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Saw Palmetto for Benign Prostatic Hyperplasia: An Update

By E-P. Barrette, MD, FACP

LOSING SLEEP OVER URINARY SYMPTOMS SEEMS LIKE ADDING insult to infirmity. It's not much fun. Since saw palmetto extract (SPE) was first reviewed in these pages,[1] further studies have been published.[2-4] Overall, SPE appears to have a modest positive effect on the symptoms of benign prostatic hyperplasia (BPH). Currently the National Center for Complementary and Alternative Medicine (NCCAM) is funding a large randomized trial of SPE.

History

Native Americans used the extract of the fruit of the dwarf palm tree (*Serenoa repens*), indigenous to the southeastern United States, for urinary complaints. In the 19th century, naturopathic physicians treated various ailments with SPE, and it was listed in, though eventually dropped from, the National Formulary.

Current Use

In Germany, herbal therapy is the preferred initial therapy for BPH. Although several agents—*Pygeum africana*, stinging nettle (*Urtica dioica*), South African star grass (*Hypoxis rooperi*), and pumpkin seeds (*Cucurbita pepo*)—often are used, saw palmetto is the most widely used for BPH.

With the resurgence of natural therapies since the passage of the Dietary Supplement Health and Education Act (DSHEA), SPE has become one of the top 10 herbal agents in the United States. The commercial harvest of saw palmetto berries in Florida yielded $50 million in 1998.[5] The majority of this is shipped to Europe, where SPE remains the first choice of therapy for BPH. A recent survey in an American academic urology practice showed significant use of phytotherapeutic agents for lower urinary tract symptoms.[6]

Mechanism of Action

SPE is a complex mixture of fatty acids, long-chain alcohols, and plant sterols including beta-sitosterol, stigmasterol, cycloartenol, lupeol, lupenone, and methylcycloartenol. Although the precise active agent in SPE is unknown, there is growing support for pure

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beta-sitosterol treatment for BPH.[7,8]

The bulk of in vitro evidence supports a mechanism similar to finasteride, i.e., inhibition of 5-alpha-reductase. Clinical trials with finasteride, a potent inhibitor of type II 5-alpha-reductase, have demonstrated a decrease in prostate volume and a decrease in prostate specific antigen (PSA) values. However, trials of SPE have not shown any effect on prostate volume or PSA values, suggesting that SPE may be exerting its effects via alternative pathways. For example, recent evidence supports blocking alpha-adrenergic receptors as an alternative mechanism.[9]

Clinical Studies

A comprehensive meta-analysis of all controlled trials of SPE in men with symptomatic BPH of at least 30 days published from 1966 through 1997 included 18 randomized controlled trials.[10] Sixteen of 18 were double-blind, and all these trials were conducted in Europe. The trials studied 2,939 men.

Of the 18 trials, 10 trials studied SPE vs. placebo, two trials compared SPE to an active control (finasteride), four trials compared SPE compounded with a second agent vs. placebo, one trial compared SPE vs. pygeum vs. placebo, and one trial compared oral vs. rectal SPE.

In 10 studies, SPE reduced nocturia, weighted mean difference -0.76 times per night (95% CI, -1.22 to -0.32). Compared to placebo, SPE improved self-rating of urinary symptoms (six studies), risk ratio 1.72 (95% CI, 1.21-2.44), and increased peak flow rates (eight studies), weighted mean difference 1.93 ml/sec (95% CI, 0.72-3.14). Peak flow improved 24% compared to placebo.

Weaknesses of these studies included the short duration of follow-up (four weeks in five trials, six weeks in two trials, eight weeks in three trials) and small sample size (≤ 30 in five trials, ≤ 80 in 12 trials). Only nine of 18 studies had adequate blinding and only three trials used a standardized symptom score.

The lack of any improvement in the placebo arm in many of these studies suggests problems with blinding or study design, since all the large trials of pharmaceutical agents have shown significant improvement in the placebo-treated subjects. In a second meta-analysis of 11 trials of Permixon (a European formulation of SPE), the peak flow rates improved 1.87 ml/sec ($P < 0.001$) and nocturia decreased by 0.55 episodes ($P < 0.001$) more than the placebo arm.[11]

Two large double-blind studies compared SPE to finasteride. In the larger study, 1,098 men were randomized to 160 mg SPE bid or 5 mg finasteride qd for six months.[12] Both treatments improved the International Prostate Symptom Score (IPSS) (37% vs. 39%, $P = 0.17$) and quality of life equally well. Peak urinary flow increased slightly more with finasteride (30% vs. 25%, $P = 0.035$). The second trial followed 543 men with mild-to-moderate BPH for 48 weeks.[13] The SPE was compounded with 120 mg stinging nettle extract. The IPSS, quality-of-life, and peak urinary flow rates improved equally in both arms. Unfortunately neither trial included a placebo arm.

In the smaller study, prazosin appeared to be slightly better than SPE when studied for 12 weeks in 45 men.[14] Alfuzosin, an alpha-adrenergic antagonist not available in the United States, also improved urinary symptoms and flow rates better than SPE.[15] The former trial used non-standardized symptoms scores and the latter trial was only three weeks in duration.

Two small U.S. trials recently have been published. In an open-labeled, uncontrolled study, 50 men with moderate BPH (IPSS ≥ 10) received 160 mg SPE bid for six months.[16] The IPSS improved from 19.5 to 12.5 ($P < 0.001$). Forty-six percent (21 of 46) had 50% or more improvement in their urinary symptoms. Interestingly, no change in either peak flows or multiple urodynamic parameters were seen.

