for general medical and psychological health in terms of stress reduction, improved coping strategies, and self-empowerment. Indeed, pharmacotherapy has been shown to boost the effectiveness of mind-body therapies in migraine prevention. Although some studies show that acupuncture is as effective as pharmacotherapy, regional and practitioner differences in the procedure and difficulty in interpretation of the studies make it difficult to judge which patients would benefit most.

Recommendation

It is important for primary care physicians to utilize International Headache Society criteria to diagnose migraine headaches in their patients and promptly

initiate therapeutic lifestyle interventions, including regular aerobic exercise, a low-fat diet, the avoidance of migraine triggers, and evaluation of the need for riboflavin, magnesium, or CoQ10 supplementation. Depending upon the patient's clinical situation, mind-body therapies can be considered alone or in combination with pharmacotherapy. The headache diary and Ped MIDAS or MIDAS questionnaires are important tools by which patient and physician can assess the impact of therapeutic interventions on the migraine history. ❖

References

1. Linde K, et al. Acupuncture for patients with migraine: A randomized controlled trial. *JAMA* 2005;293:2118-2125.
2. Diener HC, et al. The GERAC Migraine Study Group. Efficacy of acupuncture for the prophylaxis of migraine: A multicentre randomised, controlled clinical trial. *Lancet Neurol* 2006;5:310-316.
3. Birch S. Reflections on the German Acupuncture studies. *J Chin Med* 2007;83:12-17.
4. Vickers AJ, et al. Acupuncture for chronic headache in primary care: Large, pragmatic, randomised trial. *BMJ* 2004;328:744-747. Epub 2004 Mar 15.
5. Wonderling D, et al. Cost effectiveness analysis of a randomized trial of acupuncture for chronic headache in primary care. *BMJ* 2004;328:747-749.
6. Penzien DB, et al. Behavioral management of recurrent headache: Three decades of experience and empiricism. *Applied Psychophysiol Biofeedback* 2002;27:163-181.
7. The American Academy of Neurology. Behavioral and Physical Treatments for Migraine: Encounter Kit for Migraine Headache. Available at: www.aan.com/professionals/patient/hakit/pdf/beh_phy_tre.pdf. Accessed Feb. 22, 2007.
8. Lipton RB, et al. Disease management of migraine and the importance of stratified care. *Dis Manage Health Outcomes* 2003;11:379-388.
9. Holroyd KA, et al. Enhancing the effectiveness of relaxation-thermal biofeedback training with propranolol hydrochloride. *J Consult Clin Psychol* 1995; 63:327-330.
10. Nestoriuc Y, Martin A. Efficacy of biofeedback for migraine: A meta-analysis. *Pain* 2007;128:111-127.
11. Kaushik R, et al. Biofeedback assisted diaphragmatic breathing and systemic relaxation versus propranolol in long term prophylaxis of migraine. *Complement Ther Med* 2005;13:165-174.
12. Pittler MH, Ernst E. Feverfew for preventing migraine. *Cochrane Database Syst Rev* 2004;(1): CD002286.
13. Pfaffenrath V, et al. 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.
14. Diener HC, et al. Efficacy and safety of 6.24 mg t.i.d. feverfew CO_2-extract (MIG-99) in migraine prevention—a randomized, double-blind, multicenter, placebo-controlled study. *Cephalalgia* 2005;25: 1031-1041.
15. Johnson ES, Kadam NP. Efficacy of feverfew as prophylactic treatment of migraine. *BMJ* 1985;291: 569-573.
16. Paulsen E, et al. Do monoterpenes released from feverfew plants cause airborne Compositae dermatitis? *Contact Derm* 2002;47:14-18.
17. European Scientific Cooperative on Phytotherapy. *Tanaceti parthenii* herba/folium (feverfew). Exeter UK: ESCOP; 1996. Monographs on the Medicinal Uses of Plant Drugs, Fascicule 2. Feverfew Monograph.
18. Feverfew Monograph. Consumer Lab. Available at: www.consumerlab.com/tnp.asp?chunkiid=21713#ref1. Accessed April 1, 2007.
19. Consumer Lab Product Review: Magnesium. Available at: www.consumerlab.com/results/magnesium.asp. Accessed Feb. 5, 2007.
20. Consumer Lab Product Review: CoEnzymeQ10. Available at: www.consumerlab.com/results/CoQ10.asp?#cautions. Accessed Feb. 7, 2007.
21. Ernst E, White AR. Prospective studies of the safety of acupuncture: A systemic review. *Am J Med* 2001; 110:481-485.
22. Su JW, et al. Bilateral pneumothoraces as a complication of acupuncture. Available at: www.sma.org.sg/smj/4801/4801cr10.pdf. Accessed March 25, 2005.
23. Schoenen J, et al. Effectiveness of high-dose riboflavin in migraine prophylaxis. A randomized controlled trial. *Neurology* 1998;50:466-470.
24. Piekert A, et al. Prophylaxis of migraine with oral magnesium: Results from a prospective multicenter, placebo-controlled and double-blind randomized study. *Cephalalgia* 1996;16:257-263.
25. Facchinetti F, et al. Magnesium prophylaxis of menstrual migraine: Effects on intracellular magnesium. *Headache* 1991;31:298-301.
26. Hershey AD, et al. Coenzyme Q10 deficiency and response to supplementation in pediatric and adolescent migraine. *Headache* 2007;47:73-80.

