Forty percent of all menopausal women seek medical attention to alleviate symptoms of menopause, a natural physiologic process. Severe symptoms and an overall decrease in quality of life have prompted many women to demand additional information and treatment. Although menopausal hormone therapy has been the standard, increasing evidence suggests that women are looking to complementary and alternative therapies for management and treatment of menopausal symptoms. Modalities such as physical activity, diet supplements, bodywork, and mind-body techniques are often used without evaluation or treatment by conventional health care providers. Many of these treatments may present varying risks and contraindications. Consequently, there is a great need for ongoing education and research to ensure alternative therapy use is not only effective, but also safe. This paper provides a systematic review of current complementary and alternative modalities and of physical activity used in the management and treatment of menopausal symptoms. (JAMWA. 2004;59:270-277)

Women today may live as much as one-third of their lives after menopause, a natural physiologic process often accompanied by hot flashes, night sweats, vaginal dryness, irritability, and depression. With their mean life expectancy now exceeding 84 years, it is estimated that more than 60 million American women will be postmenopausal by 2025. Forty percent of all menopausal women seek medical attention for menopausal symptoms. Severe symptoms and an overall decrease in quality of life have prompted many women to demand additional information and treatment for their menopausal symptoms. When considering reasons to initiate hormone therapy, respondents to a 1997 North American Menopause Survey cited relief from physical symptoms more frequently than prevention of osteoporosis, cardiovascular disease, or Alzheimer’s disease.

Although it is not without controversy, menopausal hormone therapy (MHT), also known as hormone replacement therapy, has been the standard treatment for menopausal symptoms. Numerous studies have found it (estrogen alone or estrogen plus progestin) to be the most effective therapy for hot flashes and sleep disturbances; MHT lessens 80% to 90% of symptoms compared with other medical interventions, including vitamins, clonidine, and antidepressants, which relieve only 30% to 60% of symptoms. Although additional benefits include a decrease in vaginal dryness and urinary tract infections and increased skin elasticity and thickness, concerns about safety and efficacy are causing a retreat from the blanket use of MHT.

Before the results of the Women's Health Initiative (WHI) were released, only 50% of prescriptions written for MHT were actually filled, and less than 40% of women initiating MHT continued it for

**Complementary and Alternative Medicine and Physical Activity for Menopausal Symptoms**

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more than a year. Reasons for nonuse and early discontinuation merit serious assessment by both health care providers and women. MHT is contraindicated in women suspected of or previously diagnosed with an estrogen-dependent neoplasia (breast or advanced stage uterine cancer), active thrombotic or embolic disease, undiagnosed uterine bleeding, and active liver disease or severely impaired hepatic function. Consequently, the fear of increased risk of cancer and worrisome side effects such as uterine bleeding, headaches, and breast tenderness is a significant deterrent. In addition, many women simply view MHT as an “unnatural” method of dealing with a natural phenomenon.

The WHI has discredited the belief in the protective effects of MHT, and, in fact, has shown that it is associated with an increased risk of heart disease (29%), breast cancer (26%), and events such as strokes (41%). MHT did demonstrate a protective effect against colon cancer (37%) and hip fractures (34%) secondary to osteoporosis. WHI results in combination with clinical contraindications and generalized fear may leave some women with the impression that MHT is inappropriate for the treatment of menopausal symptoms.

Women’s interest in and use of complementary and alternative therapies have been increasing, even before the WHI results were released. Complementary and alternative medicine (CAM), defined as medical practices that are not an integral part of Western medicine, is not widely taught at medical schools or generally available from practitioners. Furthermore, these therapies are seldom eligible for reimbursement. Out-of-pocket expenses for alternative therapies were estimated at $27 billion in 1997, exceeding all out-of-pocket expenses for physician services that year. In 1998, CAM visits exceeded visits to conventional providers, and 80% of women responding to a 1997 survey reported having used some form of nonprescription therapy to manage menopausal symptoms. Therefore, it is no surprise that women generally treat menopausal symptoms with easily obtainable therapies, many of which have not been evaluated by double-blind, placebo-controlled trials.