In the second recent study, a six-month, double-blind, randomized, controlled trial of 44 men showed slightly more symptom improvement with SPE than with

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Table 1

American Urological Association Benign Prostatic Hyperplasia symptom index

Questions for patients to answer regarding their Benign Prostatic Hyperplasia condition	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always
1. Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?	0	1	2	3	4	5
2. Over the past month, how often have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5
3. Over the past month, how often have you stopped and started again several times when you urinated?	0	1	2	3	4	5
4. Over the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5
5. Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5
6. Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5
7. Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning? (Check the column that best represents the number of times you awoke each night, on average.)	0	1	2	3	4	5

Add the point value for each question to determine the symptom score. A total score of 0-7 means symptoms are considered mild; a total score of 8-19 means symptoms are considered moderate; a total score of 20-35 means symptoms are considered severe.

Adapted from: American Urological Association. Available at: www.edaptechnomed.com/aua.htm. Accessed February 20, 2001.

placebo, although it was not statistically significant.[17] Taken three times daily, SPE (106 mg) was compounded with 80 mg nettle root extract, 160 mg pumpkin seed extract, lemon bioflavonoid extract, and beta-carotene. Pre- and post-treatment prostate biopsies demonstrated a decrease in the percent epithelium in the transition zone of the prostate from 17.8% to 10.7% ($P < 0.01$) with SPE but no change in the placebo-treated men. These changes are similar to those seen with finasteride.

Adverse Effects and Drug Interactions

Mild side effects have been noted to occur at rates similar to placebo. No interactions between SPE and drugs have been reported. However, many trials have excluded men on medications.

Dosage and Formulation

The usual SPE dose is 160 mg bid. SPE frequently is sold compounded with many other herbal ingredients. In Europe SPE often is compounded with stinging nettle or pumpkin seeds. The most rigorous five trials of all the published evidence used SPE alone, 160 mg bid (three trials), or SPE with nettle, 160/120 mg bid (two trials).

Pharmaceutical Comparisons

In two large well-designed trials, SPE appeared to be as effective as finasteride. Unfortunately, neither trial included a placebo control and a recent trial of finasteride showed it to be no better than placebo.[18] Also, there are no trials comparing SPE to the commonly prescribed alpha-adrenergic antagonists terazosin, doxazosin, and tamsulosin.

Conclusion

Two meta-analyses suggest SPE has a modest benefit for BPH symptoms, improving urine flow and decreasing nocturia. However, no single trial included in these two meta-analyses is definitive. All of these studies contain one or more deficiencies, i.e., short study period, non-validated symptom scores, small numbers of subjects, and inadequate blinding. Moreover, the SPE products tested are manufactured in Europe and are not readily available in the United States. It is not certain whether U.S.-manufactured SPE is equivalent to SPE from Europe. Fortunately, a large one-year NIH- and NCCAM-sponsored placebo-controlled trial of SPE in moderate-to-severe BPH is starting.

Recommendation

Until definitive trials are published, one must use the available evidence. Decisions to start therapy for BPH with SPE, finasteride, an alpha-adrenergic antagonist, or to initiate referral to a urologist need to be negotiated with the patient. For patients wishing to try SPE for mild-to-moderate BPH, a trial of SPE alone, 160 mg bid, or SPE with nettle, 160/120 mg bid, for several

months is not unreasonable. An attempt to monitor symptoms objectively with an easily completed questionnaire, such as the American Urological Association symptom index (*See Table 1*), will help determine the benefits of treatment. ❖

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Yoga for Degenerative Joint Disease

By Sharon L. Kolasinski, MD, FACP, FACR

THE CRITICAL ROLE OF EXERCISE IN THE MANAGEMENT of chronic musculoskeletal disorders is increasingly evident.[1] Yoga is one of several traditional practices that may be useful in treating chronic conditions such as degenerative joint disease. Although yogic philosophy addresses numerous aspects of well being that might affect health and disease, the use of the physical postures, or asanas, has received some recent, noteworthy attention. Documented improvement in symptoms related to both osteoarthritis of the hands and carpal tunnel syndrome has been attributed to yoga.[2,3]

Philosophy

Yoga derives from the more than 2,000-year-old writings of Patanjali, who identified the eight disciplines of yoga.[4] One of these eight disciplines is hatha yoga, or the practice of asanas.

In traditional Eastern practice, the aim of hatha yoga is to prepare the practitioner for the spiritual experience of purifying the body. Ultimately, the goal is the achievement of harmony of body, mind, and spirit. It is purported that because no single asana meets all needs in this process, a balanced program of asanas is intended to address the physiologic functioning of the nerves, muscles, and internal organs. No postures are rigidly prescribed since they may be modified depending on the practitioner's abilities. Assistive devices may be used as

needed to achieve proper positioning and later may be discarded as the practitioner becomes more adept.

In modern Western practice, however, the use of hatha yoga techniques has emphasized achieving strength, flexibility, and relaxation.[5] Pranayama, or breathing control techniques, often are used in conjunction with asanas. The guiding principle behind pranayama is that if the breath is controlled, the mind will be

Physiologic Effects of Yoga

THE LITERATURE ASSESSING THE PHYSIOLOGIC EFFECTS OF aerobic training has relied on cardiopulmonary outcome measures. Several studies involving yoga have used these outcomes as well. Less has been quantified about yoga's effects on strength, flexibility, and standardized measures of functioning used in the assessment of arthritis therapies.