Antioxidant Vitamins, Immunity, and Endurance Exercise

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THE VALUE OF EXERCISE FOR HEALTH IS COMMONLY recognized, even if recommendations are not always acted upon. But could the old adage that "too much of a good thing is bad for you" apply to exercise? Some evidence appears to indicate so, leading to suggestions that athletes require additional vitamin intake. Prolonged exercise and heavy training impact an athlete's immune system, both acutely and chronically.[1] Endurance athletes have been shown in some studies, but not all, to be more susceptible to infections, especially upper respiratory tract infections (URTI), shortly before and immediately after marathons and ultramarathons.[2]

Of even greater concern is a small number of epidemiological studies that have compared all-cause mortality with physical activity levels measured as energy expenditure.[3] As expected, those expending the least energy through aerobic exercise had the highest death rates. Mortality rates decreased with increasing weekly energy expenditure. But then the trend reversed itself somewhat for the group with the highest energy expenditure (> 10,000 kJ/week).[3] This would be roughly 4 hours/week running at 10 miles/hour. Endurance athletes are known to have higher oxidative stress, which is associated with a number of diseases. Because antioxidants counteract oxidative stress, dietary antioxidant vitamin supplementation has been suggested to benefit endurance athletes.

Mechanism of Action

The benefits of aerobic exercise arise, in part, from increased oxygen consumption. Most of this oxygen is reduced to water and safely eliminated. However, about 4-5% is incompletely reduced to form reactive oxygen species (ROS), the best known of which are free radicals. These ROS are unstable and highly reactive, making them potentially harmful to living cells. The body therefore counteracts ROS through an elaborate antioxidant system consisting of endogenous and exogenous antioxidants. Vitamins C and E are included in the latter group. However, if the ROS levels are elevated beyond what the antioxidants can neutralize, oxidative stress results. The latter has been associated with a number of diseases, including atherosclerosis, diabetes, Parkinson's disease, Alzheimer's disease, and cancer.[3]

Oxidative stress is also believed to contribute to muscle fatigue and damage.[4] Exercise-induced muscle and lymph tissue inflammation and damage are associated with free-radical mediated processes.[5] For these reasons, supplementation with antioxidant vitamins, most commonly vitamins C and E, has also been recommended to counteract muscle fatigue and injury associated with endurance exercise.

The connection between exercise and immune dysfunction is less well understood. ROS have a direct inhibitory effect on neutrophils and other cells of the immune system. In addition, acute exercise releases a number of stress hormones such as adrenaline and cortisol.[1] Elevated levels of these compounds are associated with reduced levels of several components of the immune system. Although numerous studies document an exercise-induced immune depression, the link between this and increased incidence of illness has been difficult to establish. However, because several vitamins are essential for normal immune function, vitamin supplementation is also recommended to counteract this aspect of endurance training. Vitamins A, C, and E are most commonly recommended here.

Clinical Studies

A review published in 2006 found 41 original studies of the impact of dietary antioxidant supplementation on exercise-induced oxidative stress.[3] Although almost all were randomized and double-blind, a variety of antioxidants were used at different doses and in different regimens. The most commonly used compound was vitamin E, used in 28 of the studies (given alone in 16). Overall, the results were equivocal, with 20 studies showing that the antioxidants reduced oxidative stress, 23 studies showing no effect, and four showing increased oxidative stress. Some other observations made by the reviewers: the form of vitamin E used (whether natural or synthetic) did not impact outcomes; no association was found between outcomes and the dose of vitamin E (which ranged between 300 mg/d and 1200 mg/d); and the duration of supplementation had a significant impact. Studies which found that antioxidants significantly reduced oxidative stress assigned participants to an average of eight weeks of supplementation, while studies that found no change in oxidative stress gave the supplements for an average of four weeks.

Clinical research with vitamin E and immunity is

even less clear. The Alpha-Tocopherol Beta-Carotene Cancer Prevention (ATBC) study was conducted with 50- to 69-year-old male smokers, a population very different from endurance athletes. People were randomly assigned to receive either alpha-tocopherol (vitamin E, 50 mg/d), beta-carotene (a precursor to vitamin A, 20 mg/d), both, or a placebo.[6] While the primary endpoints being studied involved cancer prevention, supplementation did not impact the incidence of the common cold when sedentary men were compared to those whose employment involved significant physical exercise, or those who exercised vigorously during leisure time.

