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INSIDE

Rye Grass Pollen for Benign Prostatic Hyperplasia, Prostatitis, and Prostatodynia

By Darren M. Lynch, MD

BENIGN PROSTATIC HYPERPLASIA (BPH) IS A COMMON DISORDER, with increasing incidence reported with advancing age. Population studies show the frequency of moderate-to-severe BPH symptoms to be 8-31% of men in the fifth decade and up to 44% of men in the seventh decade.[1] Treatment options for symptoms include medications, surgery, and botanical treatments, the latter being most common in Europe but enjoying increasing popularity in the United States. Use of plant extracts for the treatment of BPH was described as far back as 15th century BC Egypt.[2]

Diagnosis and Treatment Guidelines

Clinical practice guidelines for BPH were published in 1994 by the Agency for Health Care Policy and Research.[3] Diagnosis is presumptive and is based on a constellation of both obstructive and irritative voiding symptoms. Obstructive symptoms include decreased force of or interrupted urinary stream, straining to void, sensation of incomplete emptying, and urinary hesitancy. Irritative symptoms include urinary frequency, nocturia, and urgency. Interestingly, prostatic enlargement is not necessary for the diagnosis of BPH, as prostate size has not been found to correlate with degree of obstruction or severity of symptoms.[4]

Chronic nonbacterial prostatitis and prostatodynia are difficult entities to treat. Chronic nonbacterial prostatitis has an unknown etiology and may represent a non-infectious inflammatory disorder. Diagnosis is based on symptoms in the absence of infectious etiology, including irritative voiding symptoms and perineal or suprapubic discomfort. Prostatodynia is a non-inflammatory disorder affecting young and middle-aged men with symptoms similar to chronic prostatitis, as well as hesitancy and possibly interruption of flow. According to Watson and Irwin, the term prostatodynia is used to designate any unexplained complaints of chronic pelvic pain associated with nonspecific voiding symptoms and/or pain located in or around the groin, genitalia, or perineum, or the absence of pyuria and bacteriuria, with or without excess white cells or bacteria, on results from Gram stain and culture of expressed prostatic secretions

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in male patients.[5] Voiding dysfunction or pelvic floor muscular impairment may be the underlying pathophysiology. Both illnesses present viable opportunities for use of botanical treatments, like rye grass pollen, as conventional medical therapies have not proven to be wholly effective.

Constituents and Formulation

The most commonly used and studied rye grass pollen extract product for BPH is Cernilton, prepared from the Swedish rye grass pollen *Secale cereale*. Cernilton is used by millions of men worldwide and is a registered pharmaceutical product throughout Western Europe, Japan, Korea, and Argentina. The extract is prepared through microbial digestion of rye grass pollen, followed by water and acetone extraction. Cernilton is composed of 60 mg of a water-soluble fraction (Cernitin T60) and 3 mg of an acetone-soluble fraction (Cernitin GBX) per tablet. Pollen extracts have been found to contain at least 21 amino acids, as well as enzymes, coenzymes, sterols, minerals, trace elements, and all known vitamins. Gas chromatography studies found the Cernitin GBX fraction to contain phytosterols and fatty acids, including alpha-linoleic acid.

Mechanism of Action

The mechanism of action of rye grass pollen is not completely understood, although a number of mechanisms have been proposed regarding its beneficial effects on the prostate. In vitro studies have shown the water-soluble fraction T60 to inhibit the growth of prostate cancer cell lines and primary cultures from BPH specimens.[6] Other in vitro data raise the possibility of anti-prostaglandin and anti-leukotriene actions by inhibiting the arachidonic acid cascade.[7] Animal studies have demonstrated a significant reduction in rat prostate size following three weeks of therapy,[8] as well as a contractile effect on the bladder and a relaxing effect on the urethra in mice and pigs.[9]

Clinical Studies

Two systematic reviews of rye grass pollen for BPH have been published. A 2002 Cochrane Systematic Review of rye grass pollen for BPH found human trials to be limited by short duration, limited number of enrollees, gaps in reported outcomes, and unknown quality of the preparations utilized.[10] However, the authors concluded that the available evidence suggests rye grass pollen is well-tolerated and modestly improves urologic symptoms including nocturia. Additional randomized controlled trials were deemed necessary to evaluate long-term clinical effectiveness and safety of rye grass pollen. These findings echoed those published in the initial systematic review a few years earlier.[1]

Two published trials supporting the use of rye grass pollen in BPH are not available in English and, therefore, were not fully reviewed by the author. The first was a German double-blind, placebo-controlled study of 103 patients followed for 12 weeks, with findings of statistically significant improvements in nocturia and post-void residual urine.[11] The second was a double-blind Japanese trial comparing two proprietary brands of rye grass pollen, Cernilton and Paraprost, the latter being a pharmacological treatment for BPH used primarily in Japan and containing a mixture of amino acids. The investigators found statistically significant self-reported improvement of symptoms in the Cernilton group.[12]

The most rigorous English language double-blind, placebo-controlled study of rye grass pollen for BPH was published in 1990.[13] Sixty patients awaiting operative treatment for outflow obstruction due to benign prostate enlargement were entered into the six-month study. The study dose was 2 tablets of Cernilton twice daily. Subjective assessment was based on the Boyarsky scoring scale for symptoms of frequency, urgency, hesitancy, intermittency, incomplete emptying, terminal dribbling, and dysuria, with a score of 0-3 for each of

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these symptoms. Objective criteria for the evaluation of outflow obstruction were urine flow rate, voided volume, ultrasound measurement of residual urine, and transrectal ultrasound measurement of prostate size. Fifty-three patients were evaluated at the end of the six-month trial, 29 in the Cernilton arm and 24 in the placebo arm, with findings of statistically significant subjective improvement in 69% of patients. Significant decreases were noted in both residual urine volume and ultrasound determined antero-posterior diameter of the prostate. No significant differences were detected in flow rate and voided volume.

Subsequent papers also report positive effects of rye grass pollen on BPH. One open study included 79 patients with mild or moderate symptomatic BPH.[14] Subjective assessment was based on the same Boyarsky scoring scale for symptoms, with an average baseline score of 9.6. Maximum flow rate, average flow rate, residual volume, and mean prostatic volume on transrectal ultrasonography were other measured baseline characteristics. The dose of Cernilton pollen extract was 2 tablets three times daily for more than 12 weeks, with substantial improvement noted in nearly all irritative symptoms, no changes in prostatic volume or urine volume, and no adverse reactions reported. Twenty-eight patients who achieved good results with short-term treatment continued treatment for more than a year, with subsequent findings of decreased prostatic volume and further reductions in symptom score and residual volume. The results of this study are difficult to extrapolate, however, as no statistical analysis was performed and there was no control group.