Raju and colleagues compared physiological parameters including heart rate, blood pressure, minute ventilation, the oxygen and carbon dioxide content of expired air and blood lactate, and pyruvate levels in two groups of elite athletes.[1] National competitors in judo, volleyball, and other sports were followed for two years by submaximal and maximal treadmill testing. One group performed their usual physical workouts, while the other group also practiced daily pranayama under the supervision of a yoga instructor.

Both groups significantly reduced oxygen consumption at rest after exercise. The experimental group also improved in oxygen consumption per unit work after exercise testing and had lower resting blood lactate levels. The authors suggested that pranayama practice could augment the known benefits of aerobic exercise. The study was limited by its small size and the heterogeneity of the participants and their training programs. Only 12 participants completed the full two-year study.

A second study used treadmill testing to evaluate the effect of four weeks of yoga training on six healthy female volunteers.[2] Eight postures and breathing techniques were practiced daily during two 90-minute sessions. Maximal exercise testing was performed before and after the four-week period. At the end of the experimental intervention, all participants showed a significant reduction in percentage body fat with a corresponding increase in lean body mass. Participants also showed significant reductions in minute ventilation, oxygen consumption per unit work, heart rate, and respiratory quotient after exercise.

While this study documented that yoga practice led to rapid improvements in cardiorespiratory efficiency, the generalizability of the results to patients impaired by musculoskeletal disease is unclear. The participants in the study were physical education teachers with a mean age of 26 years.

Another study assessed blood pressure responses in sedentary, elderly participants recruited from the community, a group perhaps more reflective of patient populations with musculoskeletal disease.[3] Two groups, comprised of 20 men and women each, underwent a six-week program of either exercycle-based or yoga-based training. The exercise bicycle was used for 20 minutes, preceded and followed by 10-minute warm-up and cool-down periods. Yoga training consisted of a warm-up followed by a series of static yoga postures and breathing exercises and a 20-minute relaxation period. At the completion of the study, both interventions had resulted in a reduction in heart rate and an increase in oxygen consumption following exercise. In addition, unlike those in the aerobic group, the yoga practitioners experienced an increase in baroreflex sensitivity, reflecting a change in parasympathetic activity, and suggesting an increase in vagal tone.

Grip strength is a standard outcome measure in studies of patients with arthritis of the hands. The effect of one pranayama (breathing control) technique on grip strength was assessed in another recent study.[4] Grip strength was measured by dynamometer in a group of 130 teenagers attending a residential Indian yoga camp. Participants were randomly divided into five groups and instructed in five different breathing techniques, in addition to the same basic yoga training. Right nostril breathing, left nostril breathing, and alternate nostril breathing techniques all led to bilateral increases in grip strength, but breath awareness and hand gesture groups showed no improvement. The authors suggested that the observed differences might be related to reduced oxygen requirements or the training effect of doing additional breathing exercises compared to the two groups who did not improve. ❖

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calm. Pranayama and meditation frequently are included in Western yoga instruction.[5]

Physiologic Effects

Although yoga was introduced in the United States in the late 1800s, the medical literature included little about the physiologic effects of yoga until the past decade. (*See "Physiologic Effects of Yoga."*)

Clinical Studies

Specific studies evaluating the role of yoga in treating musculoskeletal disorders have been performed by Garfinkel and associates. The first of these evaluated the use of yoga in treating osteoarthritis of the hands.[2] In this randomized, controlled trial (RCT), the investigators followed a population of patients with pain and/or stiffness of the distal and proximal interphalangeal joints of the hands. Patients in the yoga intervention group participated in a 10-week program, which included eight 60-minute instructional sessions, as well as pre- and post-treatment testing. During the sessions, patients were instructed in asanas aimed at stretching and strengthening. Extension and alignment were emphasized. In addition to group discussion during sessions, written instructions were provided at the end of each session. Statistically significant differences were seen in finger joint tenderness, range of motion, and hand pain during activity. Non-significant trends toward improvement were noted for hand pain at rest and hand function measured by the Stanford Hand Assessment Questionnaire.

No participant experienced any adverse effects. The study was limited by its small size; 11 patients served as controls and 19 were evaluated in the experimental group. It also lacked an active intervention control, an important criticism since it has been demonstrated repeatedly that arthritis patients have improvements in symptoms with interventions such as telephone calls and other forms of psychosocial support.

The second RCT by Garfinkel et al used a series of asanas to treat carpal tunnel syndrome in a group of participants recruited through newspaper advertising and among workers with heavy occupational computer use.[3] The control group received wrist splints. The yoga intervention group received instruction in asanas aimed at improving flexibility, correcting alignment, stretching, and increasing awareness of optimal joint position during use. Sessions were held for 60-90 minutes twice weekly for eight weeks. Pre-and post-intervention testing was carried out for grip strength, pain measured by visual analog scale, and median nerve sensory and motor conduction measured by electroneurometer. Statistically significant improvements in grip strength and pain were found in the yoga group. Criticisms of this study include the small sample size and a failure to demonstrate a change in nerve conduction studies that correlated with symptom improvement.

One additional trial, carried out in patients with longstanding rheumatoid arthritis, addressed the use of yoga in those with musculoskeletal disease.[6] Twenty patients with rheumatoid arthritis of "sufficient severity to require disease-modifying therapy" had mean disease duration of 15-20 years and were non-randomly assigned to a yoga intervention group or to receive usual medical care only. The yoga group participated in daily two-hour sessions five days a week for three weeks, then weekly for three months. Daily home practice was expected. The only variable to differ significantly between the two groups at the end of the trial was left hand grip strength. Criticisms of this study include its small size (10 participants in each group) and short duration. Furthermore, the report lacks information regarding specific clinical aspects of these patients' disease. Given the longstanding disease duration, the yoga intervention may have treated aspects of secondary degenerative disease.