A small number of studies have shown reduced levels of exercise-induced immunodepression after vitamin E supplementation, but the results have not been consistent. A recent randomized controlled trial assigned 20 men to receive either placebo or vitamin E (400 IU/d) and vitamin C (1 g/d) for 28 days.[7] Participants cycled on an exercise bicycle for 2.5 hours and had immunological analysis carried out on blood samples collected immediately before and after exercising. While the supplement group showed less of an increase in cortisol levels after exercise, no significant differences were seen in interleukin-6 or neutrophil levels, nor in oxidative stress.

Vitamin C has generated the most interest as an essential nutrient that influences the immune system.[5] A number of cells in the immune system store vitamin C in high concentrations.[8] Vitamin C is involved in a number of metabolic reactions activated during exercise, leading to suggestions that prolonged exercise may deplete vitamin C and lead to higher dietary requirements. Three controlled trials of short duration found that vitamin C supplementation (0.5-1.0 g/d for 7-14 days) did not impact immune changes after intensive exercise for 1-2.5 hours.[5]

Two other studies examined the elevated levels of several interleukins (signaling compounds important to proper immune system function) present in runners who completed a 90 km ultramarathon. The levels were significantly less elevated in those who took 1.5 g/d vitamin C for seven days prior to the competition compared to those who took 0.5 g/d vitamin C or placebo.[9] However, neither study randomly assigned participants. In a brief, randomized controlled study, 1.5 g/d vitamin C for seven days prior to an 80 km ultramarathon did not impact immune or oxidative stress levels following the event.[5]

A meta-analysis of vitamin C for the common cold found no evidence of benefit in reducing the incidence in the general population.[10] However, a sub-group analysis was conducted on six studies involving participants under heavy acute physical stress. These included marathon runners, skiers, and soldiers on sub-arctic exercises. The meta-analysis found the incidence of colds reduced by half among those taking vitamin C. Doses of vitamin C ranged from 250 mg/d to 1,000 mg/d for up to two months prior to the endurance exercise.

A small number of studies have examined the use of vitamins as ergogenic aids: to improve sports performance. A 1988 study of 30 competitive male runners used a placebo-controlled crossover design with each runner taking a multivitamin and mineral supplement for a three-month period.[11] Performance was measured in a 15 km time trial, a treadmill run to exhaustion, peak running speed, and with metabolic markers. None of these differed significantly during the supplementation period. In another double-blind study, 22 physically active men were randomly assigned to either placebo or a multivitamin and mineral supplement for 90 days.[12] No significant differences occurred between the two groups for performance in a 90-minute run, muscle strength, or metabolic markers of fitness. A more recent 2006 study likewise found no ergogenic benefit with anaerobic exercise from a multivitamin and mineral supplement.[13] For athletes consuming an adequate diet, vitamin supplements are unlikely to have a direct effect on athletic performance.

Adverse Effects

The International Olympic Committee (IOC) has warned that large doses of some essential nutrients may be harmful, but does not reference the evidence to support that claim.[14] A very small number of studies (four out of 41 reviewed) found that antioxidant supplementation increased oxidative stress.[3] Direct negative effects of supplementation were not reported in other studies. Athletes should be cautious in purchasing vitamins because, as dietary supplements, there may be significant variability in their quality.

Formulation

Another problem for those taking dietary supplements is the wide variety of formulations available, often combining different supplements in different ratios.[3] There is practically no evidence available on the best formulations or doses.

Conclusion

The literature on vitamins and exercise is clear that neither long-term nor short-term supplementation has an impact on exercise performance, aerobic performance, or muscle strength.[15] Whether supplementation

has a more subtle effect on exercise performance by reducing the incidence of infections or lowering oxidative stress is less clear. Research is presently inadequate to completely address concerns regarding excessive exercise that arose from the epidemiological studies noted at the beginning of this article.

While some studies find a beneficial impact for endurance athletes on biomedical markers associated with disease after supplementation, an almost equal number of studies have not found such benefits. This has been the case with vitamin C and vitamin E taken alone or in combination. Some of this variability may arise because of differences in dosage regimens, exercise protocols, study duration, or fitness levels of the participants. The only clear benefit demonstrated in studies is reduced incidence of colds after prolonged acute exercise when people took vitamin C supplements beforehand. At the moment, however, available evidence does not support the general use of antioxidant vitamin supplementation in endurance athletes.