Women and clinicians both need useful information and tools to help them make informed decisions regarding the more than 100 new menopausal symptom relief products that have entered the market since 1998. These products have become so popular that women have spent more than $600 million purchasing them. Ongoing education and research are essential to ensure that alternative therapies are not only effective, but also safe.

This article provides a broad overview of both physical activity and the complementary and alternative therapies currently used for menopausal symptoms, including vitamin supplements, soy products, bodywork, mind-body techniques, and herbal remedies.

Physical Activity

Physical activity may ameliorate hot flashes and insomnia by influencing opioid levels. Postmenopausal changes in opioid levels, including lowered levels of beta-endorphins and decreased central opioid activity, may lead to decreased inhibitory effects on norepinephrine. Unregulated levels of norepinephrine may initiate flushing episodes by activating the heat-loss mechanism in the medial preoptic area. Because exercise has been shown to increase central opioid activity, it may exert a beneficial effect on hot flashes. Hammer compared hot flash severity and frequency, finding that only 21.5% of physically active women (average of 3 hours/week) experienced moderate to severe flashes, compared with 44% of the control group. The proportion of women without hot flashes was comparable in both groups, indicating a decrease in severity, but not in frequency. Although promising, this study has some limitations. Although neither group used hormones, the physically active group may have been more likely to use other interventions to decrease hot flash severity.

More recent studies have also suggested that women who exercise regularly are less likely to experience severe hot flashes. A Swedish study reported that only 5% of exercising women experienced “severe” hot flashes, compared with 15% of sedentary women. Because differences in severity could not be explained by differences in body mass index, smoking, or MHT use, the authors suggested that physical activity may decrease the severity of hot flashes.

Although data supporting physical activity are still preliminary, physical activity provides numerous health benefits, including cardiovascular fitness, decreased bone resorption, weight reduction, improved lipoprotein profile, and reduced tension and anxiety. The benefits of physical activity appear to outweigh potential risks, such as...
falls and fractures, particularly when physical limitations are considered and the woman is assessed for risk factors for preexisting disease conditions before initiating an exercise program or increasing her activity level.

Vitamin E

The medical and lay literature have anecdotally suggested that vitamin E may alleviate hot flashes. A placebo-controlled trial conducted by Barton et al found a marginal clinical benefit from a daily regimen of 800 IU of vitamin E. Both the control and study groups (total n=105) experienced an average of 1.6 fewer hot flashes per day during the first treatment period (1 week). The second 4-week treatment yielded a statistically significant, but clinically negligible decline in hot flash frequency (1 fewer/day) in the vitamin E group. Researchers concluded that the potential benefit from vitamin E is small. Similarly, the North Central Cancer Treatment Group found minimal efficacy in its clinical trial. To date, clinical trial results have been insufficient to support or refute the efficacy of vitamin E to treat hot flashes. Furthermore, several potential problems have been associated with high intakes of vitamin E, including muscle weakness, fatigue, nausea, and diarrhea. Vitamin E is also contraindicated in patients taking anticoagulants.

Soy and Soy Products

Soy and soy products have been recommended for the alleviation of menopausal symptoms because they have high concentrations of phytoestrogens, nonsteroidal plant derivatives possessing mild estrogenic and antiestrogenic properties. Phytoestrogens are divided into 4 groups based on their chemical structures: isoflavonoids, flavonoids, coumestans, and mammalian lignans. The biologic actions of phytoestrogens are very complex. They competitively bind to estrogen receptors, displacing more potent estrogens, and potentially decrease the overall estrogenic effect. In addition, individual phytoestrogens may also exhibit receptor selectivity, facilitating unique, tissue/organ-specific actions. Additional mechanisms of action include inhibiting DNA topoisomerase, suppressing angiogenesis, inducing differentiation in cancer cell lines, and inducing apoptosis. These nonhormonal activities may be more important in cancer prevention than in alleviating menopausal symptoms.

