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Eating Fish to Prevent Sudden Death

By Matthew Sorrentino, MD

INCREASING EVIDENCE SUGGESTS THAT A MEDITERRANEAN DIET RICH in monounsaturated fatty acids and omega-3 fatty acids can help reduce cardiac mortality. The American Heart Association Nutrition Committee released a report in 1996 stating that the inclusion of marine sources of omega-3 fatty acids in the diet was reasonable and potentially highly beneficial.[1] Recent studies have further clarified the role of cold water fatty fish, such as salmon, herring, mackerel, and tuna, in the diet.

Physiological Effects

Fish oils have effects. Such effects include an antiarrhythmic effect; favorable changes in some lipoprotein levels, especially serum triglyceride levels; improved vascular function; reduced thrombotic effect, probably by decreasing platelet aggregation; and lowered blood pressure.

Kang and Leaf reviewed a series of studies which showed that the intravenous administration of omega-3 fatty acids can prevent ischemia-induced malignant ventricular arrhythmias in an animal model.[2] These investigators concluded that omega-3 fatty acids reduce the electrical excitability of myocytes, probably by binding to sodium channels, thus effecting an antiarrhythmic effect.

Numerous studies have evaluated the lipoprotein effects of fish oils. A meta-analysis and summary of the best designed trials showed that an average intake of 4 g/d of omega-3 fatty acids decreased triglyceride levels by 25% in normal individuals and 34% in hypertriglyceridemic subjects.[3] Low-density lipoprotein (LDL) cholesterol rose 5-10% and high-density lipoprotein (HDL) cholesterol increased minimally by 1-3%. Further evaluation should determine if the triglyceride lowering effects of fish oils change the atherogenicity of LDL particles and if the increase in total LDL cholesterol is clinically important.

Fish oils may also have a direct effect on vascular function. An in vitro study of hypercholesterolemic individuals has shown a significant improvement in endothelial function of small arteries after three

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months of high-dose fish oil supplementation.[4] This effect is probably independent of the lipoprotein effects because there was no statistically significant difference in lipoprotein values in this study.

Multiple studies have evaluated the effect of omega-3 fatty acids on platelet aggregation. A recent study attempted to determine the effects of dietary fat, dietary fish, and fish oil capsules on platelet function.[5] All groups taking omega-3 fatty acids had reduced platelet aggregation. Dietary fish was found to have a greater effect on platelet function when fish was part of a low-fat diet. Since platelets play a critical role in thrombus formation in patients with atherosclerotic disease, omega-3 fatty acids may work in part like aspirin and prevent cardiac events by inhibiting the formation of a thrombus associated with plaque rupture.

The effect of fish oils on blood pressure has been variable. A meta-analysis of 31 trials showed a small but significant effect of fish oil, lowering blood pressure approximately 3 mm Hg systolic with a mean dose of 4.8 g/d of omega-3 fatty acids.[6] This effect was more likely to be noted in hypertensive individuals.

Table 1

Dietary sources of omega-3 fatty acids

Food Source	Omega-3 Fatty Acids per 100 g Serving
Atlantic mackerel	2.5 g
Salmon	1.2-1.4 g
Canned sardine	1.7 g
Eel	1.7 g
Herring	1.6 g
Bluefish	1.2 g
Squid	0.9 g
Striped bass	0.8 g
Rainbow trout	0.5-1.0 g
Tuna	0.3 g
Flounder	0.2 g

Adapted from: Linder MC, ed. *Nutritional Biochemistry and Metabolism.* 2nd ed. Norwalk, CT: Appleton and Lange; 1991.

Epidemiological Evidence

Early epidemiological studies have suggested that populations consuming higher levels of fish have lower coronary mortality than populations eating a typical North American diet.[7] The mechanism of this apparent protective effect is unknown but may include favorable changes in lipoprotein profiles, antithrombotic effects, or antiarrhythmic effects.

Recently the Physicians' Health Study group reevaluated the cohort of more than 20,000 U.S. male physicians and assessed their fish consumption to help clarify the potentially protective effects of fish in the diet.[8]

One hundred thirty-three sudden deaths were reported in the trial. Dietary fish was associated with a reduced risk of sudden death and total mortality. These benefits were noted with the consumption of one fish meal per week or greater. There was, however, no associated change in the risk of myocardial infarction or non-sudden cardiac death. These findings suggest that a component of fish may have antiarrhythmic qualities that may prevent cardiac arrest.

Clinical Studies

Prescribing a diet rich in fish oils may offer protection against sudden cardiac events. The GISSI investigators reported a secondary prevention trial of patients who had recently had a myocardial infarction.[9]

Patients were randomized to a daily dose of omega-3 fish oil capsules (850-882 mg eicosapentenoic acid and docosahexenoic acid) in addition to a Mediterranean diet (100 g [3.3 oz] of fatty fish per day). Treatment with the fish oil capsules significantly decreased the primary endpoints of death, nonfatal myocardial infarction, and

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stroke in treated individuals. The latter two benefits were primarily attributable to a decrease in the risk of death, again suggesting that an antiarrhythmic effect may be important.