Recommendation

National Dietary Guidelines take into account everyone's need for antioxidants, including antioxidant vitamins. These are most readily available by consuming a diet rich in fruit and vegetables. However, these guidelines were developed with an average energy expenditure in mind and to prevent deficiency states, but not necessarily to optimize health or performance.[3] Athletes, especially endurance athletes, will likely have higher energy expenditure. This should lead to endurance athletes increasing the amount of fruit and vegetables in their diet, and taking a general multivitamin. Elite athletes, or those undertaking prolonged endurance training, should consider consulting a qualified sports nutritionist to ensure they are meeting their dietary requirements. At this point, there is insufficient evidence to recommend that endurance athletes consistently take high doses of antioxidant vitamin supplements. ❖

References

1. Gleeson M. Can nutrition limit exercise-induced immunodepression? *Nutr Rev* 2006;64:119-131.
2. Himmelstein SA, et al. Vitamin C supplementation and upper respiratory tract infections in marathon runners. *J Exerc Physiol Online* 1998;1.
3. Williams SL, et al. Antioxidant requirements of endurance athletes: Implications for health. *Nutr Rev* 2006;64:93-108.
4. Barclay JK, Hansel M. Free radicals may contribute to oxidative skeletal muscle fatigue. *Can J Physiol Pharmacol* 1991;69:279-284.
5. Nieman DC, et al. Influence of vitamin C supplementation on oxidative and immune changes after an ultramarathon. *J Appl Physiol* 2002; 92:1970-1977.
6. Hemilä H, et al. Physical activity and the common cold in men administered vitamin E and β-carotene. *Med Sci Sports Exerc* 2003;35:1815-1820.
7. Davison G, et al. Antioxidant supplementation and immunoendocrine responses to prolonged exercise. *Med Sci Sports Exerc* 2007;39:645-652.
8. Peake JM. Vitamin C: Effects of exercise and requirements with training. *Int J Sport Nutr Exerc Metab* 2003;13:125-151.
9. Nieman DC, et al. Influence of vitamin C supplementation on cytokine changes following an

ultramarathon. *J Interferon Cytokine Res* 2000; 20:1029-1035.
10. Douglas RM, et al. Vitamin C for preventing and treating the common cold. *Cochrane Database Systematic Rev* 2004;4.
11. Weight LM, et al. Vitamin and mineral supplementation: Effect on the running performance of trained athletes. *Am J Clin Nutr* 1988;47:192-195.
12. Singh A, et al. Chronic multivitamin-mineral supplementation does not enhance physical performance. *Med Sci Sports Exerc* 1992;24:726-732.
13. Fry AC, et al. Effect of a liquid multivitamin/mineral supplement on anaerobic exercise performance. *Res Sports Med* 2006;14:53-64.
14. International Olympic Committee. IOC consensus statement on sports nutrition 2003. Available at http://multimedia.olympic.org/pdf/en_report_723.pdf. Accessed April 30, 2007.
15. Evans WJ. Vitamin E, vitamin C, and exercise. *Am J Clin Nutr* 2000;72:647S-652S.

CME Questions

CME Instructions: Physicians participate in this continuing medical education program by reading the articles, using the provided references for further research, and studying the CME questions. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material.

After completing this activity, participants must complete the evaluation form provided at the end of each semester (June and December) and return it in the reply envelope provided to receive a credit letter. When an evaluation form is received, a credit letter will be mailed to the participant.

23. Sham acupuncture is viewed by most experts not to be an inert placebo control when compared to verum acupuncture, as light touch or needling employed with this technique can stimulate C-tactile afferent nerves, which can result in analgesic effects.
a. True
b. False

24. The Multidisciplinary U.S. Headache Consortium concluded that behavioral treatments may be most suitable for which patients?
a. Those who prefer this approach.
b. Those who cannot tolerate pharmacologic treatment secondary to side effects.
c. Those who are currently or will imminently be pregnant or nursing.
d. Those who have a long history of frequent or excessive analgesic medication use.
e. All of the above

25. Due to its use as a folk remedy for abortions, which of the following should not be used in pregnant women?
a. CoQ10
b. Feverfew
c. Magnesium
d. Riboflavin

26. Antioxidant vitamins are suggested for endurance athletes to:
a. reduce antioxidant stress.
b. counteract exercise-induced immunosuppression.
c. prevent exercise-related injuries and inflammation.
d. All of the above

27. The beneficial effect of antioxidant vitamins in endurance athletes with the best support from clinical research is that:
a. vitamin E reduces the risk of heart disease.
b. vitamin C reduces the incidence of colds after an acute incidence of endurance exercise.
c. vitamin C combined with vitamin E prolongs life.
d. vitamin E improves exercise performance.

Answers: 23. a, 24. e, 25. b, 26. d, 27. b.

With Comments from Russell H. Greenfield, MD

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Tea Time Will Never Be the Same Again: Tea and Milk

Source: Lorenz M, et al. Addition of milk prevents vascular protective effects of tea. *Eur Heart J* 2007;28:219-223.

Goal: To determine whether milk impacts the cardioprotective effects of drinking tea.

Study design: Controlled crossover clinical trial together with in vitro data.

Subjects: Healthy, postmenopausal women recruited through advertisements (n = 16, mean age 59.5 years).