Adverse Effects

Few adverse effects of yoga have been reported. Two case reports suggest that left vertebral artery occlusion, documented angiographically, occurred in two young adults following yoga exercises involving weight bearing on and maximal range of motion of the cervical spine.[7,8] A third case of arterial occlusion recently was reported involving the basilar artery and leading to multiple infarcts in a healthy 34-year-old who developed symptoms after head standing.[9] One case of precipitation of symptoms of closed angle glaucoma was reported in a 47-year-old after performing salabhasana, a posture in which the practitioner lies prone with the cervical spine in extension and the legs elevated by extension at the hips.[10] The authors hypothesized that this posture increased intraocular pressure in this subject predisposed to glaucoma, but the authors did not believe that yoga caused the glaucoma. A benign finding of asymptomatic, bilateral conjunctival varix thromboses in a 60-year-old who had practiced head standing 10 times/d for 10 years also has been reported.[11] Finally, reversible foot drop was diagnosed in a 22-year-old who assumed a kneeling position during chanting for up to six hours/d.[12] The degree of supervision of these practitioners was not made clear in the case reports, but only the case of symptoms related to glaucoma appeared to have occurred while a practitioner attended regular instruction. The others apparently occurred during unsupervised home practice.

Contraindications and Precautions

Patients embarking on a new exercise program should seek prior medical evaluation, especially if they previously have been sedentary or have cardiovascular risk factors. Physicians should question patients about their exercise habits. Patients with arthritis or other musculoskeletal complaints should be asked to discuss the specifics of their exercise regimen, particularly if the patient undertakes an exercise program to treat symptoms.

Yoga complications involving the cervical spine have occurred in practitioners without known history of neck problems. It would be prudent to avoid exercises requiring prolonged flexion and extension or extremes of rotational motion in patients with known cervical spine osteoarthritis, cervical degenerative disc disease, or known atherosclerotic or other vascular disease.

Conclusion

Yoga is an ancient and complex practice, one aspect of which involves physical exercise that reportedly has a variety of benefits. The benefits to the musculoskeletal system itself are perhaps the least well documented. Some work suggests that yoga can be helpful in overall conditioning, as well as in treating specific complaints including those related to degenerative joint disease and carpal tunnel syndrome. How yoga should best be used as an intervention to treat musculoskeletal disorders remains unclear. However, if the goals of treatment include pain reduction, improvement in grip strength, and improvement in joint range of motion, data from well-designed clinical trials support the use of yoga.

Recommendation

If the physician wishes to prescribe yoga to treat symptoms, the goals of therapy and the type of hatha yoga should be made clear to the patient. In particular, in those patients with inflammatory arthritis, it is unlikely that aspects of inflammation such as warmth or erythema are likely to respond. For those patients with degenerative joint disease, however, a two-month trial of weekly supervised yoga instruction may be beneficial.

Physicians should be familiar with Western variations on traditional hatha yoga, including "power yoga" classes that involve vigorous participation, often in highly heated rooms. Yoga practice should be medically supervised in the same manner as any other exercise program. Particular attention should be paid to the actual asanas to be performed. Common sense precautions for those with degenerative arthritis include not performing postures beyond the limits of comfort and avoiding excessive repetitions. Patients should be encouraged to inform their yoga instructors of their medical history prior to the start of the class and to point out any difficulty they may have in assuming certain asanas during class. ❖

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Acupuncture for Migraine Headaches

By Alan D. Forker, MD, FACC

ALTHOUGH ACUPUNCTURE CAN BE TRACED BACK AT least 2,000 years in China, only since James Reston visited China in 1971 and wrote about his post-surgical acupuncture experience in the American press did

Western clinicians become more aware of acupuncture. However, many doctors consider acupuncture a placebo, primarily because of no access to reliable data.

English texts on acupuncture now are available,[1,2] and there has been an explosion of published reports in the literature, though many trials are uncontrolled and the number of patients studied with adequate controls is small. A boost to clinicians' interest occurred with publication of the NIH Consensus Development Conference on Acupuncture in 1998[3] and Eisenberg et al survey data.[4]

TCM Acupuncture vs. Western Adaptation

For the traditional Chinese practitioner, acupuncture is part of the therapeutic package. Understanding the flow of energy or *qi* (chee) through meridians, the balance of yin and yang, the diagnosis of diseases by a multitude of tongue abnormalities and palpation of the peripheral pulse (18 tongue findings and 29 types of pulse for starters[2]), and the treatment acupoints all over the body challenge the non-TCM trained practitioner in more ways than one. For instance, 10 different patients with migraine headache might be treated in 10 different ways by TCM.[1] The goal in migraine TCM treatment is "keeping a clear head, so lucid yang can ascend and turbid yin descend."[5]

It would help our Western understanding if anatomic/physiologic demonstrations of qi, meridians, and acupoints were possible; and some valid research is starting to appear.[6]

Mechanism of Action

Acupuncture owes some of its recent respectability to the discovery of the release of opioid peptides, such as beta-endorphins, met-enkephalin, substance P, plus noradrenaline and 5-hydroxytryptamine.[1] Plausible additional mechanisms of action are needed since opioid release may not explain potential long-term benefits such as psychoneuroimmune modulation, altered autonomic tone, and muscle relaxation and decreased emotional stress.