Another study involved 89 BPH patients, 51 of whom received Cernilton and 38 who received Tadenan (*Pygeum africanum*, traditionally used in Europe for BPH) over a four-month period.[15] The two groups were compared using a subjective symptoms score devised by the author and objective evaluation by physical exam, uroflowmetry, and ultrasound determination of residual urine and prostate size. Subjective improvement was found in 78% of the Cernilton group compared to 55% of the Tadenan-treated group. Improvements also were noted in urine flow rate, residual urine volume, and prostate size. Again, no statistical analysis was performed, raising questions about the significance of the study. It is interesting that Cernilton outperformed a more widely recognized botanical BPH treatment.

Two studies have evaluated the treatment of chronic prostatitis and prostatodynia with pollen extract. The first was an open trial of 15 patients with either diagnosis suffering with symptoms for periods ranging from five months to seven years.[16] Nearly all complained of irritative urinary symptoms, mainly dysuria and frequency, and all complained of pain or discomfort. Duration of treatment lasted from one to 18 months. Complete resolution of symptoms was found in seven of 15 patients and another six patients were markedly improved. Most patients (11/15) did not experience improvement in signs and symptoms until three months after starting treatment.

A larger study of 90 patients treated with 1 tablet of Cernilton three times daily for six months was subsequently conducted.[17] The patients were divided into two groups: those without associated complicating factors (n = 72) and those with complicating factors, such as urethral strictures, prostatic calculi, and bladder neck sclerosis (n = 18). This division was employed because of significant differences at initial presentation and in response to treatment. Subjective symptoms of discomfort, nocturia, frequency, and dysuria, as well as findings from digital rectal prostate exams and uroflowmetry, were recorded at baseline, three months, and six months. Other measurements included urine leukocyte counts and measurement of complement C3/ceruloplasmin in the ejaculate, regarded as an extremely sensitive index of inflammation within the prostate.

Patients with associated complicating factors responded poorly to treatment. Both symptoms and urine flow measurements improved in the group without complicating factors; there was an overall positive clinical response in 56 of 72 of these patients. Complement C3/ceruloplasmin levels were reduced as well, suggesting an anti-inflammatory mechanism. Again, lack of statistical analysis and absence of a control group make the results of this study difficult to apply widely.

Adverse Effects

Adverse effects were not reported in any of the aforementioned studies.

Dosage

Dosing was different in nearly every study mentioned, but Graminex, the manufacturer of Cernilton, lists 6 tablets daily as the recommended dose for prostate conditions.

Conclusion

Rye grass pollen extract appears to be a safe, well-tolerated, and moderately effective botanical treatment for use in prostate disorders, with some studies following patients for as long as 12 months. More extensive evidence supports its use for BPH than for chronic prostatitis or prostatodynia, though the relative lack of effective treatments for these latter conditions makes the use of rye grass pollen extract compelling. The effect of rye

grass pollen on development of urinary retention or need for surgery with BPH has yet to be determined. More rigorous controlled studies are needed to fully assess the efficacy of rye grass pollen extract in prostate disorders.

Recommendation

Rye grass pollen can be an effective, evidence-based herbal treatment for prostate disorders; however, long-term safety data are lacking. ❖

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References

1. MacDonald R, et al. A systematic review of Cernilton for the treatment of benign prostatic hyperplasia. *Br J Urol Int* 1999;85:836-841.
2. Lowe FC, Ku JC. Phytotherapy in treatment of benign prostatic hyperplasia: A critical review. *Urology* 1996; 48:12-20.
3. McConnell JD. *Benign prostatic hyperplasia: Diagnosis and treatment.* Benign Prostatic Hyperplasia Guideline Panel. Clinical practice guideline no. 8, publication no. 94-0582. Rockville, MD: U.S. Dept. of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research, 1994.
4. Dull P, et al. Managing benign prostatic hyperplasia. *Am Fam Physician* 2002;66:77-84.
5. Watson RA, Irwin RJ. Prostatodynia. Available at: www.emedicine.com/med/topic1992.htm. Accessed Sept. 1, 2003.
6. Habib FK, et al. In vitro evaluation of the pollen extract, cernitin T-60, in the regulation of prostate cell growth. *Br J Urol* 1990;66:393-397.
7. Loschen G, Ebeling L. Inhibition of arachidonic acid cascade by extract of rye pollens [in German]. *Arzneimittelforschung* 1991;41:162-167.
8. Ito R, et al. Cernitin pollen extract (Cernilton); antiprostatic hypertrophic action of Cernitin pollen extract (Cernilton). *Pharmacometrics* 1986;31:1-11.
9. Kimura M, et al. Micturition activity of pollen extract: Contractile effects on bladder and inhibitory effects on urethral smooth muscle of mouse and pig. *Planta Medica* 1986;2:148-151.
10. Wilt T, et al. Cernilton for benign prostatic hyperplasia. *Cochrane Database Syst Rev* 2003;(1): CD001423.
11. Becker H, Ebeling L. Konservative therapie der benignen prostata-hyperplasie (BPH) mit Cernilton N. *Urologe B* 1988;28:301-306.
12. Maekawa M, et al. Clinical evaluation of Cernilton on benign prostatic hypertrophy—a multiple center double-blind study with Paraprost. *Hinyokika Kiyo* 1990;36:495-516.
13. Buck AC, et al. Treatment of outflow tract obstruction due to benign prostatic hyperplasia with the pollen extract, cernilton. A double-blind, placebo-controlled study. *Br J Urol* 1990;66:398-404.
14. Yasumoto R, et al. Clinical evaluation of long-term treatment using cernitin pollen extract in patients with benign prostatic hyperplasia. *Clin Ther* 1995; 17:82-87.
15. Dutkiewicz S. Usefulness of Cernilton in the treatment of benign prostatic hyperplasia. *Int Urol Nephrol* 1996;28:49-53.
16. Buck AC, et al. Treatment of chronic prostatitis and prostatodynia with pollen extract. *Br J Urol* 1989;64: 496-499.
17. Rugendorff EW, et al. Results of treatment with pollen extract (Cernilton N) in chronic prostatitis and prostatodynia. *Br J Urol* 1993;71:433-438.

DHEA for Women with Systemic Lupus Erythematosus

By Dónal P. O'Mathúna, PhD

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) IS A CHRONIC, inflammatory, autoimmune disease of connective tissue characterized by injury to many organs, especially the skin, joints, kidneys, nervous system, and mucous membranes. The American College of Rheumatology has developed, updated, and revised criteria for classifying SLE.[1] Up to 10 times as many women as men are affected by the disease. Clinical manifestations of SLE are very diverse due to its widespread impact. Common symptoms include fever, joint pain, a characteristic butterfly rash, pleural effusion, and nephritis. Patients with SLE usually go through periods of remission and exacerbation, referred to as flares. SLE frequently leads to glomerulonephritis, cardiovascular diseases, pulmonary diseases, and gastrointestinal disturbances. Patients have high levels of various autoantibodies, especially those directed against cell nucleus molecules.