Methods: Subjects were instructed to abstain from drinking tea for four weeks prior to and during the study. During the trial, participants drank 500 mL of boiled water (control), freshly brewed black tea with 10% water, or black tea with 10% skim milk while they enjoyed a croissant for breakfast. Tea preparation was standardized. Subjects underwent three clinical evaluations after fasting overnight, each at least three days apart from one another. Flow-mediated dilation (FMD) and nitro-mediated dilation (NMD, referring to measurements taken after 0.4 mg sublingual nitroglycerin spray and reflecting endothelial independent vasodilatation), were measured before and two hours post-ingestion of the beverages using high-resolution vascular ultrasound following cuff occlusion of the forearm for five minutes. Changes in brachial artery diameter were measured every 15 seconds for up to two minutes. Bench studies were also performed. Bovine aortic endothelial cells were treated with black tea, milk, and milk proteins, and vasorelaxation studies were performed using isolated rat thoracic aorta rings. In cell culture experiments, the production of nitric oxide in response to tea with or without milk was measured.

Results: Tea ingestion significantly increased FMD compared to control, but this effect was abolished with the addition of milk. Tea's effects on NMD (endothelial independent vasodilatation), however, were not affected by the addition of milk. Tea significantly increased endothelial nitric oxide synthase (eNOS) activity in cell culture, but addition of 10% milk completed eliminated the rise in eNOS activity. Experiments with single milk proteins showed that casein (all three forms tested) blunted eNOS activity in a manner similar to milk. In contrast, albumin, lactalbumin, and lactoglobulin had little effect on eNOS activity. Further study showed that tea-induced eNOS phosphorylation, which regulates eNOS activity, is blocked by both milk and single milk caseins. Tea relaxed pre-contracted aortic rings, which was prevented by the NOS-inhibitor L-NAME. Similarly, 10% milk also completely inhibited tea-induced relaxation. When β-casein was added to tea, aortic ring relaxation was likewise inhibited, whereas bovine serum albumin had little effect. Additional studies showed that addition of 10% milk selectively and markedly decreased concentrations of various catechins in the supernatant of centrifuged tea, whereas content of caffeine and gallic acid was unaffected, suggesting a complex formation between catechins and milk proteins.

Conclusion: Milk may counteract the favorable health effects of tea on vascular function.

Study strengths: Human exposure, cell culture, and functional models assessed; degree of detail.

Study weaknesses: Lack of generalizability (subjects were healthy postmenopausal women); very small sample size.

Of note: Ten percent milk was added to black tea to mimic common practice in the United Kingdom; vegetarians and regular drinkers of large amounts of tea were excluded from the study; participants had to have normal values on screening parameters that included lipid levels, blood pressure, thyroid-stimulating hormone, and body mass index; worldwide, tea is second only to water in terms of public consumption; data suggest that polyphenols possess a high binding affinity for proteins high in proline, such as caseins; prior data indicate that adding milk to tea inhibits tea's antimutagenic actions; studies assessing milk's effect on the antioxidant capacity of tea have yielded conflicting results.

We knew that: Tea exerts antioxidant, vasodilatory, and anti-inflammatory effects; the health effects of tea have been tied to its flavonoid content, especially catechins; studies suggest that tea drinking is inversely related to cardiovascular disease morbidity and mortality; FMD is evoked by nitric oxide generated by eNOS during a short period of shear stress; eNos is important for ischemia-mediated arteriogenesis and blood flow stimulated angiogenesis; the major catechin in tea (epigallocatechin-3-gallate) induces eNOS activation in endothelial cells and leads to vasorelaxation in rat aortic rings; tea polyphenols have long been known to interact with milk proteins.

Comments: Until recently, nowhere in the West has the ritual enjoyment of drinking tea become so ingrained in society as in Britain. Indeed, with positive trials of the health benefits of tea piling up over recent years it's clear the Brits (as well as traditional Asian peoples long before) have been on to something. Surprising it is, however, to find that the genteel manner of enjoying afternoon tea with milk appears to counteract important health benefits of tea drinking on endothelial function. Additional studies should be performed that examine other types of tea, but the results of this small, yet in-depth, study raise questions that few would have considered prior. For those who drink tea for their hearts, it may be best to

eschew milk. For those who drink tea for their souls, a little milk remains permissible.

What to do with this article: Keep a hard copy in your file cabinet. ❖

Adults, Herbs, and Evidence-based Medicine

Source: Bardia A, et al. Use of herbs among adults based on evidence-based indications: Findings from the National Health Information Survey. *Mayo Clin Proc* 2007;82: 561-566.

Goal: To examine indications that consumers report for taking individual herbs, determine whether these are in accordance with available evidence, and identify factors that predict evidence-based use.

Design: Cross-sectional complex survey (data taken from the Alternative Health/Complementary and Alternative Medicine [CAM] supplement of the 2002 National Health Interview Survey, or NHIS).

Subjects: Survey respondents who used a single popular herbal remedy to treat a specific medical condition within the prior 12 months (n = 609, of whom 65% were women, mean age 41 years).