Pathophysiology of Migraine

The pathophysiology and etiology of migraine headaches are still unknown. In addition, the current pharmacologic therapy of migraine is complex and difficult to understand. This leaves plenty of room for patients to utilize complementary therapies, including acupuncture, chiropractic, and relaxation, the latter two of which are more common than acupuncture for treating headaches.[4] (*See Table 1 for Acupuncture Procedures*.)

Clinical Trials and Placebos

Searches of MEDLINE, PubMed (only English), the Cochrane Library, and Best Evidence on the web yielded few high-quality clinical trial data. Literature and pain meta-analysis reviews also emphasize that point.[7-11] The meta-analyses made the following conclusions:

- Most acupuncture results utilizing an adequate placebo control are equivocal.
- The majority of studies in the treatment of pain and migraine are methodologically poor.
- Necessary improvements include longer studies with more patients, better statistics with power calculations, independent assessment of outcomes needed, adequate control group, standardization of acupuncture techniques, description of therapists' training and experience, and cost-effectiveness analysis.

Headache is particularly responsive to placebo therapy. For example, Xiuying et al treated 100 patients with "intractable migraine": 94% were improved and 57% cured. However, no control group was utilized and no description of methods for evaluation was given.[5]

Quality sources evaluating acupuncture for migraine all come back to the same four articles, which include a total of 211 patients.[12-15] Two of these studies used a beta-blocker comparison plus trigger point stimulation primarily.[12,15] Although both studies compared with a beta-blocker achieved greater benefit with acupuncture, again acceptable controls were not present. In one trial, Hesse et al created a placebo control as "touched superficially with a blunt end" of the needle.[15]

Three choices for an acceptable control are mock transcutaneous electrical nerve stimulation (TENS), sham acupuncture, and minimal acupuncture.[1] However, mock TENS does not mimic needle insertion accurately. Instead it involves placement of patches and then showing patients the equipment although no current is given. Dowson et al used mock TENS in 48 patients and found no difference from classical acupuncture.[13] Theoretically, mock TENS could be used in patients with head and neck pain, especially with trigger points, if the practitioner performed blind credibility testing that the patients found to be reliable.

The difference between sham and true acupuncture is that the sham acupoint is located approximately one inch away from the true acupoint, but depth and stimulation remain the same. None of the migraine trials utilized this description of sham acupuncture. Even if utilized, it may not be a good placebo, as it has a strong possibility of diffuse noxious inhibitory control like TENS.[1]

Minimal acupuncture involves a shallow insertion (approximately 2 mm) with very slight stimulation, usually located away from the typical acupoint. This appears to be the best placebo, and the only quality article in the literature utilized it.

Table 1

Types of acupuncture procedures

1. Classical **traditional Chinese** medicine or "different strokes for different folks"
2. Scientific, Westernized or **formula**: more of a cook-book approach with a routine set of acupoints
3. Focus on **trigger points**, especially in the head and the neck region for migraine headache
4. With or without mechanical, electrical, or thermal (moxibustion) **needle stimulation**

Adapted from: Filshie J, White A. *Medical Acupuncture: A Western Scientific Approach*. Edinburgh: Churchill Livingstone; 1998.

Vincent, a London neurologist, recruited 30 migraine patients and utilized weekly TCM acupoints compared with minimal acupuncture.[14] No baseline data were provided. Interestingly, the author says "classical TCM acupoint locations were used, although I do not believe they are essential for a therapeutic effect." Vincent predominately treated acupoints in the head and shoulder area. Weekly headache pain score decreased 43% at four months and 38% at one year in the acupuncture group; this was statistically significant compared to the minimal acupuncture group. In addition, the control patients were tested with a four-question credibility scale with the conclusion that minimal acupuncture was equally credible as true acupuncture.[1] No other trial reproduces these results utilizing these techniques.

Adverse Effects

Norheim described 78 reports of adverse effects from MEDLINE between 1981 and 1994.[16] Most serious adverse events arise because of incorrect treatment in sensitive treatment locations (i.e., chest wall and ear), lack of sterility and disposable needles, and inadequate training. Twenty-three patients had a pneumothorax with chest wall acupuncture including one death in a chronic obstructive pulmonary disease patient with bilateral treatment. This can be avoided by not utilizing chest acupoints and by using less depth in puncture. In addition, 100 cases of hepatitis, 16 cases of auricular chondritis (two with necrosis and ear deformity), and one death in an asthmatic have been reported. Few of these reports describe technique, type of acupuncture, or education of the therapist.

Current Western Guidelines

The Canadian Headache Society Consensus Conference in 1995 concluded that biofeedback, relaxation therapy, cognitive-behavioral therapy, and chiropractic cervical manipulation may be of some value in migraine but that a "lack of firm evidence" was available for acupuncture.[17]

The NIH Consensus Conference in 1997 concluded there were "promising results" of acupuncture in adult postoperative and chemotherapy-induced nausea and vomiting and in postoperative dental pain. Acupuncture "may be useful" in migraine headache as an adjunct or alternative in a comprehensive management program.[3]

In 2000, the British Medical Association concluded that studies "suggest" acupuncture is more effective than controls for low back pain, dental pain, nausea and vomiting especially in postoperative adults, and migraine. Acupuncture has not been subject to a formal audit in the United Kingdom, and the National Institute of Clinical Excellence was established to evaluate and produce guidelines.[18]

Licensure and Regulation

Thirty-three states and the District of Columbia had acupuncture certification or licensure in 1999; acupuncture is recognized as within the scope of practice for physicians in 42 states and the District of Columbia.[19] Seventy-nine percent of general practitioners in the United Kingdom would like to see acupuncture provided by the National Health Service.[18]

Conclusion

It is uncertain whether acupuncture has a valid role in the treatment of migraine headache. At this point only one trial of 30 patients, utilizing minimal acupuncture as placebo, supports its use.