The traditional Mediterranean diet is rich in fish and plant fatty acids, and lean in red meat and saturated fats. The diet has been championed as cardioprotective. To test whether a Mediterranean diet compared with a Western diet may reduce the risk of cardiac events after a first myocardial infarction, investigators initiated and designed the Lyon Diet Heart Study—a randomized, single-blind secondary prevention trial.[10] The combined outcome of cardiac death and nonfatal myocardial infarction was significantly reduced in the Mediterranean diet group as opposed to the Western diet group. This protective effect was maintained up to four years after the first heart attack. The study was not designed to determine which factor of the diet may have provided the benefit. These results support the recent findings of the GISSI study group.

Dosage and Formulation

A minimum of one fish meal per week seems to give benefit. (*See Table 1 for dietary sources of omega-3 fatty acids.*) There is no evidence of a dose effect since the Health Professionals Follow-up Study found that increasing doses of fish did not further decrease the risk of heart disease.[11] The GISSI trial is the first major trial to suggest that fish oil capsules at a reasonable dose of less than 1 g/d may give the same benefit as fish in the diet, although all patients in this trial were instructed to eat a Mediterranean diet as well.

Adverse Effects

Possible side effects of fish oil capsules are listed in Table 2.

Table 2

Potential side effects of fish oil capsules

- Fishy odor, gastrointestinal upset
- May increase bleeding time
- Increase caloric intake and weight gain
- May increase LDL cholesterol in some individuals
- May decrease immune response
- Unrefined fish oil preparations may contain pesticides
- Vitamin A and D toxicity with some preparations

Source: Stone NJ. Fish consumption, fish oil, lipids, and coronary heart disease. *Circulation* 1996;94:2337-2340.

Conclusion

The GISSI trial and the Lyon Diet Heart Study support the recommendations of the American Heart Association Nutrition Committee.[1] There is compelling evidence that a diet rich in omega-3 fatty acids is protective against sudden cardiac events. Omega-3 fatty acids may function as antiarrhythmic agents in patients with ischemic heart disease as well as lower triglyceride levels, improve endothelial function, decrease thrombogenicity, and slightly lower blood pressure.

Recommendation

We recommend inclusion of at least one to two marine fish meals per week in the diet of all patients with coronary heart disease or with risk factors for heart disease. We prefer fish in the diet to fish oil capsules since dietary fish appears to be effective, less expensive, and better tasting, and free of the potential side effects of the fish oil capsules. In addition, a Mediterranean diet may contain antioxidants and additional fatty acids (such as the monounsaturates within olive oil) that may offer further cardiovascular benefits. ❖

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Cordyceps for Improved Energy Levels and Sports Performance

By Dónal P. O'Mathúna, PhD

CORDYCEPS IS AN ANCIENT CHINESE HERBAL REMEDY made from the fungus *Cordyceps sinensis*. The fungus grows in the Himalayan regions of China and Tibet. Public attention was drawn to the herb when unknown female Chinese runners swept the long-distance events at the 1993 world championships and later broke a number of world records.[1] The following year, female Chinese swimmers performed similarly at their world championships.[2] In spite of many accusations, Chinese coaches denied their athletes were using banned drugs, and instead attributed the improvements to rigorous training and a special diet that included cordyceps.

Could this product bring such amazing performance improvements to athletes? If it benefits athletes, what might it do for your patients' everyday energy levels?

Background

Cordyceps has been used for centuries in China as a food supplement and tonic beverage, but only for the very rich because of a limited supply. Harvesting cordyceps remains controversial because devout Buddhists living where cordyceps grows naturally view the fungus as sacred, and oppose harvesting it for profit. The scarcity of the wild form stimulated researchers to produce strains that could be grown using fermentation technology.[3] These products have allowed widespread use of cordyceps. The most commonly used extract is called Cs-4 and is available in the United States as CordyMax™ (Pharmanex, Inc.).

Life Cycle

The Latin term *cordyceps* means "swollen head" and its Chinese names convey some of the fungus' fascinating appearance and life cycle. Half of the three-inch-long harvested fungus looks like a mummified caterpillar and the other half looks like a brown blade of grass. Its Chinese names literally mean "winter worm, summer grass" or "caterpillar fungus."[4] The parasitic fungus grows inside several caterpillar species during winter until nothing remains except a mummified caterpillar shell. When summer arrives, the cordyceps' fruiting body bursts through the caterpillar's head, looking like a blade of grass.

General Uses

Cordyceps is traditionally used as a general tonic or to rejuvenate people after sickness or overexertion. It is said to be more potent than ginseng. The herb is also used to treat a wide variety of illnesses, including respiratory, renal, liver, and cardiovascular diseases, sexual dysfunction, hyperlipidemia, and cancer.

Pharmacology

Cordyceps extracts contain a wide variety of constituents, including proteins, unusual cyclic dipeptides, sugars, sterols, nucleosides, fatty acids, vitamins, and minerals.[3] It contains a relatively high level of adenosine and adenosine derivatives. Adenosine is a vital constituent of DNA, RNA, and adenosine triphosphate (ATP), the high-energy molecule fueling many cellular processes. Cordyceps extracts also contain high levels of the essential amino acid tryptophan (24 mg/g), which can have a calming effect on humans.[4]

Mechanism of Action

According to traditional Chinese medicine, the components in cordyceps go to the lung and kidney Qi meridians to provide lung protection, kidney improvement, and "Yin-Yang double invigoration."[3]

The mechanism of action for cordyceps is poorly understood, but a number of active ingredients have the potential to impact exercise performance.