Epidemiological data suggest an inverse relationship between menopausal symptom severity and isoflavone intake from soy products. Asians typically consume 20 to 80 mg of isoflavones daily (compared with less than 5 mg in Western countries) and rarely report menopausal symptoms. Cultural norms may also explain lower hot flash frequencies in Asian countries; however, it is socially unacceptable for Asian women to discuss menopausal symptoms, and some Asian languages even lack terms or idioms to describe hot flashes. Thus rates of frequency and severity may be underestimated.

Clinical trials have yielded a continuum of results both substantiating and refuting the benefits of soy. A recent study conducted by Albertazzi et al found a significant reduction in hot flashes in the treatment group compared with the placebo group (45% and 30% respectively). Subsequent trials have reported vasomotor improvements, as well as significant declines in total cholesterol (6%), low-density lipoprotein cholesterol (7%), and diastolic blood pressure (5 mm Hg). Murkies et al randomized 58 postmenopausal women to receive servings of wheat or soy flour. The wheat group experienced a 25% and the soy group a 40% reduction in hot flash frequency. The soy treatment was of limited practical benefit, however, because the 15% difference was equivalent to 1 hot flash per day. Another study compared the use of such dietary supplements as soy, Ginkgo biloba, and black cohosh with MHT use. Although less satisfied with symptom control, the supplement group reported the highest quality of life.

Studies of soy and soy protein are not always comparable. The amount and type of phytoestrogen used and methods of preparation and extraction may vary widely. For example, the active or aglyconic forms of isoflavones are alcohol soluble; however, most store-bought soy milk and tofu are alcohol washed and do not contain active isoflavones. Because isoflavone concentrates and extracts are manufactured by alcohol washing and evaporation, the effects of soy protein found in whole foods, soy protein isolates, and isoflavone isolates may vary.

Although soy has been associated with such additional benefits as maintaining bone density, improving lipoprotein...
profiles, and preventing breast and prostate cancer. Safety remains a concern, including development of breast cancer and increased growth of existing tumors. However, high excretion of phytoestrogens in plasma and urine, indicating high intake, has been associated with a low incidence of breast cancer in 2 Australian case-control studies. Moreover, countries with high dietary intakes of phytoestrogens have many of the world’s lowest incidences of breast cancer and cardiovascular disease. Phytoestrogen use has also been found to affect concentrations of throxine, insulin, and glucagon. One randomized trial noted a decrease in insulin, reduced insulin resistance, and improved glycemic control, and another documented an increase in serum-free throxine concentrations. Although phytoestrogen consumption is not recommended during critical stages of embryological reproductive tract development (between the 5th and 8th weeks of pregnancy) or in high doses, it is unlikely that a diet incorporating moderate amounts (25 g = 2 soy burgers or 2 soy bars) of soy and soy products will cause adverse events.

**Bodywork**

Bodywork therapies, including massage, touch therapies, movement therapies, acupuncture, acupressure or shiatsu, rolfing/structural integration, chiropractic therapy, and osteopathy, use physical manipulation to alleviate clinical symptoms. In 1996, a large health maintenance organization (HMO) surveyed alternative therapy use among its clinicians and members and found that manipulative therapies, such as chiropractic, acupuncture, and therapeutic massage, were the alternative therapies most frequently used by both members and clinicians. In addition, primary care physicians and HMO members were more interested in coverage for manipulative and behavioral therapies than for conventional treatments.