Methods: Data were extracted from the survey with particular emphasis on answers regarding use of herbs in the prior year, and if so whether they were employed to address a specific medical condition. Subjects were asked to specify the clinical indication for use of the herb from a list of 73 specific health conditions. They were also asked to list independently herbs they took during the previous year from a list of 35 commonly used botanicals. Only responses from subjects who used a single herb from the list of 35 and who said they were taking it to address a specific malady were included in the analysis. Ultimately, analysis was limited to individuals who took one of six herbs in the prior 12 months (echinacea, garlic, ginseng, kava, soy, and St. John's wort).

Results: Overall 54.9% of respondents used herbs consistent with evidence-based medicine (EBM) guidelines (range of 68% for echinacea to 4% for ginseng); however, only about one-third of people using garlic, kava, soy, or St. John's wort did so in accordance with EBM guidelines. For five of the herbs (not echinacea, for which no such pattern was identified), older, non-Hispanic white women with higher levels of education were more likely to use the agents in an evidence-based manner.

Conclusion: More than 60% of adult respondents to a nationally representative survey used a sampling of commonly consumed single herbal remedies to address specific health conditions in ways not supported by the scientific literature.

Study strengths: Large sample size; multivariable logistic regression analysis.

Study weaknesses: Response rate to the Alternative Health/CAM supplement was not noted; analysis only possible for use of a single herb, when clinical experience suggests that many people use more than one herbal remedy at a time, or combination therapy; no information provided on specific products used by respondents, dosages employed, or perceived efficacy.

Of note: The response rate to the overall 2002 NHIS questionnaire was almost 75%; a single database was used to develop the evidence-based standards for herb use as applied in this study; sales of dietary supplements have increased more than any other segment of CAM since the 1990s; data suggest that consumers believe their conventional medical doctors are not in favor of supplement use; the survey employed in this study distinguished "natural herbs" from vitamins and minerals; the 10 most commonly endorsed herbs in the survey were noted to be echinacea, ginseng, ginkgo, garlic, St. John's wort, peppermint, ginger, soy, ragweed, and kava; the authors were not able to assess ginkgo for claudication, dementia or cerebral insufficiency, nor were they able to assess ginger for nausea and vomiting, because these conditions were not listed in the survey's 73 specific health conditions; the database employed for this study did not identify any established use of peppermint; it is striking that ragweed was listed as one of the 10 most commonly endorsed herbs in the survey; ginseng for "mental performance" was not assessed in this trial, only its use in the setting of diabetes; despite a spate of articles questioning its efficacy against the common cold, echinacea remains the single most popular herbal remedy in the United States.

We knew that: Most people do not discuss their use of CAM therapies, including supplements, with their conventional doctors; in addition, conventional medical providers are often not well-versed in CAM therapies, including the use of supplements; the NHIS is a large, nationally representative household survey that uses a national sample of the civilian, non-institutionalized U.S. population, sampling approximately 30,000 adults each year (with over-sampling of both black and Hispanic populations); the NHIS has been conducted continuously since 1957, and data are released annually; the survey includes a core set of questions with additional questions asked periodically, and detailed questions asked of one randomly selected adult and one child per household; the Dietary Supplement Health and Education Act (DSHEA) of 1994 established that dietary supplements be regulated under an FDA category different from both foods and drugs; under DSHEA, supplement labels can only claim that the product contained therein supports the "structure and function of the body," and cannot offer claims that the supplement can help "diagnose, treat, cure, or prevent any disease."

Clinical import: The authors of this study call for health care professionals to proactively educate consumers regarding existing evidence either for or against the use of specific herbs to address health conditions. Such a call is laudable, and problematic. The majority of conventional medical practitioners has little or no knowledge of the proper use of supplements, is uncertain where to turn for credible information in this regard, and is struggling to stay up to date in their own fields let alone learn

about CAM therapies. In addition, data suggest that the majority of practicing physicians do not follow EBM guidelines with respect to specific therapeutic interventions, thus it cannot be surprising that the lay public often pays little heed to the medical research, choosing to rely more on personal experience, tradition, and popular opinion than on professional advice. The study itself is significantly flawed in ways delineated, but the underlying theme that people are using CAM therapies without guidance from, or at least partnership with, their conventional doctors is important to emphasize, even though already commonly accepted.

What to do with this article: Remember that you read the abstract. ❖

One Does not Equal Two—Cinnamon and Diabetes Mellitus

Source: Altschuler JA, et al. The effect of cinnamon on A1C among adolescents with type I diabetes. *Diabetes Care* 2007;30: 813-816.

Goal: To determine the effect of cinnamon on glycemic control in adolescents with Type 1 diabetes mellitus (DM).

Study design: Prospective, randomized, double-blind, placebo-controlled study performed over 90 days.

Subjects: Adolescents with Type 1 DM (n = 72, with 57 completing the trial) treated as outpatients.

Methods: Subjects were randomized to receive either 1 g/d of cinnamon in pill form or placebo (a lactose pill). A three-month supply was provided to participants at the time of enrollment, and instructions were offered to take the pills at the same time each day. Subjects were asked to maintain a logbook of insulin usage during the course of the study. Primary outcome measures were total A1c and change in A1c. Additional endpoints included total daily insulin use and adverse events. Subjects were called every two weeks both to assess compliance and collect data.