Recommendation

I currently would recommend the following approach in treatment of migraine headache: First, identify and avoid emotional and environmental triggers; second, try a 5-HT receptor agonist; third, consider riboflavin, and/or feverfew, and/or a beta blocker; fourth, add biofeedback, and/or relaxation, and/or massage therapy; and fifth, if nothing else works or excessive side effects occur with the above, then try acupuncture. ❖

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Reader Question

Comment: Professionals who work in nutrition are aware that everything from psychotropic medications[1] to hyperinsulinemia[2] to emotional eating[3] can cause weight gain.

We have been successful in changing not only weight but other parameters such as glucose, blood pressure, and lipid levels. A simple suggestion to refer to those professionals would have been a much better recommendation than to spend 30 seconds discussing something in which one lacks expertise (possibly driving a patient to more self-blame, dangerous supplements, and fad diets) and to suggest that patients sit while eating and not eat from the refrigerator. (See *Alternative Medicine Alert*, February 2001, pp. 23-24.)

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Response: *Ms. Lasslo-Meeks has misread and misunderstood the evidence-based support to physicians to regard obesity as a disease, and to offer patients ways to create behavioral change as a first step in treating obesity.*

Study after study has demonstrated that if physicians simply encourage patients who want to lose weight, patients are far more successful than if they had never been to the office. Sensible behavioral steps are an easy way to start.

Treating obesity is difficult, and each obese person is ill in his or her own way. But in just the title, Geneen Roth's When You Eat At The Refrigerator, Pull Up a Chair *captures the need for recognizing portion size and improving self-esteem—too often a shared problem, especially for women. Teams of clinicians, including dietitians, exercise physiologists, clinical psychologists and physicians, can learn from each other while offering the time and expertise that so many patients need.*

John La Puma, MD, FACP
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CME Questions

10. Which of the following therapies are FDA-approved for benign prostatic hyperplasia?
a. Terazosin, prazosin, finasteride, saw palmetto extract
b. Terazosin, doxazosin, prazosin, saw palmetto extract
c. Terazosin, doxazosin, prazosin, finasteride
d. Terazosin, doxazosin, finasteride

11. Which of the following should be used to assess the benefits or lack of benefits of saw palmetto extract for BPH?
a. Daily diary noting times of urination
b. AUA symptom index
c. Measurement of peak urine flow at the start and again in two months
d. Measurement of post void residual volumes

12. In one trial of yoga for osteoarthritis of the hands, researchers did not find statistically significant differences in:
a. finger joint tenderness.
b. range of motion.
c. hand pain during activity.
d. hand pain at rest.

13. U.S., British, and Canadian experts conclude acupuncture is an established treatment for migraine?
a. True
b. False

14. Acupuncture has a scientifically proven mechanism of action?
a. True
b. False

Clinical Briefs

With Comments from John La Puma, MD, FACP

Ginkgo biloba for Tinnitus

Source: Drew S, Davies E. Effectiveness of *Ginkgo biloba* in treating tinnitus: Double-blind, placebo-controlled trial. *BMJ* 2001; 322:73.

TO DETERMINE WHETHER *GINKGO BILOba* is effective in treating tinnitus, we designed a double-blind, placebo-controlled trial using postal questionnaires and self-reported data.

We enrolled 1,121 healthy people aged between 18 and 70 years with tinnitus that was comparatively stable; 978 participants were matched (489 pairs). These pairs were given 12 weeks' treatment with either 50 mg *Ginkgo biloba* extract LI 1370 tid or placebo. Our main outcome measures were participants' assessment of tinnitus before, during, and after treatment. Questionnaires included items assessing perception of how loud tinnitus was and how troublesome it was. Changes in loudness were rated on a six-point scale. Changes in troublesomeness were rated on a five-point scale.

We found no significant differences in primary or secondary outcome measures between the groups. Thirty-four of 360 participants receiving active treatment reported that their tinnitus was less troublesome after 12 weeks of treatment compared with 35 of 360 participants who took placebo. We conclude that 50 mg *Ginkgo biloba* extract LI 1370 given three times daily for 12 weeks is no more effective than placebo in treating tinnitus.

COMMENT

Ringing in the ears is common enough to be troublesome to many people—it's one of those annoyances that has no effective pharmacologic treatment, and about which doctors have little helpful to recommend.

So the idea that ginkgo leaf extract, probably effective in increasing cerebral blood flow and widely used for anything the least bit neurological, might be helpful was enough to have these University of Birmingham (UK) investigators give the Commission E standardized abstract to pairs of people with their ears buzzing, even without audiologic exams. The extract contained 25% flavonoids, 3% ginkgolides, and 5% bilobalides.

Alas, no go—10% response in both ginkgo and control groups.

Curiously, "one or more beneficial effects, such as improvements in general well-being, circulation, and hearing, were reported by 24/489 (4.9%) participants in the active treatment group and 11/489 (2.2%) in the placebo group. This difference was statistically significant (95% confidence interval 0.4%-4.9%)." No more is said about this finding. The study was funded by the British Tinnitus Association in conjunction with Lichtwer Pharma UK, manufacturer of the extract used in this study.

Recommendation

Ginkgo leaf extract cannot be recommended for tinnitus. Because it may increase the risk of bleeding with anticoagulant and antiplatelet drugs, it should not be co-administered with them. ❖

Adverse Events from Hydrazine Sulfate

Source: Hainer MI, et al. Fatal hepatorenal failure associated with hydrazine sulfate. *Ann Intern Med* 2000;133:877-880.