Mice fed a cordyceps extract showed a significantly higher ATP/inorganic phosphate (Pi) level ($P < 0.05$) compared to controls.[5] This metabolic high energy state returned to normal within one week of stopping cordyceps supplementation. A number of other Chinese studies with mice fed Cs-4 water extracts (0.2 or 0.4 g/kg) gave an average ATP/Pi ratio increase of 45-55% ($P < 0.001$).[3] Higher ATP levels could in theory boost sports performance, primarily in short-duration events.

Use of cordyceps in treating respiratory diseases led to several Japanese studies showing that cordyceps relaxes the trachea of animals and allows better ventilation.[4]

Other studies show that cordyceps can activate the immune system, with the potential to speed recovery from exercise or illness.[6] Its proposed anticancer effects may also be mediated through an immune response.[7] Finally, studies on the use of cordyceps for sexual dysfunction revealed some male sex hormone-like effects in rabbits and castrated mice.[3] All of these mechanisms and effects are intriguing, but none have demonstrated improved athletic performances with cordyceps.

Clinical Studies

The results of extensive animal and clinical research in China are available primarily in Chinese. However, Zhu, Halpern, and Jones recently reviewed this research in English, making the conclusions available to Western medicine.[3,8] Their review found studies to support many of the uses of cordyceps. They did not state how exhaustively they searched the Chinese literature, and discussed only studies with positive results. The authors did describe an unpublished, uncontrolled study in which 82.9% of patients with respiratory diseases performed better on a 200-meter jog compared to 40.2% of those taking another herbal remedy.[3]

Only one exercise-related clinical study was found after a search of MEDLINE, TOXLINE, International Pharmaceutical Abstracts, Conference Papers Index, and the Cochrane Library. This 1999 study with CordyMax was a placebo-controlled trial involving 30 healthy, elderly people.[9] Sixteen subjects (average age, 64 years) took 3 g/d cordyceps for six weeks while the control group (n = 14; average age, 66 years) took identical placebo capsules. Exercise performance was measured before and after treatment using a cycle ergometer.

Those taking cordyceps increased their VO_{2max} from 1.88 to 2.00 L/min (P = 0.05) while the values for the placebo group were unchanged. The anaerobic thresholds for those taking cordyceps increased from 1.15 to 1.30 L/min (P = 0.01), while a non-significant decrease occurred in those taking the placebo.

Adverse Effects

Some animal researchers report being unable to attain an LD_{50}, as no mice died within seven days of being given 80 g/kg.[8] Cordyceps caused no liver damage to mice at 200 mg/kg/d.[5] Animals fed cordyceps for three months showed no detectable differences compared to controls.[8] Subjects in clinical trials report some mild GI discomfort, such as dry mouth, nausea, and stomach discomfort, and one patient had an allergic reaction.[8]

Drug Interactions

Drug interactions have not been studied. Research has shown that cordyceps has monoamine oxidase (MAO) inhibitory effects, warranting caution with patients taking other MAO inhibitors or consuming foods containing large amounts of tyramine.[3] Cordyceps can interfere with platelet aggregation and may magnify anticoagulant therapy.[10] Its effect on relaxing the trachea may also accentuate epinephrine bronchodilators.[4]

Formulation

CordyMax contains 525 mg of a dried extract standardized to contain at least 0.14% adenosine. The extract is made from cultivated *Cordyceps mycelia* (the underground portion of the fungus). The manufacturer recommends taking two capsules, two or three times daily. The traditional recommendation is to include 3-9 g/d cordyceps in a hot tea or cooked meals.

Conclusion

Cordyceps enjoys a long tradition of use in China. Recent fermentation technology has overcome scarcity problems, making it available to consumers and researchers. Early results show it contains numerous biologically active ingredients. Some of these lend support to the wide variety of conditions for which cordyceps is traditionally used. Very little clinical evidence exists regarding cordyceps' effects on exercise performance, though limited results are encouraging, at least for the elderly. No clinical studies were found on its effect on athletic performance.

Recommendation

It is premature to recommend cordyceps to patients: Too little is known. The wide variety of active ingredients present in cordyceps suggests caution in those already taking other medications, especially MAO inhibitors, anticoagulants, and bronchodilators. Athletes considering using cordyceps can rely only on anecdotal evidence, though the improvements seen among Chinese athletes are intriguing, and cordyceps by itself appears to be very safe. Dietary supplements, however, will never replace the need to train, whether for general exercise benefits or a competitive edge. ❖

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Hypnosis for Treatment of Acute, Malignancy-Related, and Chronic Pain

By Nicole Nisly, MD
and Teresa Klepser, PharmD

DESPITE THE ADVENT OF EFFECTIVE PHARMACOLOGICAL interventions, pain remains a difficult and prevalent problem. This is particularly troublesome to clinicians facing children who need to undergo multiple painful procedures or older patients fearing and suffering from advanced malignancy. Despite the recognized importance of psychosocial and behavioral factors in pain perception and response, treatment strategies have focused primarily on biomedical interventions such as drugs and surgery. Pain may be classified as acute, cancer-related, or chronic nonmalignant. We assess below the evidence for the use of hypnosis as an effective adjunctive or alternative procedure in the treatment of pain.[1]

Historical Background

In the 18th century, Franz Mesmer made popular the use of hypnosis, also known as mesmerism. About 40 years ago, the American Medical Association recognized hypnosis as a valid medical technique. Recently, renewed interest in this technique has merited its use in a variety of conditions with strong psychological components, such as asthma, insomnia, irritable bowel syndrome, and acute and chronic pain syndromes. Recent hypnosis studies have improved our understanding of mechanism of action. A growing number of randomized controlled trials (RCTs) in the field of psychoneuroimmunology are adding scientific heft to historical models.