Results: No statistically significant differences were identified between the two groups with respect to total daily insulin intake, final mean A1c, mean change in A1c, or number of hypoglycemic episodes. With respect to the last parameter, however, subjects in the cinnamon group experienced 39% more hypoglycemic episodes than those in the placebo arm, but the result did not reach statistical significance.

Conclusion: Cinnamon is not effective for improving glycemic control in adolescents with Type 1 DM.

Study strengths: Compliance assessed by regular phone contact in addition to pill count (however, level of compliance is not stated in the paper); intention-to-treat analysis.

Study weaknesses: Source of cinnamon and type is not detailed except to say that the pills were prepared by the University of California-San Francisco Investigational Pharmacy; significant dropout rate; short duration of trial.

Of note: Adolescents with Type 1 DM were chosen for study because they are deemed a high-risk group; adolescents have unique challenges in trying to maintain adequate glycemic control that include increasing insulin resistance, and both physiologic (rapid growth) and psychosocial issues; data point to an increase in A1c in those with DM from age 13 to 19 years; for inclusion, subjects had to have carried the diagnosis of Type 1 DM for at least 18 months and have avoided inpatient care for at least 12 months; in this study, A1c levels were taken from medical records at the time of enrollment and then repeated approximately 90 days later; a subject in the cinnamon arm experienced a hypoglycemic seizure one day after enrollment and withdrew from the study; study results tended to favor the placebo group.

We knew that: A1c (also called glycohemoglobin) provides an estimate of blood sugar control over the prior few months, and is the single best predictor for risk of complications in people with either Type 1 and Type 2 DM; specialists typically recommend that people with DM keep their A1c as close to 6% or below as possible (4-6% is considered normal); a slim majority of studies has shown that cinnamon may be an effective aid in achieving enhanced glycemic control for people with Type 2 DM; results of a number of in vitro studies suggest that cinnamon may sensitize individuals to the effects of insulin, with some researchers hypothesizing the presence of a synergistic effect; other researchers posit that cinnamon may actually increase endogenous insulin production; the majority of data supporting a therapeutic benefit of cinnamon in the setting of Type 2 DM focuses on fasting blood sugar, which contributes relatively little to A1c.

Comments: While the potential benefit of adding cinnamon to the diet for people with Type 2 DM has long been considered, the same cannot be said for the setting of Type 1 DM. Many practitioners simply assumed that cinnamon must be good for anyone with "diabetes," though the basis for specific therapeutic intervention differs considerably between Types 1 and 2. The present study raises questions about the efficacy of cinnamon for people with either type of DM, but is far from definitive. One major concern is the type of cinnamon employed by the pharmacists. To lump all forms of cinnamon together is simplistic, if not misguided, as there are many. The majority of data showing a beneficial effect on blood sugar has used *Cassia cinnamon*. The form of cinnamon employed in this trial was not disclosed. To their credit, the researchers do question whether a larger dose of cinnamon might be necessary to show an effect in Type 1 DM, and note that a 90-day intervention is shorter than the typical 120-day lifespan of the human red blood cell (thus potentially having an impact on A1c). In addition, it is interesting to note the statistically nonsignificant rate of hypoglycemia in the cinnamon group (39%), a rate that would certainly be deemed clinically significant. The questions raised by this trial are important, but further research is clearly warranted.

What to do with this article: Keep a copy of the abstract on your computer. ❖

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ALTERNATIVE MEDICINE ALERT™

A Clinician's Evidence-Based Guide to Alternative Therapies

Migraine Headaches: A Patient Handout

MIGRAINE HEADACHES ARE USUALLY CHARACTERIZED BY SEVERE PAIN ON ONE OR BOTH sides of the head, an upset stomach, and at times disturbed vision. Sensitivity to light is a standard symptom of the two most prevalent types of migraine-caused headache: classic and common.

The major difference between the two types is the appearance of neurological symptoms 10-30 minutes before a classic migraine attack. These symptoms are called an aura. The person may see flashing lights or zigzag lines, or may temporarily lose vision. Other classic symptoms include speech difficulty, weakness of an arm or leg, tingling of the face or hands, and confusion.

The pain of a classic migraine headache may be described as intense, throbbing, or pounding and is felt in the forehead, temple, ear, jaw, or around the eye. Classic migraine starts on one side of the head but may eventually spread to the other side. An attack lasts 1-2 days.

Common migraine—a term that reflects the disorder's greater occurrence in the general population—is not preceded by an aura. But some people experience a variety of vague symptoms beforehand, including mental fuzziness, mood changes, fatigue, and unusual retention of fluids. During the headache phase of a common migraine, a person may have diarrhea and increased urination, as well as nausea and vomiting. Common migraine pain can last 3-4 days.