Source: Black M, Hussain H. Hydrazine, cancer, the Internet, isoniazid, and the liver. *Ann Intern Med* 2000;133:911-913.

THE INTERNET HAS REVOLUTIONIZED the manner in which patients obtain information about health care. This technology also has allowed patients to obtain directly both prescription and nonprescription therapies.

We report a case of fulminant hepatorenal failure associated with the use of hydrazine sulfate, an unregulated alternative remedy for cancer marketed on the Internet. A 55-year-old man with squamous cell cancer of the left maxillary sinus obtained hydrazine sulfate

through an Internet site, self-medicated with hydrazine sulfate, and developed hepatic encephalopathy, renal failure, and profound coagulopathy. Severe gastrointestinal hemorrhage developed. Autopsy revealed autolysis of the kidneys and submassive bridging necrosis of the liver.

Fatal hepatorenal failure may occur after the use of hydrazine sulfate. This fatal complication must be considered in anyone taking or contemplating the use of hydrazine sulfate.

COMMENT

This is more complicated than it looks. Hydrazine sulfate inhibits gluconeogenesis and thus may interrupt protein wasting and cancer cachexia. The drug has been found to have some effectiveness in non small cell lung cancer, with an increase in patient caloric intake, though without an improvement in survival. Randomized control trials have not shown it to be effective in other cancers (*Journal of Clinical Oncology* 1994;12:1113-20), though these NCI-sponsored trials have been criticized as less than definitive.

The hubbub here is the drug's easy availability and some Web sites' advocacy for it as virtually harmless. While it does appear to be less harmful in people, generally speaking, than in animal models, this is small comfort to the family of the man described in this case report. He reportedly had declined surgery, radiation, and chemotherapy for his tumor, and had no reported risk factors for liver disease. He had discontinued use of 180 mg/d for four months after a rash developed. Two weeks later he was admitted, and a week later he was dead.

Recommendation

Any physician can contact Medwatch via telephone (800-FDA-1088), fax (800-FDA-0178), or the Internet (http://www.accessdata.fda.gov/scripts/medwatch). Physicians should use this privilege when they suspect an adverse drug, herbal or supplement event—the reporting mechanism is the same. ❖

Acupuncture for Pain in Pregnancy

Source: Thomas CT, Napolitano PG. Use of acupuncture for managing chronic pelvic pain in pregnancy. A case report. *J Reprod Med* 2000;45:944-946.

CHRONIC PELVIC PAIN IS A HEALTH problem that affects many reproductive-age women. During reproduction the dilemma is even more challenging. The growing uterus often exacerbates pain, and treatment is limited by the effect on the fetus. A multispecialty approach and alternative medicine are often effective. Recently, the FDA announced the use of acupuncture and acupressure as officially recognized modalities for treatment of chronic pain in oncology patients.

We report a case of chronic pelvic pain in a 23-year-old primigravida at 27 weeks' gestation on narcotics. After organic causes were ruled out, acupuncture was employed successfully. Outpatient management for the duration of the pregnancy included acupuncture and narcotics for breakthrough pain while maintaining activities of daily living. Spontaneous vaginal delivery without complications at 38 5/7 weeks produced a 3,305 g female infant. The pain resolved immediately following delivery.

We believe that this case demonstrates the benefit of combined allopathic with alternative forms of medicine. With the use of acupuncture, narcotic use was limited in this gravida while adding to her quality of life by allowing her to maintain normal activity.

COMMENT

This case, reported by a captain and a major at Travis Air Force Base Medical Center, is worth noting both for the patient's clinical course and for the potential it has for stirring the thinking of hospitalists and those who employ them.

A 27-year-old with laparoscopy-diagnosed endometriosis since age 15 and on Lupron® prior to conception, the patient presented with right flank pain and hematuria. Nephrolithiasis was diagnosed. She had three days of intravenous narcotics and five subsequent in-hospital days of 7-10 tablets/d of oral oxycodone/acetaminophen, without complete pain relief. Biofeedback for a day, followed by trigger point injections, was also unsuccessful.

On the 11th hospital day, acupuncture at the helix of the ear was performed. The needles were left in place for eight hours, without the need for pain medicine. The patient required four treatments over three days, and was discharged. Outpatient acupuncture treatment occurred two to five times weekly, with the addition of three to five oxycodone/acetaminophen tablets until delivery.

Though it is unclear from the report whether the pain treated was that of a renal stone or of underlying endometriosis, if acupuncture can shorten hospital stays and reduce narcotic use in pregnancy, it may emerge as an available procedure in obstetric and gynecologic suites where women have a choice.

Whether acupuncture works by increasing endogenous opioid release and changing sympathetic tone, and whether it alters the perception of pain or actually changes its level is unknown. But it probably does work for some people in some circumstances. And it seldom does any harm, when carefully administered. That should be music to the ears of those who count dollars and days in acute care settings, and set the scene for local, innovative, community hospital-based research trials.

Recommendation

Keep an open mind about acupuncture and pain relief. ❖

In Future Issues:

Chromium for Weight Loss

Light Therapy for Seasonal Affective Disorder

Traditional Chinese Medicine for Fibroids

Supplement to *Alternative Medicine Alert*
March 2001

ALTERNATIVE MEDICINE ALERT™
A Clinician's Guide to Alternative Therapies

The B Vitamins: Part II

Vitamin B_3 (niacin, nicotinic acid, and nicotinate)

SEVERE VITAMIN B_3 DEFICIENCY IS KNOWN AS PELLAGRA AND IS CHARACTERIZED BY DERMATItis, dementia, and diarrhea. Pellagra is limited to areas where nutrition is severely limited and based on corn.