Like exercise, therapies that increase central opioid activity may be responsible for decreased frequency, duration, and intensity of hot flashes. Wyon et al randomized 21 women into an electroacupuncture group using 2 Hz and a control group with superficial needle insertion for 8 weeks. Hot flashes in both groups declined by more than 50%; however, only the electroacupuncture group sustained the effect after 6 months, suggesting that electroacupuncture has a sustaining effect on opioid activity. Scores on the Kupperman index, a weighted measure of the 11 most common menopausal symptoms, also declined significantly during and after both treatments though electroacupuncture did not appear to affect sleep dysfunction during the treatment period. A more recent study found a 4-fold increase in the use of bodywork among those suffering from chronic sleep disturbances compared with nonsufferers. Recommendations for bodywork to treat menopausal symptoms are limited, as the data are inconclusive; however, current research has documented little to no risk in the use of these therapies.

**Mind-Body Techniques**

Mind-body techniques include meditation, biofeedback, yoga, tai chi, and other voluntary manipulations of body-process perceptions. Because catecholamines have been suggested as catalysts of many relaxation pathways, meditation, paced respiration, and progressive muscle relaxation may have a positive effect on hot flashes.

Irvin et al compared the effects of relaxation response and attention-control training in 33 women and found that hot flash intensity and tension-anxiety and depression decreased in the relaxation response group. Another trial randomized postmenopausal women to compare 3 types of training: paced respiration, muscle relaxation, and alpha-wave electroencephalographic biofeedback and found that paced respiration was most effective in reducing hot flashes. A third study examined applied relaxation techniques, which included 10 to 12 sessions of progressive relaxation, release-only relaxation, cue-controlled relaxation, differential relaxation, rapid relaxation, application training, and maintenance training. Hot flash incidence declined for all 6 patients from 59% to 100% (mean 73%) during the 12-week training period and was sustained for 6 months following the training.

Although studies have shown promising results, the benefits of mind-body techniques may be limited in clinical practice, as they require extensive training, discipline, and time by certified or licensed professionals to be effective.

**Botanical and Herbal Therapies**

The German Commission E has defined herbal therapies as those whose active ingredients are derived exclusively from plant materials or from vegetable drug preparations, which are plant materials used for medicinal purposes. Botanicals and herbal remedies that have been suggested to relieve menopausal symptoms include ginseng, bee pollen, red sage, gotu kola, sarsaparilla, licorice root, wild yam root, dandelion, raspberry, motherwort, black cohosh, damiana, dong quai, evening primrose, red clover, saw palmetto, flaxseed, sage, chamomile, ginkgo, hops, passion flower, St. John’s wort, and valerian. The many claims of purported
remedies are exhaustive, confusing, and often lacking in scientific validity.

Manufacturers are expected to have some scientific evidence to conclude that dietary ingredients, which are components of dietary supplements (vitamins, minerals, herbs or other botanicals, amino acids, metabolites, or extracts), are reasonably safe. However, these ingredients are not subject to Food and Drug Administration (FDA) approval. Functional foods, which provide health benefits beyond energy and essential nutrients and dietary supplements, are allowed to carry “structure/function claims on their labels,” claims that they affect the function or structure of the body, but not that they reduce disease risk. For example, calcium supplements claim to improve bone health, but do not reduce disease risk by treating or preventing osteoporosis. Consumers may misunderstand structure/function claims and risk ineffective treatments or side effects.

The FDA does not require content testing of herbal products, so it is possible for the product to be unsafe even though the herb has been approved by academic researchers. Many factors, including variable growth environments, differing plant species, parts of plant used, and possible adulteration or substitution, contribute to efficacy and safety variations among products. The FDA has received 2797 reports of adverse events potentially associated with dietary supplements, including 105 deaths, since 1993. Because the reporting system is voluntary, the incidence of adverse events may be seriously underreported.

A national consumer survey conducted by Prevention magazine in 1999 found that 12% of consumers, or approximately 11.9 million people, had experienced adverse reactions from herbal dietary supplements.