Definition

Hypnosis induces a deeply relaxed state with increased suggestibility, in which emotional and physiological responses can be modified and modulated. This deeply relaxed state permits selectively focused attention. In combination with enhanced imagery,[1] a patient's selective focusing can be used to therapeutic benefit. (*See box on page 31 for hypnosis terminology.*)

Mechanism of Action

Hypnosis may alleviate pain by blocking pain's neurological pathways. Two pain transmission circuits[1] have been suggested: 1) A spinal cord-thalamic-frontal-cortex-anterior cingulate pathway may play a role in the subjective psychological and physiological responses to pain, and 2) The spinal cord-thalamic-somatosensory cortex pathway may play a role in pain sensation.

It has been hypothesized that hypnosis blocks pain impulses from entering consciousness by activating the frontal-limbic attention system, thus inhibiting pain impulse transmission from thalamic to cortical structures.

Hypnosis does not appear to influence endorphin production, and its role in the production of catecholamines is unknown.

Procedure

A typical treatment course for a patient with chronic pain takes place over four or five sessions lasting 45-60 minutes each.

In the first session, the therapist assesses the pain characteristics, identifies associations between pain sensation and emotions or images, and describes the procedure. The therapist attempts to assess which images cause relaxation for the patient and which hypnotic suggestions may be well accepted based on the patient's emotions and personal belief system.

The patient is then guided to a state of deep relaxation, through the use of imagery, deep breathing, or progressive muscle relaxation. When that state is achieved the therapist may suggest that the patient visualize being

in a pleasant place rather than the procedure room or change the image of pain from a dark gloomy color to a bright, pleasant one.

During the next sessions, the therapist will repeat the procedure, evaluate the response, and modify the suggestion technique and content to produce the desired outcome. The therapist will teach the patient to induce hypnosis at home by following the same procedure learned at the therapist's office. A tape recording of the therapist's suggestions may be used to help the patient achieve the desired response.

Human Studies—Acute Pain

Some evidence exists that hypnosis may be used for reducing postoperative pain and the pain of procedures. Ashton et al evaluated 32 patients undergoing elective coronary bypass surgery for the first time, in an age- and gender-stratified RCT using self-hypnosis vs. standard care control.[2] The night before surgery, patients were instructed to focus on and practice breathing deeply, relaxing their jaw and throat muscles, keeping the incisions free from infection, minimizing bleeding, reducing pain and discomfort, and maintaining normal blood pressure. After surgery, they were asked to practice relaxing to reduce pain, discomfort, and infection; to normalize blood pressure and appetite; to heal quickly; and to return to "normal or customary lifestyle."

The authors evaluated the use of intra-operative pharmacotherapy, the amount of analgesic needed for the five initial postoperative days, the Profile of Mood States (POMS), and the length of intensive care and hospital stay. The self-hypnosis group showed a significant reduction in tension (POMS) or anxiety following surgery. No significant differences were found in any other POMS categories. Patients who practiced the self-hypnosis technique postoperatively (65% of hypnosis group) used significantly less medication than those who did not. No other significant differences were found between the groups, including differences in medication use. Three complications, including a sternal dehiscence, occurred in the hypnosis group; one occurred in the control group. Study weaknesses include the small number of patients and the fact that measures of pain were not assessed objectively.

Lang and colleagues evaluated the ability of self-hypnotic (SH) relaxation during interventional radiological

Hypnosis Terminology[1-3]

Hypnotic Trance or Pre-Suggestion Component is a deeply relaxed state with increased suggestibility and reduced critical faculties. Trances involve attention focusing through the use of imagery, distraction, or relaxation. Subjects focus on relaxation and disregard intrusive thoughts.

Direct Hypnotic Suggestion is a proposal made to a person in a hypnotic trance or a deeply relaxed state, characterized by the introduction of specific goals. The suggestion encourages changes in behavior, in the perception of symptoms, or in the control of physiological bodily functions. Examples of therapeutic direct hypnotic suggestions include reducing anxiety during dental procedures, decreasing perception of pain during labor, and controlling bleeding during surgery.

Post-Hypnotic Component is a proposal made to a person during hypnotic trance or deeply relaxed state which involves continued use of a new behavior, following termination of hypnosis. The post-hypnotic component aims to alter behavior, perception, or physiological control. Examples are recommending smoking cessation and teaching the ability to self-hypnotize. The ability to create self-hypnosis is the most important outcome from hypnosis teaching because it allows patients to recreate what the therapist has taught them.

Hypnotizability is how readily people respond to hypnosis techniques. Measured on scales or tests that score responsiveness to suggestion, a person's hypnotizability can be graded as high, medium, or low. The ability to respond to many or a few suggestions is distributed on a bell-shaped curve. People who are low on hypnotizability can improve their response with practice.