Treatment for the underlying disease is not available. Patients are typically instructed to avoid exposure to sunlight and ultraviolet radiation. Active disease and flares are treated with topical steroids, salicylates, systemic corticosteroids, and immunosuppressive agents. Given the adverse effects associated with these medications, agents with better side effect profiles are actively

being sought. One that has generated much interest is the adrenal hormone, dehydroepiandrosterone (DHEA).

Pharmacology

DHEA is a steroid hormone, closely related to testosterone and estrogen. DHEA is converted endogenously into its sulfate ester (DHEAS), the predominant form in which it circulates.[2] DHEA and DHEAS are metabolically interconvertible and therefore their endogenous levels follow the same pattern.[2] DHEA levels rise in humans, reaching a peak in their mid-20s, and then fall over the rest of their lives. This has led to unsubstantiated claims that DHEA supplementation could be the "elixir of youth."[3] The precise role played by DHEA in normal metabolism is not known, except that it affects many body systems.[4]

Mechanism of Action

Use of DHEA to treat SLE has been explored because of the female preponderance of SLE, low circulating levels of DHEA and DHEAS in SLE, the immunomodulatory effects of DHEA, and the beneficial effects of DHEA when given to mice with SLE.[4] In SLE, serum levels of adrenal androgens are lower than normal.[4] Systemic inflammation leads to a shift in hormone secretion away from adrenal androgens to maintain cortisol levels. Glucocorticoids are administered to help maintain cortisol levels. Detailed studies with 72 patients revealed that those with SLE had severely reduced serum levels of DHEA and DHEAS, probably due to changes in the enzymes involved in adrenal steroidogenesis.[5]

Clinical Studies

An early study involved 10 patients with SLE given 200 mg/d DHEA.[6] After 3-6 months of treatment, improvements were seen in patients' symptom reports using the SLE Disease Activity Index (SLEDAI), physicians' assessments, and need for corticosteroid use. In a double-blind, randomized controlled trial (RCT), 28 women with SLE received either DHEA (200 mg/d) or placebo. Patient SLEDAI scores, patients' and physicians' overall assessments, and corticosteroid use all improved significantly over the three months of the study ($P = 0.022$). Those taking placebo had more SLE flares ($P = 0.053$). Another open study found statistically significant improvements in these same outcomes, compared to baseline, when 50 patients took DHEA (50-200 mg/d) for six or 12 months.[8]

The aforementioned studies enrolled patients with mild-to-moderate SLE. Patients with severe SLE were enrolled in one study adding DHEA to conventional treatment with high-dose corticosteroids, with or without immunosuppressant agents.[9] Responders were defined as those whose major SLE manifestation was stabilized after six months. The study authors randomized 21 patients to either placebo or 200 mg/d DHEA. No statistically significant differences were found between the two groups of subjects. However, the two study groups were found to have statistically significant differences at baseline in both the severity of SLE symptoms ($P < 0.05$) and types of other conditions. Those randomized to the DHEA group had greater disease activity and more instances of nephritis. These baseline differences may limit the generalizability of these results, and reflect a difficulty inherent to the study of diseases manifesting a variety of symptoms.[10]

The first relatively large RCT assigned 120 subjects to either DHEA (200 mg/d) or placebo.[4] The subjects were all adult Chinese women with mild-to-moderate SLE who also were taking standard SLE medication (glucocorticoids and immunosuppressants). No significant differences were found in disease activity scores using two measures to compare baseline scores with those at the end of the six-month study. However, subjects taking DHEA had significantly fewer serious SLE disease flares and went longer before experiencing flares ($P = 0.044$). Patients' global assessment scores were significantly improved ($P = 0.005$), but not physicians' evaluations. DHEA was well-tolerated, although expected increases in serum testosterone levels and incidence of acne did occur.

A larger RCT examined the hypothesis that DHEA could allow corticosteroid-dependent women (taking 10-30 mg/d prednisone) to reduce their dose without increasing SLE activity.[11] The 191 subjects were randomized to receive either placebo, 100 mg/d DHEA, or 200 mg/d DHEA. Prednisone doses were reduced at monthly intervals by predetermined increments if patients' SLEDAI scores were stable or improved. Successful responders were those who achieved a prednisone dose of ≤ 7.5 mg/d within seven months. The study was continued to nine months if the dose was still being successfully reduced but subjects had not yet reached or become stabilized at ≤ 7.5 mg/d. Among all subjects, the higher DHEA dose demonstrated a nonsignificant trend toward more responders than the lower dose or placebo (55%, 44%, 41%, respectively). Prior to unblinding, subjects were divided into those with active (SLEDAI score > 2) or inactive disease (SLEDAI score ≤ 2). Among those with active SLE, significantly greater numbers of responders were found among those taking 200 mg/d DHEA compared to 100 mg/d DHEA or placebo (51%, 38%, 29%, respectively; $P = 0.031$). Among subgroups, as the baseline SLEDAI score

increased, the proportion of responders increased. The researchers concluded that in future DHEA trials only those with active SLE should be enrolled.

Adverse Effects

Patients taking DHEA have dose-related increases in serum DHEAS and testosterone levels. Use of DHEA, therefore, can lead to androgenic effects. In one study, 41% of corticosteroid-dependent patients receiving DHEA (100 or 200 mg/d) experienced an increased incidence of mild acne compared to 19% of those taking placebo ($P < 0.05$).[11] Hirsutism and menstrual abnormalities also increased, but were not significantly different from those in the placebo group. Abdominal discomfort, including stomach cramping and pain, is commonly reported, but usually is transient and relieved by H2-receptor antagonists. No drug interactions have been reported with DHEA.

Epidemiological studies have noted a positive correlation between serum DHEA levels and incidence of breast cancer in postmenopausal, but not premenopausal, women.[12] This correlation needs to be more fully researched, but is of particular concern for obese postmenopausal women.

Formulation

DHEA is most commonly available as 50 mg capsules, with 200 mg usually taken in the morning. DHEA also is known by its United States Adopted Names Council designation, prasterone, and by its Genelabs formulation, GL701.[11] Concern has been raised regarding the quality of DHEA products available on the U.S. market because of its regulatory status. The FDA categorized DHEA as an unapproved drug in 1985, making it available only by prescription. The 1994 Dietary Supplement Health and Education Act reclassified it as a dietary supplement, making it readily available over the counter. A 1998 study found commercial products containing 0-150% of the labeled amount, with nine of the 16 products failing to meet standard pharmaceutical specifications of 90-110% of labeled amount.[13]

Conclusion

SLE is a chronic, debilitating disease with many different manifestations. Current conventional treatment relies upon the use of medications associated with serious adverse effects. Although only a relatively small number of clinical trials have examined the effectiveness of DHEA in SLE, the results have been generally positive. Reduction in the severity of the illness itself and the ability to reduce the dose of concurrent medications have been documented. However, none of the studies have extended beyond one year, which is important given the cyclic nature of SLE and the likelihood that medications will be taken for many years. Long-term studies also are needed to resolve questions regarding adverse effects.