Both classic and common migraine can strike as often as several times a week, or as rarely as once every few years. Both types can occur at any time. Some people, however, experience migraines at predictable times—for example, near the days of menstruation or every Saturday morning after a stressful week of work.

The migraine process. Research scientists are unclear about the precise cause of migraine headaches. There seems to be general agreement, however, that a key element is blood flow changes in the brain. People who get migraine headaches appear to have blood vessels that overreact to various triggers.

Scientists have devised one theory of migraine which explains these blood flow changes and also certain biochemical changes that may be involved in the headache process. According to this theory, the nervous system responds to a trigger such as stress by causing a spasm of the nerve-rich arteries at the base of the brain. The spasm closes down or constricts several arteries supplying blood to the brain, including the scalp artery and the carotid or neck arteries. As these arteries constrict, the flow of blood to the brain is reduced. At the same time, blood-clotting particles called platelets clump together—a process which is believed to release a chemical called serotonin. Serotonin acts as a powerful constrictor of arteries, further reducing the blood supply to the brain.

Reduced blood flow decreases the brain's supply of oxygen. Symptoms signaling a headache, such as distorted vision or speech, may then result, similar to symptoms of stroke. Reacting to the reduced oxygen supply, certain arteries within the brain open wider to meet the brain's energy needs. This widening or dilation spreads, finally affecting the neck and scalp arteries. The dilation of these arteries triggers the release of pain-producing substances

called prostaglandins from various tissues and blood cells. Chemicals that cause swelling and inflammation, and substances that increase sensitivity to pain, are also released. The circulation of these chemicals and the dilation of the scalp arteries stimulate the pain-sensitive nociceptors. The result, according to this theory: a throbbing pain in the head.

Women and migraine. Although both males and females seem to be equally affected by migraine, the condition is more common in adult women.

The relationship between female hormones and migraine is still unclear. Women may have "menstrual migraine"—headaches around the time of their menstrual period—which may disappear during pregnancy. Other women develop migraine for the first time when they are pregnant. Some are first affected after menopause.

The effect of oral contraceptives on headaches is perplexing. Some women with migraine who take birth control pills experience more frequent and severe attacks. However, a small percentage of women have fewer and less severe migraine headaches while taking birth control pills. And women who do not suffer from headaches may develop migraines as a side effect when they use oral contraceptives.

Triggers of headache. Although many sufferers have a family history of migraine, the exact hereditary nature of this condition is still unknown. People who get migraines are thought to have an inherited abnormality in the regulation of blood vessels.

Migraine triggers include stress and other normal emotions, as well as biological and environmental conditions. Fatigue, glaring or flickering lights, changes in the weather, and certain foods can set off migraine. Some scientists believe that foods such as yogurt, nuts, and lima beans (and several others) contain chemical substances, such as tyramine, that constrict arteries—the first step of the migraine process. Other scientists believe that foods cause headaches by setting off an allergic reaction in susceptible people.

How Is Migraine Headache Treated?

Drug therapy, biofeedback training, stress reduction, and elimination of certain foods from the diet are the most common methods of preventing and controlling migraine and other vascular headaches.

Regular exercise, such as swimming or vigorous walking, can also reduce the frequency and severity of migraine headaches.

During a migraine headache, temporary relief can sometimes be obtained by applying cold packs to the head or by pressing on the bulging artery found in front of the ear on the painful side of the head.

Biofeedback and relaxation training. Drug therapy for migraine is often combined with biofeedback and relaxation training. Biofeedback refers to a technique that can give people better control over such body function indicators as blood pressure, heart rate, temperature, muscle tension, and brain waves. Thermal biofeedback allows a patient to consciously raise hand temperature. Some patients who are able to increase hand temperature can reduce the number and intensity of migraines.

A patient learning thermal biofeedback wears a device that transmits the temperature of an index finger or hand to a monitor. While the patient tries to warm his hands, the monitor provides feedback either on a gauge that shows the temperature reading or by emitting a sound that increases in intensity as the temperature increases. The patient is not told how to raise hand temperature, but is given suggestions such as "imagine your hands feel very warm and heavy."

In another type of biofeedback called electromyographic (EMG) training, the patient learns to control muscle tension in the face, neck, and shoulders.

Although biofeedback can be practiced at home with a portable monitor, the ultimate goal is to wean the patient from the machine. The patient can then use biofeedback anywhere at the first sign of a headache.

The antimigraine diet. Scientists estimate that a small percentage of migraine sufferers will benefit from a treatment program focused solely on eliminating headache-provoking foods and beverages.

Other migraine patients may be helped by a diet to prevent low blood sugar. Low blood sugar, or hypoglycemia, can cause headache. This condition can occur after a period without food: overnight, for example, or when a meal is skipped. People who wake up in the morning with a headache may be reacting to the low blood sugar caused by the lack of food overnight.

Treatment for headaches caused by low blood sugar consists of scheduling smaller, more frequent meals. A special diet designed to stabilize the body's sugar-regulating system is sometimes recommended.

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