Hypnotizability Scales are qualitative and quantitative measures of a person's ability to respond to suggestions following hypnotic induction. Typically a trained hypnotist will read a script consisting of a hypnotic induction, followed by a series of test suggestions that vary in difficulty level. ❖

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procedures to reduce the need for intravenous sedation.[3] In a pilot study, 16 male patients were randomized to the SH group and 14 to the control group. Both groups had patient-controlled analgesia. The hypnotherapy staff gave the SH group very brief self-hypnosis training and performed a Hypnotic Induction Profile Test prior to beginning the procedure. The therapist accompanied the patients throughout the length of the procedure and continually reinforced the hypnotic suggestion.

The SH group had significantly less use of medication (12/16 in the SH group did not request medication at all vs. 1/14 in the control group). Pain was classified on a scale of 0 to 10. The maximum pain perception in the SH group (2/10) was much lower than in the control group (5/10). Oxygen desaturation and hemodynamic instability were noted to be worse in the control group. Actual benefit did not correlate with individual hypnotizability.

Based on this pilot, in 1998 the National Center for Complementary and Alternative Medicine (NCCAM) at the NIH funded a larger controlled study at the University of Iowa, now awaiting publication.

Patterson reports a RCT of 61 burn patients undergoing painful treatments.[4] Two groups (hypnosis and control attention/relaxation group) had a VAS (visual analogue scales) measurement of pain at two consecutive daily wound debridement sessions. On the first day, both groups submitted baseline VAS ratings. On the second day, subjects received either hypnosis or control attention/brief relaxation instructions from a psychologist during debridement. The post-treatment VAS scores of the two groups did not differ, but hypnosis patients who reported high baseline levels of pain reported less post-treatment pain. The same author participated in two other burn-unit studies,[5,6] yielding conflicting results.

Human Studies—Cancer-Related Pain

Liossi and Hatire conducted a RCT comparing the efficacy of clinical hypnosis vs. cognitive behavioral coping skills (CBCS) vs. no intervention for alleviating pain and distress of 30 pediatric patients (ages 5-15 years) undergoing bone marrow aspirations.[8] Assessment of pain and pain-related anxiety involved both behavioral observation and self-reports. Nurses observing the procedure completed the Procedure Behavior Checklist, a checklist of distress behaviors. The hypnosis and CBCS groups reported less pain and anxiety than the control group. A self-reported pain scale and an observed distress grading system completed by the nurse observing the procedure indicated that hypnosis and CBCS were similarly effective for pain. Hypnosis was more effective than CBCS for anxiety and distress. The study concluded that hypnosis and CBCS are effective in preparing pediatric patients for bone marrow aspirations.

Syrjala conducted a RCT evaluating the effectiveness of psychological techniques for reducing cancer pain and post-chemotherapy nausea or vomiting in 67 adult, bone marrow patients with hematological malignancies.[9] Prior to the beginning of the treatment, patients were randomized to four groups: hypnosis (HYP), cognitive behavioral coping skills training (CBCST), therapist attention control (TC), and treatment as usual (TAU) control group. Patients in the HYP, CBCST, and TC groups met with a clinical psychologist for two pretransplant sessions and a total of 10 sessions during the course of transplantation.

Forty-five patients completed the study. Analysis of the study variables indicated that hypnosis was effective in reducing reported and nurse-observed/nurse-rated oral pain from chemotherapy-related mucositis, but opioid use did not differ significantly between the groups. The other symptoms measured, including nausea and vomiting, did not differ significantly between the four groups.

Steggles published an extensive annotated bibliography of the scientific literature published in English from 1985-1995. The bibliography included 37 articles on hypnosis and pediatric cancer patients and covered case reports or studies to experimental and non-experimental group designs.[10] In 1995, an NIH Technology Assessment group concluded that hypnosis' evidence of effectiveness for cancer-related pain is strong.[1]

Human Studies—Chronic Nonmalignant Pain

Haanen conducted a RCT on 40 patients with refractory fibromyalgia, randomized to either hypnosis or physical therapy for 12 weeks and then followed for another 12 weeks.[11] The hypnosis group had significantly less pain and fatigue and had better sleep and global assessments at 12 and 24 weeks. But these improvements were not reflected in an improvement of the "total myalgic score," measured with a dolorimeter.

Dinges followed prospectively a cohort of patients (children, adolescents, and adults) with sickle cell disease who reported experiencing three or more episodes of vaso-occlusive pain the preceding year.[12] Following a four-month baseline phase of conventional treatment only, the patients received self-hypnosis training sessions that were implemented over an 18-month period. The sessions took place once a week for the first six months, biweekly for the second semester, and every third week for the remaining six months. This intervention was associated with a significant decrease in the number of "pain days" and the use of pain medications during the self-hypnosis intervention

period. Sleep also improved.

Safety

Gravitz describes difficulties in ending the hypnotic trance in two subjects: a medical resident participating in a workshop and a 36-year-old women with chronic pain.[13,14] Other similar isolated communications were reported in the literature and reviewed by this author. Concerns have been raised about using these therapies with individuals who have psychotic conditions as well as personality disorders.[15] These individuals should be treated only under the supervision of an experienced, licensed health care provider with expertise in the use and limitations of hypnosis in the setting of psychiatric disorders.[16]

Training and Scope of Practice

Only health care professionals authorized to see patients, including PhD psychologists, counselors, and social workers licensed in counseling, can perform hypnosis. A Certified Hypnotist credential requires 40 hours of education and training, a health care professional degree, and two years' experience using hypnosis in clinical practice. A Consulting Hypnotist credential requires 120 hours of education and training, a health care professional degree, and evidence of advanced standing in their primary profession.[17]

Hypnosis training is not considered sufficient to allow for independent practice. The American Psychological Association (APA) Division of Psychological Hypnosis states that hypnosis is not a treatment in and of itself, like psychoanalysis or behavior therapy, but rather a procedure used to facilitate therapy. The APA believes that clinical hypnosis should be performed only by qualified health care professionals who use this procedure within the scope of their specific area of professional expertise.[16] For example, a dentist or a social worker may use hypnosis within a profession-specific scope of practice and follow the standards dictated by their particular state licensing boards.[16,17] Of course, the patient needs to consent to the use of hypnosis by any health care professional.