Recommendation

Adult women with SLE may find symptom relief from 200 mg/d DHEA and/or may be able to reduce doses of other medications. However, DHEA should be employed only under close medical supervision, especially if other medications are being scaled back. The ready availability of DHEA as a dietary supplement means that patients should be advised about where to obtain high-quality products. Recommendations for using DHEA in men with SLE cannot yet be given as studies have not been reported with male subjects. ❖

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References

1. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1997;40:1725. Available at: www.rheumatology.org/research/classification/1982SLEupdate.html. Accessed Aug. 14, 2003.
2. Baulieu EE. Dehydroepiandrosterone (DHEA): A fountain of youth? *J Clin Endocrinol Metab* 1996;81:3147-3151.
3. O'Mathúna DP. DHEA supplementation during menopause. *Altern Med Alert* 1999;2:113-116.
4. Chang DM, et al. Dehydroepiandrosterone treatment of women with mild-to-moderate systemic lupus erythematosus: A multicenter randomized, double-blind, placebo-controlled trial. *Arthritis Rheum* 2002;46:2924-2927.
5. Vogl D, et al. Serum levels of pregnenolone and 17-hydroxypregnenolone in patients with rheumatoid arthritis and systemic lupus erythematosus: Relation to other adrenal hormones. *J Rheumatol* 2003;30:269-275.
6. van Vollenhoven RF, et al. An open study of dehydroepiandrosterone in systemic lupus erythematosus. *Arthritis Rheum* 1994;37:1305-1310.
7. van Vollenhoven RF, et al. Dehydroepiandrosterone in systemic lupus erythematosus. Results of a double-blind, placebo-controlled, randomized clinical trial. *Arthritis Rheum* 1995;38:1826-1831.

8. van Vollenhoven RF, et al. Treatment of systemic lupus erythematosus with dehydroepiandrosterone: 50 patients treated up to 12 months. *J Rheumatol* 1998;25:285-289.
9. van Vollenhoven RF, et al. A double-blind, placebo-controlled, clinical trial of dehydroepiandrosterone in severe systemic lupus erythematosus. *Lupus* 1999;8: 181-187.
10. Lahita RG. Dehydroepiandrosterone (DHEA) for serious disease, a possibility? *Lupus* 1999;8:169-170.
11. Petri MA, et al. Effects of prasterone on corticosteroid requirements of women with systemic lupus erythematosus: A double-blind, randomized, placebo-controlled trial. *Arthritis Rheum* 2002;46:1820-1829.
12. Stoll BA. Dietary supplements of dehydroepiandrosterone in relation to breast cancer risk. *Eur J Clin Nutr* 1999;53:771-775.
13. Parasrampuria J, et al. Quality control of dehydroepiandrosterone dietary supplement products. *JAMA* 1998;280:1565.

Clinical Hypnosis and Surgery

By Steven Gurgevich, PhD

THE LATEST FIGURES FROM THE CENTER FOR HEALTH Statistics report nearly 72 million surgical procedures performed in the United States in 1996. No one needs to be reminded of the financial expense associated with surgery, but the cost in terms of anxiety and pain can be just as staggering to the patient. Mind-body methods, such as clinical hypnosis and guided imagery, hold great promise in reducing both the psychic costs of suffering as well as the financial expense of surgery.

Mind-body methods for medical and surgical applications date back to the Ebers papyrus in Egypt, Aesclepius' sleep-healing temples in ancient Greece, and the "cult of the magnet" represented by Franz Antoine Mesmer.[1,2] Although Mesmer's methods were discredited, British physicians Elliotson and Esdaile documented and published hundreds of cases of mesmerism applied successfully for anesthesia and analgesia in surgical procedures.[3]

Esdaile, a surgeon practicing in India in the 1840s, documented major surgery—from limb amputations to eye surgery—using hypnosis as the anesthetic. His use of hypnosis was particularly noteworthy because only 5% of his surgical patients died, when the standard surgical mortality rate was 40%. He felt that the "mesmeric" relief of pain accounted for the greater survival. His critics said that it was only out of deference to him as a white, British doctor that his patients did not complain. He responded that they must be surviving out of deference as well. Ultimately, Esdaile too was discredited and the Royal Medical Society banned the practice of mesmerism. Esdaile said that "… not many of this generation will live to benefit from mesmerism, if they wait till it is admitted into the Pharmacopoeia."

For the past two and a half centuries, however, mind-body methods have continued to be used despite resistance from some conventional medical institutions.[4] Various methods have been identified by many names, but it was the British physician James Braid who first used the label "hypnosis."[5] Finally, in 1955 and 1957, the British and American medical associations deemed hypnosis an acceptable medical procedure. Initial research studies sought to determine whether hypnosis was beneficial. That question has been addressed in numerous studies and meta-analyses of research findings.[6-9] Today, investigations have shifted from determining if hypnosis works to exploring how and in what ways may it be used to help surgical patients.

For example, Montgomery et al performed a meta-analysis of 20 published controlled studies using hypnosis in surgical applications.[6] They found that the surgical patients in hypnosis treatment groups experience better outcomes than 89% of those in control groups across six clinical outcome categories: negative affect, degree of pain, amount of pain medication used, physiological indicators, recovery time, and treatment time.

What is Hypnosis?

There are many competing theories as to what exactly constitutes and defines hypnosis. Marmer describes hypnosis as a psychophysiological tetrad of altered consciousness consisting of narrowed awareness, restricted and focused attentiveness, selected wakefulness, and heightened suggestibility.[10] The Spiegels describe hypnosis as a psychophysiological state of arousal, attentive receptive focal concentration, with a corresponding diminution in peripheral awareness.[11] They give examples of naturally occurring trance, such as daydreaming, intense concentration, distraction, and motivation for selective perception. Brown and Fromm call it, "A special state of consciousness in which certain human capabilities are heightened and others may fade into the background."[12]

Most will agree that hypnosis involves a system of skills and methods that allow the individual's mind and body to share information more effectively to achieve a therapeutic outcome. One of those methods is called

trance, or a conscious state of awareness, in which an individual can be absorbed in his own thoughts and ideas so well that he may perceive and respond to those thoughts and ideas as if they were real.

And most will certainly agree that all hypnosis actually is self-hypnosis. The therapist or clinician provides instructions and guides the patient in shifting consciousness to become absorbed in pleasantly relaxing thoughts, ideas, images, and feelings, and to be distracted from aversive or noxious internal or external stimuli. This process is called hypnotic induction. It allows and empowers the patient to experience greater control over sensory and physiological experience, facilitating a greater openness and receptivity to therapeutic suggestions. The trance state, along with hypnotic suggestions, is called hypnotic utilization. Thus, there are two main aspects of the process of hypnosis: induction of trance and utilization of the trance state.