Dietary Reference Intakes (DRI)

2 mg/d for children 0-6 mo
4 mg/d for children 6 mo-1 y
6 mg/d for children 1-3 y
8 mg/d for children 4-8 y
12 mg/d for children 9-13 y
16 mg/d for men 14 y and older
14 mg/d for women 14 y and older

Food Sources

- Both niacin and one of its precursors, tryptophan, are considered when determining niacin food content.
- Dietary sources of niacin and tryptophan include lean meats, poultry, fish, peanuts, organ meats, brewer's yeast, milk, legumes, and some cereals, especially enriched grains and flours.
- Niacin also is synthesized by intestinal bacteria.

Mechanism of Action

- Vitamin B_3 functions as a component of the pyridine nucleotides: nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP).
- NAD and NADP are involved in more than 200 different reactions in the metabolism of carbohydrates, fatty acids, and amino acids.
- Important in the oxidation-reduction reactions in the Krebs cycle involving the production of energy from carbohydrates.
- Critical for the step-wise transfer of electrons in mitochondria.
- Has been shown to have anti-anxiety activity resembling benzodiazepines.
- Has been identified as part of the glucose tolerance factor of yeast which enhances response to insulin.

Clinical Uses

- To treat elevated blood cholesterol levels, reducing LDL and triglycerides and increasing HDL.
- At dosages of about 2 g/d, to reduce the recurrence rate for heart attacks by 30% and overall mortality by 11%.
- To prevent the development of diabetes in high-risk children.
- To preserve residual beta-cell function and improve glycemic control in adult diabetics.
- To improve flexibility and reduce inflammation in osteoarthritics.
- To reduce benzodiazepine withdrawal.
- To reduce the occurrence of cataracts.
- To control fluid loss caused by cholera.

Adverse Effects/Toxicity
- Naturally occurring niacin in food causes no known adverse effects.
- Large doses may cause transient side effects (e.g., tingling sensations, flushing of the skin, and head throbbing), which subside within 20-30 minutes and usually disappear entirely with continued use.
- Sustained release forms of vitamin B_3 may be hepatotoxic, and should be avoided if possible and used only with physician supervision.
- Chronic use of large amounts has been associated with rash, hyperpigmentation, dry skin, xerostomia, hyperuricemia, gout, peptic ulcer, amblyopia, proptosis, nervousness, panic, hyperglycemia, abnormal glucose tolerance and glycosuria, hepatotoxicity, abnormal prothrombin times, and hypoalbuminemia.
- Higher doses can cause significant increases in homocysteine levels.

Interactions/Nutrient Depletion
- Drugs that deplete vitamin B_3 include: aminoglycosides, cephalosporins, chlortetracycline, demeclocycline, doxycycline, fluoroquinolones, isoniazid, macrolides, minocycline, oxytetracycline, penicillins, sulfonamides, tetracyclines, and trimethoprim.
- Symptoms of deficiency include cracked, scaly dermatitis, especially on those areas exposed to the sun; inflammation of the mucous membranes of the GI tract, causing swollen tongue and diarrhea; and mental confusion and disorientation, leading to psychosis or delirium.

Vitamin B_5 (pantothenic acid)

Vitamin B_5 is involved in a number of essential metabolic roles including the production of some hormones and neurotransmitters, as well as the metabolism of all carbohydrates, fats, and proteins. Upon absorption, vitamin B_5 first is converted to a sulfur-containing compound called pantetheine, then into co-enzyme A (CoA), the only known biologically active form of vitamin B_5.

Vitamin B_5 is present in so many foods that deficiency in humans is virtually unknown. Experimentally induced deficiencies present as skin, liver, thymus, and nervous disorders.

Dietary Reference Intakes (DRI)
1.7 mg/d for children 0-6 mo
1.8 mg/d for children 6 mo-1 y
2 mg/d for children 1-3 y
3 mg/d for children 4-8 y
4 mg/d for children 9-13 y
5 mg/d for men and women 14 y and older

Food Sources
Vitamin B_5 is present in all plant and animal tissues. Good dietary sources include eggs, liver, fish, chicken, whole grain breads, cereals, legumes, cauliflower, broccoli, lean beef, white and sweet potatoes, and tomatoes.

Mechanism of Action
- As a constituent of CoA, vitamin B_5 participates in a wide variety of enzymatic reactions.
- CoA is involved in the release of energy from carbohydrates in the Krebs cycle.
- CoA is necessary for the synthesis of steroid hormones and proper functioning of the adrenal glands.
- CoA also functions in the production of fats, cholesterol, and bile acids.
- Vitamin B_5 is necessary for the synthesis of acetylcholine, phospholipids, and porphyrin in the hemoglobin of red blood cells.

Clinical Uses
- To boost energy and athletic ability.
- To detoxify alcohol.
- To improve the stress reactions of well-nourished individuals.
- To relieve the "burning feet" syndrome of diabetic neuropathy.
- To decrease cholesterol (pantetheine form only).
- To decrease the symptoms of rheumatoid arthritis in a subset of patients.

Adverse Effects/Toxicity
- There are no known toxic effects.
- Large doses may cause diarrhea.

Resources

Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline. Washington, DC: National Academy Press; 1999. Available at http://books.nap.edu/books/0309065542/html/index.html. Accessed December 27, 2000.

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