Compensation

The charge for hypnosis depends on the setting and the geographic location. A one-hour session with a PhD psychologist may cost from $70-150. Hypnosis may be offered as a small portion of the consultation or treatment, as with a dentist or interventional radiologist providing hypnosis in place of medication, analgesia, or sedation. The charge typically would not be coded as hypnosis, but as stress management, counseling, or pain management, and as such, may be covered by insurance.

Conclusion

In a patient population subject to life-long unpredictable episodes of pain and for whom few safe, cost-effective medical alternatives exist, an adjunctive program that involves regular contact with a self-hypnosis team and emphasizes patient self-management techniques is very appealing. Hypnosis appears to be effective and safe as an adjunct or substitute for pharmacological treatment of acute pain and anxiety related to painful medical procedures for both adults and children.[3] It may be helpful in the treatment of burns,[7] but further studies are needed to confirm this. It is effective as an adjunct treatment of chronic pain associated with cancer, specifically that related to oral mucositis.

Recommendation

Hypnosis should be considered in the adjunctive treatment of acute, chronic, and cancer-related pain, when serious mental health illness has been ruled out. Hypnosis should be administered under the supervision of a licensed health care professional who is trained in the use of hypnosis and who is using this procedure within his or her scope of practice and training. ❖

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Note to Readers

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CME Questions

15. Omega-3 fatty acids have been shown to:
a. reduce platelet aggregation.
b. decrease risk of nonfatal myocardial infarction and stroke.
c. lower triglyceride levels.
d. All of the above.

16. Fish oil capsules have fewer side effects and are preferred over dietary fish.
a. True
b. False

17. The nucleoside found in high quantities in cordyceps is:
a. adenosine.
b. guanine.
c. cytosine.
d. thymine.

18. The available evidence for the exercise performance enhancement effects of cordyceps is based on a study with:
a. trained athletes.
b. recreational joggers.
c. elderly people.
d. teenagers.

19. In clinical trials of self-hypnosis:
a. patients had a significant reduction in tension and anxiety and used significantly less medication postoperatively.
b. chronic pain patients experienced no change in the number of pain days.
c. None of the above.

With Comments from John La Puma, MD, FACP

Aerobic Exercise and Breast Cancer Risk

Source: Rockhill B, et al. A prospective study of recreational physical activity and breast cancer risk. *Arch Intern Med* 1999;159:2290-2296.

INCREASED PHYSICAL ACTIVITY HAS been hypothesized to prevent breast cancer, largely by reducing cumulative lifetime exposure to circulating ovarian hormones.

We analyzed data from the Nurses' Health Study, a prospective study of women aged 30-55 years in 1976. In 1980 and on subsequent surveys, women were asked about the average number of hours per week spent in various moderate and vigorous recreational physical activity during the past year. We computed a "baseline-only" (1980) measure of hours per week of physical activity, as well as a cumulative average measure that used updated reports on physical activity.

During 16 years of follow-up, we identified 3,137 cases of invasive breast cancer (1,036 premenopausal and 2,101 postmenopausal women). Data were analyzed by use of multivariate pooled logistic regression to produce relative risks of breast cancer, and the associated confidence intervals.

Women who were more physically active in adulthood had a lower risk of breast cancer than those who were less physically active. Comparing those who reported engaging in moderate or vigorous physical activity for seven or more hours per week with those who engaged in such physical activity for less than one hour per week, the relative risk was 0.82 (95% confidence interval [CI] 0.70-0.97), using the cumulative average updating. The dose-response trend was statistically significant (P = 0.004). Using the baseline-only measure of physical activity produced slightly weaker relative risks. Higher levels of adult physical activity afford modest protection against breast cancer.

COMMENT

In this epidemiological study, Harvard-associated investigators show once again that a few hours of prevention is worth more than a few minutes. And time does seem to be the relevant variable, one which Americans have less of every day. Women concerned about what they can do to reduce their risk for breast cancer may have to take the long road, but it looks like it may lead where they want to go.

The evidence for breast cancer risk reduction techniques is much better than the evidence for breast cancer treatment or prevention against recurrence. Nevertheless, an eight-week pilot study of an exercise-diet intervention in breast cancer patients in Seattle (*Cancer Epidemiol Biomarkers Prev* 1998;7:477-481) indicated that Stage 1 and 2 breast cancer patients who attended aerobic exercise sessions three times weekly and ate a low-fat diet (20% calories from fat), lost weight, inches, body fat, and blood pressure points, and gained lean body mass. Obesity, of course, is a risk factor for breast cancer development.