As with most phenomena, there is a normal distribution of ability and receptiveness, which is called hypnotizability. Most research studies employ one of the many scales designed to measure hypnotizability in children and adults.[10,13-18] Although one would think that greater hypnotizability would correlate with greater therapeutic response, some have discovered that hypnotizability does not necessarily correlate with therapeutic benefit in surgical applications. This is due to the many co-mediating factors that also influence the responsivity to hypnosis, such as personality, motivation, belief and faith, positive or negative expectancy, and therapeutic rapport.[19]

Hypnosis in the Operating Room: Pain

A recent research study by Lang et al garnered high visibility in the popular media.[20] The authors randomly assigned 241 patients undergoing percutaneous vascular and renal procedures to three groups: standard care (n = 79), structured attention (n = 80), and self-hypnotic relaxation (n = 82). All patients had access to patient-controlled analgesia with fentanyl and midazolam. The patients rated their pain and anxiety on a visual analogue scale (VAS) every 15 minutes during and after the procedure. The investigators found that the standard care group used significantly greater amounts of analgesic medication: 1.9 units vs. 0.8 and 0.9 for the structured attention and hypnosis groups, respectively. Only one patient in the hypnosis group became hemodynamically unstable, compared to 10 structured attention patients (P = 0.004) and 12 standard care patients (P = 0.0009). The procedure times were significantly shorter (P = 0.0016) in the hypnotic group (61 minutes) than the standard care group (78 minutes) and the structured attention group (67 minutes). Overall, the study demonstrated benefits of hypnotic relaxation in reducing pain, lessening need for medication, decreasing anxiety, and achieving greater hemodynamic stability. These results were consistent with the findings of their previous study, which examined self-hypnotic relaxation during interventional radiological procedures.[21] In this previous study, an extra person was available in the operating room to guide the patients into visualizations of places the patients found pleasant.

Mauer et al examined the use of medical hypnosis for orthopedic hand surgery, which commonly results in severe postoperative pain, as well as for the painful therapy exercises and wound care required shortly after surgery.[22] In a quasi-experimental research design with 60 hand surgery patients receiving either usual treatment or usual treatment plus hypnosis, the hypnosis group exhibited significantly lower measures of perceived pain intensity, perceived pain affect, and state anxiety. The physical ratings of progress were significantly higher for the hypnosis subjects than the controls, and the hypnosis group had significantly fewer postoperative complications.

Defechereux et al used hypnoanesthesia for 197 thyroidectomies and 21 surgical explorations for hyperparathyroidism between 1994 and 1997.[23] The operative data and postoperative course were compared to 119 patients who had declined hypnosis or were judged unsuitable for it and underwent general anesthesia. The patients using hypnoanesthesia experienced less postoperative pain, less analgesic medication usage, shorter hospital stay, and improved postoperative convalescence.

Hypnosis in the Operating Room: Nausea and Vomiting

Up to 70% of surgical patients receiving general anesthesia experience postoperative nausea and vomiting (PONV). Eberhart et al conducted a double-blind randomized study of 100 patients undergoing thyroidectomy.[24] Patients were randomly assigned to a suggestion group that had an audiotape playing throughout the entire operation, or to a control group that had a blank tape playing throughout surgery. A classic droperidol-fentanyl-N_2O anesthesia technique was used to preserve the neuropsychological functions required to process the therapeutic suggestions offered on the audiotape during the operation. The suggestion group had significantly less PONV: 47.2% vs. 85.7% for the control group. The suggestion group also required less anti-emetic treatment: 30.6% vs. 68.6% for the control group. Williams et al reported similar findings for a double-blind

randomized study of 60 women receiving peri-operative suggestions during gynecological surgery.[25]

Enqvist et al studied the pre-operative use of hypnosis to reduce postoperative vomiting in 50 female patients undergoing breast surgery.[26] They randomly assigned the women to control or hypnosis groups. The hypnosis group listened to an audiotape daily for 4-6 days prior to surgery. Hypnotic induction with suggestions for relaxation and sensations of thirst and hunger (positive suggestions incompatible with nausea) were provided. The patients in the hypnosis group had significantly less vomiting: 39% vs. 68% in the control group. They also reported less nausea and less need for analgesic medication postoperatively. This study may not fit perfectly under our heading—as the intervention came prior to surgery, not in the operating room—but it is a compelling example of how easy it can be to prepare patients with both self-hypnosis and post-hypnotic suggestions for positive therapeutic effects.

Hypnosis in the Operating Room: Blood Loss

Enqvist et al examined the effects of pre-operative and intra-operative suggestion on blood loss and recovery from maxillofacial surgery.[27] Sixty patients were assigned to three groups. Eighteen patients listened to a hypnosis audiotape containing pre-operative therapeutic suggestions (group A), 18 patients listened to a hypnosis audiotape containing pre- and intra-operative suggestions (group B), and 24 patients listened to a hypnosis audiotape with only intra-operative suggestions (group C). Each of these groups was compared to a group of matched control patients. Groups A and B listened to the audiotape 1-2 times daily for the two weeks before surgery. The audiotapes provided therapeutic suggestions for improved healing, less bleeding, lower blood pressure, and faster recovery. The audiotape was 17 minutes in length. During surgery, Group B also heard an audiotape, which contained similar positive therapeutic suggestions. No differences in somatic response were found for patients in groups A and B assessed with the Stanford Hypnotic Susceptibility Scale. Group A, which received pre-operative therapeutic suggestions, had 30% less blood loss ($P = 0.008$) than its matched control. Group B, receiving pre- and intra-operative therapeutic suggestions, had 26% ($P = 0.09$) less blood loss than its controls. And group C, only receiving intra-operative therapeutic suggestions, experienced 9% less blood loss than its control group.

Hypnosis in the Operating Room: Wound Healing

Ginandes et al published the results of a clinical trial that examined the effect of hypnosis on postsurgical wound healing in 18 women undergoing reduction mammaplasty.[28,29] All the women received the same surgical protocol and postoperative care, and were randomly assigned to usual care, adjunctive supportive attention, or adjunctive hypnosis. The hypnosis group was seen weekly for eight weeks (two weeks prior to surgery until six weeks after) for administration of a scripted hypnotic induction. The induction was recorded on audiotape at each session and provided to the patient. The hypnosis group received therapeutic suggestions for decreased inflammation, visible soft-tissue restoration, and accelerated tissue remodeling via direct, indirect, structured, and open-ended suggestion. During the eight sessions they also were provided with positive expectancy for comfort and rapid wound healing, diminished bleeding, healing imagery, and hypnotic skills for positive time distortion.

The supportive attention group paralleled the hypnosis group, receiving weekly 30-minute sessions that emphasized focused attention about feelings toward the surgery and surgical experience. Digital photographs of the incision were assessed at one and seven weeks with a wound assessment inventory (WAI) measuring edema, erythema, and exudates (which was substituted for open wound size). Subjective ratings of pain and perceived healing at one and six weeks were obtained along with an objective functional recovery assessment, which was determined using an SF-36 health survey completed at enrollment and seven weeks postoperative.

Nurse ratings on the WAI were significant for accelerated healing in the hypnosis group ($P < 0.001$). The hypnosis group had the most rapid healing over time, followed by the supportive attention group; the usual care control group had the slowest rate of healing. Physicians' ratings from digitized photographs did not achieve statistical significance, but trends were consistent with the pattern observed from nurses' WAI ratings. Similarly, patients also noted a trend toward greater wound healing in the predicted pattern, but the finding also did not achieve statistical significance.

Pediatric Surgical Applications

Children are excellent hypnotic subjects and also experience significant benefits from the application of clinical hypnosis for surgical procedures.[30,31] Lambert randomly assigned 52 children, matched by age, sex, and diagnosis, to hypnosis and control groups.[32] The hypnosis group was taught imagery and received suggestions for a positive postoperative experience. The hypnosis group showed significantly lower postoperative pain ratings, shorter hospital stays, and less anxiety compared with the control group.

Cost Effectiveness of Hypnosis for Surgery

Lang and Rosen examined the cost data for the patients involved in their 2000 study referenced earlier.[33] They found that the average cost associated with standard sedation was $638 per case, whereas the cost for patients receiving both sedation and hypnosis was only $300 per case. This represents an average of more than 50% (or $338) cost savings per procedure.

Side Effects of Hypnosis and Cautions

Clinical application of hypnosis, when administered by qualified practitioners, typically is benign and effective. Perhaps the greatest danger would be in using hypnosis to remove pain before it has been adequately evaluated. However, there can be complications arising out of heightened transference, such as unexpected feelings of disorientation or hostility toward the clinician.[34] There also have been reports of unexpected amnesia, disorientation, paralysis, and unexpected catharsis. These are not direct and predictable side effects of hypnosis per se, and are attributable to the psychodynamics involved, and to the personal characteristics of the patient.

A frequent caution about hypnosis involves its use by untrained or unqualified people. A simple rule of thumb is that a clinician should not be using clinical hypnosis to treat a condition unless he or she also is qualified to treat the condition without hypnosis.

Finding Qualified Professionals

The majority of states have not legislated or established guidelines for the certification and practice of hypnosis. However, the American Society of Clinical Hypnosis (ASCH, www.asch.net) has established a process for certifying professionals who have completed accredited training and approved hours of individual supervision. Both ASCH and the Society for Clinical and Experimental Hypnosis offer training workshops and scientific programs for physicians, psychologists, dentists, and social workers. Another professional association is the American Psychotherapy and Medical Hypnosis Association (www.apmha.com).

Conclusion

The public's well-recognized interest in using alterative and complementary therapies that can be safe, effective adjuncts to conventional care[35] also extends into the operating suite. Prior to the availability of chemical anesthesia, hypnosis was the standard form of anesthesia. It has been shown repeatedly that hypnosis is a benign and effective adjunct for the surgical patient. Results of experimental studies have demonstrated that hypnosis is beneficial in reducing anxiety, lowering pain perception, lessening postoperative nausea and vomiting, reducing blood loss, achieving greater hemodynamic control, accelerating wound healing, lowering complication rates, shortening hospital stays, creating greater compliance with postoperative treatment, and enhancing both patient and clinician satisfaction. And in those cases where chemical anesthesia is not advisable or safe, clinical hypnosis is an effective option.[36]

One of the frequently mentioned deterrents of using hypnosis in surgical procedures is that it may be too time-consuming. However, many of the studies cited in this article have relied upon standard scripted hypnotic inductions that can be administered in as little as 10 minutes. Montgomery et al used a 10-minute standardized hypnotic induction prior to surgery for women undergoing excisional breast biopsy.[8] The results demonstrated significantly less postoperative pain ($P = 0.001$) and distress ($P = 0.025$).

It also has been found that audiotape recordings may be an effective and efficient way of administering hypnosis.[37] The benefits of hypnosis in surgical applications, along with cost savings and efficiency of administration, make hypnosis both feasible and accessible to the rising number of individuals who want to use alternative and complementary methods to enhance their healing experience.

Recommendation

Questions about the usefulness of hypnosis for surgery have been answered both clinically and empirically. The list of benefits of hypnosis for surgical patients, clinicians, and health care organizations are expanding and becoming more rigorously documented. The next greatest question for research on this subject may well be, "Why isn't hypnosis offered to every patient undergoing surgical procedures?" *[Editor's note: The author would like to thank Dr. D. Corydon Hammond for his assistance in the literature review for this paper.]* ❖

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References

1. Kroger W. *Clinical and Experimental Hypnosis.* Philadelphia, PA: JB Lippincott; 1963.
2. Tinterow M. *Foundations of Hypnosis: From Freud to Mesmer.* Springfield, IL: Charles C. Thomas; 1970.
3. Esdaile J. *Mesmerism in India and Its Practical Application in Surgery and Medicine.* Hartford, CT: Silve Andrus and Son; 1851.