Recommendation

Women, especially those at risk for breast cancer, should include regular aerobic exercise as a central part of their prevention regimen. ❖

Vitamin C and E Supplementation and Pre-eclampsia

Source: Chappell LC, et al. Effect of antioxidants on the occurrence of pre-eclampsia in women at increased risk: A randomised trial. *Lancet* 1999;354:810-816.

OXIDATIVE STRESS HAS BEEN IMPLIcated in the pathophysiology of pre-eclampsia. Two hundred eighty-three women were identified as being at increased risk of pre-eclampsia by abnormal two-stage uterine-artery Doppler analysis or a previous history of the disorder. They were randomly assigned vitamin C (1,000 mg/d) and vitamin E (400 IU/d) or placebo at 16-22 weeks' gestation. Plasma markers of endothelial activation (plasminogen-activator inhibitor 1 [PAI-1] and placental dysfunction [PAI-2]) were measured every month until delivery. The ratio of PAI-1/PAI-2 is high in pre-eclampsia, and normal in normal pregnancies. Pre-eclampsia was assessed by the development of proteinuric hypertension, according to the International Society for the Study of Hypertension in Pregnancy Guidelines. Analyses were done by intention to treat in the cohort that completed the study.

Supplementation with vitamins C and E was associated with a 21% decrease in the PAI-1/PAI-2 ratio during gestation (95% CI 4-35, P = 0.015). In the intention-to-treat cohort, pre-eclampsia occurred in 24 (17%) of 142 women in the placebo group and 11 (8%) of 141 in the vitamin group (adjusted odds ratio [OR] 0.39 [0.17-0.90], P = 0.02). Of those in the cohort who completed the study (81 placebo group, 79 vitamin group), the OR for pre-eclampsia was 0.24 (0.08-0.70, P = 0.002). Supplementation with vitamins C and E may be beneficial in the prevention of pre-eclampsia in women at increased risk of the disease.

COMMENT

Pre-eclampsia still has little effective treatment: Diuretics, magnesium, zinc, fish oils, and antihypertensives have only modest effects, and sometimes none at all.

This well-done, impressive study was stopped at the interim analysis because the outcome ratio was already statistically different. The ratio could not be compared between groups: Some women were dropped at 24 weeks because of nonadherence, transfer of care, and unwillingness to continue.

Only high-risk women were studied.

Vitamins C and E are considered Pregnancy Category A drugs in doses up to the RDA. There is a single case report linking anencephaly and high-dose vitamin C (and in this case, multiple other nutrients and drugs); I was unable to find case reports for infants harmed by vitamin E.

Whether supplementation reduces the incidence of pre-eclampsia in low-risk women; whether the timing and dosages are optimal; and whether food containing 1,000 mg of vitamin C has the same effect (food with 400 IU of vitamin E has way too many calories even for those eating for two) should be studied.

Recommendation

Women at high risk for pre-eclampsia should know about these results, and strongly consider supplementing with 1,000 mg vitamin C and 400 IU vitamin E in mid-pregnancy, if not before. ❖

Vegan Diet and Diabetes Management

Source: Nicholson AS, et al. Toward improved management of NIDDM: A randomized, controlled, pilot intervention using a lowfat, vegetarian diet. *Prev Med* 1999; 29:87-91.

We investigated whether glycemic and lipid control in patients with non-insulin-dependent diabetes (NIDDM) can be significantly improved using a very low-fat, vegetarian (vegan) diet. Thirteen subjects with NIDDM (ages 34-74) recruited from the community were randomly assigned to a very low-fat high complex carbohydrate vegan diet (seven subjects) or a conventional low-fat diet (four subjects); 11 completed the study. The diets were not designed to be isocaloric. Fasting serum glucose, body weight, medication use, and blood pressure were assessed at baseline and biweekly thereafter for 12 weeks. Serum lipids, glycosylated hemoglobin, urinary albumin, dietary macronutrients, and exercise levels were assessed at baseline and 12 weeks.

We observed a 28% mean reduction in fasting serum glucose in the experimental group, from 10.7 to 7.75 mmol/L (195 to 141 mg/dL), which was significantly greater than a 12% decrease, from 9.86 to 8.64 mmol/L (179 to 157 mg/dL), for the control group ($P < 0.05$). The mean weight loss was 7.2 kg in the experimental group, and 3.8 kg in the control group ($P < 0.005$). Of six experimental group subjects on oral hypoglycemic agents, medication use was discontinued in one and reduced in three. Insulin use was reduced in both experimental group patients on insulin. No patient in the control group reduced medication use.

Differences between the diet groups in the reductions of serum cholesterol and 24-h microalbuminuria did not reach statistical significance; however, high-density lipoprotein concentration fell more sharply (0.20 mmol/L) in the experimental group than in the control group (0.02 mmol/L) ($P < 0.05$). The use of a very low-fat, vegan diet in patients with NIDDM was associated with significant reductions in fasting serum glucose concentration and body weight in the absence of recommendations for exercise.

COMMENT

Most type II diabetic patients are obese. Current nutritional wisdom counts on counting carbohydrates for better glycemic control. These investigators took a different approach.

They show that motivated, overweight, and medication-dependent diabetics can eat a very low-fat diet, reduce their body weight, and lower their fasting glucose levels over a 12-week period. Changes in glycosylated hemoglobin were not significantly different between the two groups at 12 weeks.