4. Gravitz M. Early uses of hypnosis as surgical anesthesia. *Am J Clin Hypnosis* 1988;30:201-208.
5. Braid J. *Neurypnology: Or the Rationale of Nervous Sleep.* London: Churchill; 1843.
6. Montgomery GH, et al. The effectiveness of adjunctive hypnosis with surgical patients: A meta-analysis. *Anesth Analg* 2002;94:1639-1645.
7. Lynn SJ, et al. Hypnosis as an empirically supported clinical intervention: The state of the evidence and look into the future. *Int J Clin Exp Hypn* 2000;48: 239-259.
8. Montgomery GH, et al. A meta-analysis of hypnotically induced analgesia: How effective is hypnosis? *Int J Clin Exp Hypn* 2000;48:138-153.
9. Blankfield RP. Suggestion, relaxation, and hypnosis as adjuncts in the care of surgical patients: A review of the literature. *Am J Clin Hypn* 1991;33:172-186.
10. Marmer J. *Hypnosis in Anesthesiology.* Springfield, IL: Charles C. Thomas; 1959.
11. Spiegel H, Spiegel D. *Trance and Treatment: Clinical Uses of Hypnosis.* Washington, DC: American Psychiatric Press; 1978.
12. Brown DP, Fromm E. *Hypnosis and Behavioral Medicine.* HIllsdale, NJ: Lawrence Erlbaum Associates; 1987.
13. Weitzenhoffer AM, Hilgard ER. *Stanford Hypnotic Susceptibility Scale (SHSS) forms A&B.* Palo Alto, CA: Consulting Psychologists Press; 1959.
14. Shore RE, Orne EC. *Harvard Group Scale of Hypnotic Susceptibility (HGSHS).* Palo Alto, CA: Consulting Psychologists Press; 1962.
15. Morgan AH, Hilgard JR. The Stanford Hypnotic Clinical Scales for adults. *Am J Clin Hypnosis* 1978/79;21: 134-147.
16. Tellegen A, Atkinson G. Openness to absorbing and self-altering experiences ("absorption"), a trait related to hypnotic susceptibility. *J Abnorm Psychol* 1974;83: 268-277.
17. Weitzenhoffer AM, Hilgard ER. *Stanford Profile Scales of Hypnotic Susceptibility (SPS).* Palo Alto, CA: Consulting Psychologists Press; 1963.
18. London P. *Children's Hypnotic Susceptibility Scale (CHSS).* Palo Alto, CA: Consulting Psychologists Press; 1962.
19. Kessler R, Dane JR. Psychological and hypnotic preparation for anesthesia and surgery: An individual difference perspective. *Int J Clin Exp Hypn* 1996;44: 189-207.
20. Lang EV, et al. Adjunctive non-pharmacological analgesia for invasive medical procedures: A randomised trial. *Lancet* 2000;355:1486-1490.
21. Lang EV, et al. Self-hypnotic relaxation during interventional radiological procedures: Effects on pain perception on intravenous drug use. *Int J Clin Exp Hypn* 1996;44:106-119.
22. Mauer MG, et al. Medical hypnosis and orthopedic hand surgery: Pain perception, postoperative recovery, and therapeutic comfort. *Int J Clin Exp Hypn* 1999;47: 144-161.
23. Defechereux T, et al. Hypnoanesthesia for endocrine cervical surgery: A statement of practice. *J Altern Complement Med* 1999;5:509-520.
24. Eberhart LH, et al. Therapeutic suggestions given during neurolept-anaesthesia decrease post-operative nausea and vomiting. *Eur J Anaesthesiol* 1998;15:446-452.
25. Williams AR, et al. The incidence and severity of postoperative nausea and vomiting in patients exposed to positive intra-operative suggestions. *Anaesthesia* 1994; 49:340-342.
26. Enqvist B, et al. Preoperative hypnosis reduces postoperative vomiting after surgery of the breasts. A prospective, randomized and blinded study. *Acta Anaesthesiol Scand* 1997;8:1028-1032.
27. Enqvist B, et al. Pre- and perioperative suggestion in maxillofacial surgery: Effects on blood loss and recovery. *Int J Clin Exp Hypnosis* 1995;43:284-294.
28. Ginandes CS, Rosenthal DI. Using hypnosis to accelerate the healing of bone fractures: A randomized controlled pilot study. *Altern Ther Health Med* 1999;5: 67-75.
29. Ginandes CS, et al. Can medical hypnosis accelerate post-surgical wound healing? Results of a clinical trial. *Am J Clin Hypnosis* 2003;4:333-351.
30. Smith J, et al. A comparison of hypnosis and distraction in young children undergoing painful medical procedures. *J Counseling Psychol* 1996;43:187-195.
31. Olness K, Kohen DP. *Hypnosis and Hypnotherapy with Children.* 3rd ed. New York: Guilford Press; 1996.
32. Lambert, SA. The effects of hypnosis/guided imagery on post-operative course of children. *J Developmental Behav Ped* 1996;17:307-310.
33. Lang EV, Rosen MP. Cost analysis of adjunct hypnosis with sedation during outpatient interventional radiologic procedures. *Radiology* 2002;222:375-382.
34. Barber J. When hypnosis causes trouble. *Int J Clin Exp Hypn* 1998;46:157-170.
35. Eisenberg DM, et al. Unconventional medicine in the United States: Prevalence, costs, and patterns of use. *N Engl J Med* 1993;328:246-252.
36. Morris DM, et al. Hypnoanesthesia in the morbidly obese. *JAMA* 1985;253:3292-3294.
37. Hammond DC, et al. Comparison of self-directed and tape-assisted self-hypnosis. *Am J Clin Hypn* 1988;31: 129-137.

CME Questions

CME Instructions: Physicians participate in this continuing medical education program by reading the article, using the provided references for further research, and studying the CME questions. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. After completing this activity, you must complete the evaluation form provided at the end of each semester (June and December) and return it in the reply envelope provided to receive a certificate of completion. When your evaluation is received, a certificate will be mailed to you.

51. Diagnosis of BPH is presumptive and based on both obstructive and irritative voiding symptoms.
a. True
b. False

52. Two systematic reviews of rye grass pollen for BPH concluded:
a. that rye grass pollen is well-tolerated.
b. that rye grass pollen modestly improves urologic symptoms.
c. Both a and b are correct.

53. Women taking DHEA for systemic lupus erythematosus:
a. may find symptom relief.
b. may be able to reduce dosages of other medications.
c. should be monitored closely by a physician.
d. All of the above

54. Significant cost savings have been documented among patients receiving hypnosis in addition to standard sedation.
a. True
b. False

Answer key: 51. a, 52. c, 53. d, 54. a.

Clinical Briefs

With Comments from Russell H. Greenfield, MD

LCPUFAs, Infant Formula, and Blood Pressure

Source: Forsyth JS, et al. Long chain polyunsaturated fatty acid supplementation in infant formula and blood pressure in later childhood: Follow up of a randomised controlled trial. *BMJ* 2003;326:953.

Goal: To determine whether supplementation of infant formula with long-chain polyunsaturated fatty acids (LCPUFAs) has an effect on blood pressure later in life.

Design: Follow-up of a randomized, controlled multicenter trial.

Subjects: A total of 147 formula-fed children and a reference group of 88 breast-fed children (mean age 70.1 months).

Methods: In 1992, children from six European centers were randomized to receive either standard infant formula, or a formula supplemented with docosahexaenoic acid (DHA) and arachidonic acid (ARA) that was otherwise nutritionally similar, during the first four months of life. Blinding with respect to the type of formula received was maintained. Approximately six years later participants had their blood pressures determined and questionnaires were completed.

Results: The children who had received formula supplemented with LCPUFAs had a lower diastolic and lower mean blood pressure than those who received the non-supplemented formula. The blood pressure of breast-fed children did not differ significantly from those who had received LCPUFAs, but the diastolic blood pressure was noted to be significantly lower than that of the non-supplemented group.

Conclusion: Dietary supplementation with LCPUFAs in formula-fed infants is associated with lower blood pressure in later childhood when compared to those having received standard infant formulae.

Study strengths: Multicenter design that ensured sex matching; all centers used the same type of automated blood pressure monitor.

Study weaknesses: Many of the initial study participants were not available for follow-up (50/126 in the supplementation group, 40/111 in the non-supplemented group, and 51/139 in the breast-fed group)—the majority of those lost to follow-up could not be traced or had relocated; data on diet after age 4 months were not collected.

Of note: The authors state that direct comparison of the supplemented formula group and the breast-fed group was not possible due to confounding variables.

We knew that: Deviations from normal blood pressure in childhood trace into adulthood; breast milk contains LCPUFAs, and breast-fed children have lower blood pressures than those fed standard formulae.

Clinical import: Tremendous advances have been made toward the treatment of cardiovascular disease, yet an increasing prevalence of hypertension, heart disease, and stroke clearly point to a need for added emphasis on prevention. For those mothers who cannot or who choose not to breast-feed, supplementation of infant formula with LCPUFAs may offer their children additional health benefits. Supplemented formulae, however, also are associated with additional cost, and programs must be developed to permit widespread availability across socioeconomic strata.

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Supplement to *Alternative Medicine Alert*
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ALTERNATIVE MEDICINE ALERT™
A Clinician's Evidence-Based Guide to Alternative Therapies

Complementary Approaches to Postoperative Pain, Nausea, and Vomiting

RESEARCHERS AT THE UNIVERSITY OF CHICAGO HOSPITALS RECENTLY PUBLISHED RESULTS from a national survey of patients who had undergone surgical procedures.[1] Patients were asked about the severity of postsurgical pain, treatment, satisfaction with pain medication, patient education, and perceptions about postoperative pain and pain medications. Of the 250 patients surveyed, approximately 80% experienced acute pain after surgery. Of these patients, 86% reported moderate, severe, or extreme pain, with more patients experiencing pain after discharge than before discharge.

Experiencing postoperative pain was the most common concern (59%) among patients. Almost 25% of patients who received pain medications experience adverse effects; however, nearly 90% of them were satisfied with their pain medications. Approximately two-thirds of patients reported that a health care professional talked with them about their pain.

In addition to postoperative pain, many patients suffer from postoperative nausea and vomiting. A 1994 study found the incidence of postoperative nausea and vomiting to be 37% and 20%, respectively. [2]

Despite an increased focus on pain management programs, development of new standards for pain management, and efforts to reduce postoperative nausea and vomiting, many patients continue to suffer from pain, nausea, and vomiting after surgery. Several complementary therapies increasingly are being employed to meet patients' postoperative needs.

Music therapy and guided imagery

A Swedish study compared the effect of intra-operative to postoperative music on postoperative pain in a controlled trial.[3] A total of 151 patients undergoing day case surgery for inguinal hernia repair or varicose vein surgery under general anaesthesia were randomly assigned to one of three groups: Group 1 listened to music intra-operatively; group 2 listened to music postoperatively; and group 3, the control group, listened to white noise. Results showed that patients exposed to music intra-operatively or postoperatively reported significantly lower pain intensity at hours 1 and 2 postoperatively and patients in the postoperative music group required less morphine at hour 1 compared to the control group.

In an experimental pilot study, researchers examined the effects of music therapy, guided imagery, and standard care on postoperative pain, postoperative nausea and vomiting, and length of stay for gynecologic laparoscopic patients.[4] Results indicated that patients in both the music therapy and guided imagery groups had significantly less pain on discharge than the patients in the standard care group.

Ginger (*Zingiber officinale*)

Researchers from Thailand recently published the results of a randomized, controlled clinical trial assessing the efficacy of ginger to prevent nausea and vomiting after outpatient gynecological laparoscopy.[5] Eighty patients were randomly assigned to group A (n = 40) or

group B (n = 40). Group A received 2 capsules of ginger (1 capsule contained 0.5 g of ginger powder) one hour before the procedure while the patients in group B received placebo. Visual analogue nausea scores (VANS) and vomiting times were evaluated at two, four, and 24 hours after the operation.

There was a significant difference in the incidence of nausea between group A (12, 30%) and group B (24, 57.5%). The VANS was lower in group A than in group B at two and four hours ($P < 0.05$), but no difference was found at 24 hours. Incidence and frequency of vomiting in group A were lower than group B, but this result did not reach statistical significance.

Acupressure

A study from the University of Exeter assessed the effectiveness of continuous PC6 acupressure as an adjunct to anti-emetic drug therapy in the prevention and control of nausea and vomiting in the first 24 hours after myocardial infarction.[6] A total of 301 consecutive patients (205 males, 96 females) were included in this study: The first 125 patients received no additional intervention. Subsequent patients were randomized to receive either continuous PC6 acupressure or placebo acupressure.

There were no significant differences between the groups for the whole 24-hour treatment period. However, the PC6 acupressure group experienced significantly lower incidence of nausea and/or vomiting during the last 20 hours (18%) compared with the placebo (32%) or control (43%) groups ($P < 0.05$). The severity of symptoms and the need for anti-emetic drugs also were reduced in the acupressure group, but these differences were not statistically significant.

Acupuncture

Researchers from South Korea recently conducted a study on the effect of auricular acupuncture on postoperative nausea and vomiting.[7] One hundred female patients undergoing transabdominal hysterectomy were entered into the study. The patients were divided into two groups (auricular acupuncture treatment group and non-treatment group) in order to test the effectiveness of auricular acupuncture. There was no significant difference in age, weight, height, or duration of anesthesia among the two groups of patients.

There was a significant difference between the control and auricular acupuncture treatment groups in the incidence of vomiting 12 hours after surgery (68% and 30%, respectively, $P < 0.01$). No noteworthy side effects from treatment were observed.

In another study, researchers compared acupuncture to sham acupuncture in arthroscopic acromioplasty subjects to determine whether they would manifest significantly better recovery as demonstrated by: UCLA shoulder scale, improved range of motion, diminished pain, decreased need and duration of analgesic use, and enhanced patient satisfaction.[8]

Thirty-five subjects completed the four-month study. Real acupuncture subjects scored significantly better on UCLA shoulder scale ($P < 0.000$); pain intensity ($P < 0.022$); self-reported analgesic use ($P < 0.008$); angles of abduction ($P < 0.046$); and in six of eight health status questionnaire components. The authors concluded that acupuncture offered significantly greater improvement with regard to: pain level, analgesic use, range of motion, and patient satisfaction.

References

1. Apfelbaum JL, et al. Postoperative pain experience: Results from a national survey suggest postoperative pain continues to be undermanaged. *Anesth Analg* 2003;97:534-540.
2. Quinn AC, et al. Studies in postoperative sequelae. Nausea and vomiting—Still a problem. *Anaesthesia* 1994;49:62-65.
3. Nilsson U, et al. A comparison of intra-operative or postoperative exposure to music—A controlled trial of the effects on postoperative pain. *Anaesthesia* 2003; 58:699-703.
4. Laurion S, Fetzer SJ. The effect of two nursing interventions on the postoperative outcomes of gynecologic laparoscopic patients. *J Perianesth Nurs* 2003;18: 254-261.
5. Pongrojpaw D, Chiamchanya C. The efficacy of ginger in prevention of post-operative nausea and vomiting after outpatient gynecological laparoscopy. *J Med Assoc Thai* 2003;86:244-250.
6. Dent HE, et al. Continuous PC6 wristband acupressure for relief of nausea and vomiting associated with acute myocardial infarction: A partially randomised, placebo-controlled trial. *Complement Ther Med* 2003; 11:72-77.
7. Kim Y, et al. Clinical observations on postoperative vomiting treated by auricular acupuncture. *Am J Chin Med* 2003;31:475-480.
8. Gilbertson B, et al. Acupuncture and arthroscopic acromioplasty. *J Orthop Res* 2003;21:752-758.