These investigators prescribed Dean Ornish's original heart disease reversal diet, minus the egg whites: 10-15% protein, <10% fat, and the remainder ad lib unrefined complex carbohydrates. B_{12} supplements alone were recommended after the study period. Catered lunches and dinners were distributed over the 12-week study; most participants used them. Twice-weekly support groups of uncertain duration and participation, as well as cooking and nutrition classes, were offered. Subjects met with a physician or a nurse every two weeks to assess medication needs, and to measure vital signs, weight, and fasting glucose.

Weaknesses in this study include the small numbers over a short period; inequalities at baseline in exercise and urinary albumin; uncertainty about the method of randomization; and the likely difficulty in reproducing these methods in a general or even specific population. It is not clear whether the benefit derived was from the diet or from weight loss.

Recommendation

Recommend that your diabetic patients find a medically based weight management plan that serves them when eating in and when eating out, for the long term. The healthiest way to do this overall is to put fruits, vegetables, grains, and legumes in the middle of the plate, and fish and other animal foods on a side plate. ❖

In Future Issues:

Turmeric as an Anti-Inflammatory

Chromium for Treatment of Diabetes

Acupuncture for Allergies

Homeopathy for Otitis Media

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Supplement to *Alternative Medicine Alert*
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ALTERNATIVE MEDICINE ALERT™

A Clinician's Guide to Alternative Therapies

Clinician Fact Sheet: Review of Herbal Supplements

Cranberry (*Vaccinium macrocarpon* Ait. Family: Ericaceae)

1998 Retail Sales: $10,378,810[1]

Part Used: Juice and extract from ripe fruit

Intended Indications
Prevention of urinary tract infections

Formulation and Dosage
- 300-400 mg of concentrated cranberry juice extract bid
- 300 ml/d commercial cranberry juice cocktail drink

Adverse Effects
Doses in excess of 3 L/d can produce GI upset and diarrhea; diabetic patients should use sugar-free varieties of cranberry juice; lactating women, children under 12 years, and patients with a history of oxalate stones should limit intake to 1 L/d

Interactions
- No significant interactions have been reported

Contraindications
- No significant contraindications have been reported
- Safety not determined in pregnancy and lactation, but likely safe at food doses

Valerian Root (*Valeriana officinalis* L. Family: Valerianaceae)

1998 Retail Sales: $8,650,521[1]

Part Used: Root

Intended Indications
Anxiety, insomnia, nervousness, stress

Formulation and Dosage
- For anxiety, nervousness, and stress, 2-3 g/d dried valerian root as tea or in capsules up to four times daily
- For chronic insomnia, 600 mg dried aqueous/alcoholic extract standardized from 0.4-0.8% valerenic acid, 1-2 hours before bedtime
- For full effect in chronic insomnia, take for at least two weeks and preferably four weeks

Adverse Effects
Generally well-tolerated, classified as GRAS for food use, occasional mild morning sedation and headache

Interactions
- Valerian may potentiate other sedatives

- Although valerian does not potentiate the effects of alcohol, it should not be combined with alcohol

Contraindications
- Valerian should not be used concomitantly with other sedatives or alcohol
- Patients should avoid driving and operating machinery for several hours after taking valerian
- Safety not determined in pregnancy and lactation

Evening Primrose (*Oenothera biennis* L. Family: Onagraceae)

1998 Retail Sales: $8,552,860[1]

Part Used: Seed oil from flowers

Intended Indications

Atopic and irritant contact dermatitis, atopic eczema, cardiovascular disease, diabetes-related problems, endometriosis, mastalgia, multiple sclerosis, PMS, rheumatoid arthritis, Sjögren's syndrome

Formulation and Dosage
- Most products contain 300 mg linoleic acid and 40-45 mg essential fatty acid GLA
- 2-4 g/d; the higher doses are reserved for dermatitis, eczema, and rheumatoid arthritis

Adverse Effects

Nausea, indigestion; headaches; softened stools; weight gain is possible if large doses are taken; may effect lipid profile

Interactions
- Evening primrose oil should not be used concomitantly with anticonvulsants because it may lower the seizure threshold
- Avoid in schizophrenic patients taking phenothiazine and epileptogenic drugs as evening primrose may increase the risk of temporal lobe epilepsy

Contraindications
- Avoid in patients taking anticonvulsants
- Safety not determined in pregnancy and lactation, but GLA is secreted into breast milk

Bilberry (*Vaccinium myrtillus L.* Family: Ericaceae)

1998 Retail Sales: $6,441,501[1]

Part Used: Extract of dried fruit and dried leaf

Intended Indications

Extract of dried bilberry fruit may promote healthy vision, increase visual pigment regeneration, treat diarrhea in children, and protect human LDL against oxidative injury, presumably by scavenging free radicals; bilberry leaf is frequently used in conjunction with diabetes, arthritis, gout, dermatitis, and hemorrhoids

Formulation and Dosage
- 80-160 mg fruit extract tid
- Standardized to contain 25% anthocyanosides
- Dosage recommendations for bilberry leaf are not provided because of lack of efficacy information

Adverse Effects

Chronic ingestion or higher doses of bilberry leaf in animals has resulted in cachexia, anemia, icterus, excitation, and death

Interactions
- No significant interactions have been reported with bilberry fruit extract
- Theoretically, bilberry leaf might lower serum triglyceride and blood glucose levels; dosing adjustments may be necessary if used concomitantly with antidiabetes drugs

Contraindications
- Safety not determined in pregnancy and lactation

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