Ginseng

Ginseng (Panax ginseng, Panax quinquefolius), a historical anecdote, is thought to have aphrodisiac and estrogenic effects, although there is no scientific evidence to support these claims. There are several varieties of ginseng, including Oriental, wild red American, Chinese, and Korean red, each claiming differing properties. Numerous studies and the lay literature have recommended ginseng for menopausal symptoms, including depression, decreased libido, and perceived poor quality of life. Evidence suggesting ginseng is effective against fatigue is minimal.

Tode et al observed that anxiety levels in climacteric women declined to normal after 30 days of ginseng treatment. In addition, both cortisol and dehydroepiandrosterone showed statistically significant decreases. The study demonstrated marked improvement in the Cornell Medical Index and the State-Trait Anxiety Inventory, but did not attribute anxiety decline to decreased fatigue and insomnia. Another study examined the effects of Korean red ginseng and found that quality of life improved in the treatment group; however, as in subsequent studies, researchers were unable to detect somatic or vasomotor benefits.

Several studies have reported estrogen-like effects on vaginal mucosa associated with ginseng use. Ginseng extract has also been reported to compete with estradiol for estrogen and progesterone binding sites in human myometrial cytosol. Several case reports have cited vaginal bleeding in postmenopausal women taking ginseng. This may be attributed to ginseng’s estrogen-like effects. Side effects associated with excess ginseng use include nervousness, sleeplessness, diarrhea, hypertension, and mastalgia.

Although the German government has approved ginseng (200 mg/day) for the treatment of fatigue, diminished work capacity, and loss of concentration, it opposes use in excess of 3 months.

Black Cohosh

Black cohosh (Cimicifuga racemosa), a popular botanical, is commonly used to treat hot flashes. Often referred to as black snakeroot, women’s root, bugbane, richweed, rattleweed, and squawroot, black cohosh was also used by early Native American cultures to promote gynecologic health. According to the German Commission E Monographs, black cohosh has estrogen-like action, suppresses leutinizing hormone (LH) preventing activation of central nervous system pathways that induce hot flashes, binds to estrogen receptors, has no contraindications to use, and produces gastric discomfort as the only potential side effect. However, manufacturers of black cohosh have sponsored much of the data generated by these studies.

Although the mechanism of action for black cohosh is not well understood, recent findings have been inconsistent with and have refuted prior claims of estrogenic activity, including LH and follicle stimulating hormone (FSH) reduction. Jacobson’s randomized, placebo-controlled trial found no significant changes in the global rating scale or in FSH and LH levels. Similarly, a German study also found no change in LH and FSH levels, although Kupperman index scores improved significantly in all groups.

Potential side effects include hypotension and digitalis-like cardiac effects. In addition, in large doses, black
Dong Quai

Dong quai (Angelica sinensis), also known as dang gui, Tang Kuei,4 and women’s ginseng,16 has been used in traditional Chinese medicine for menstrual and menopausal symptoms for more than 2000 years.65 Despite its long history of use, there is little scientific evidence to support its efficacy and safety.4,65 One 24-week randomized clinical trial of 71 women showed no significant difference in relief of menopausal symptoms in either group.66 Both the dong quai and placebo group took 3 capsules 3 times daily; after 24 weeks, study participants were unable to distinguish between the active drug and placebo. Researchers concluded that when used alone, dong quai was no more useful than placebo in the treatment of menopausal symptoms; however, Chinese herbalists maintain that the synergistic effect of dong quai and other herbs accounts for its beneficial effects.83 Scientific evidence has not substantiated dong quai’s benefits to date. In fact, according to the American College of Obstetricians and Gynecologists, the study dose of dong quai (4.5-6.0 g/day) is potentially toxic and contains numerous coumarin-like derivatives that may cause excessive bleeding or interactions with other anti-coagulants4,60 and photosensitization.86

St. John’s Wort

St. John’s wort (Hypericum perforatum), a popular antidepressant, has been used for centuries. Increasing data suggest that St. John’s wort is effective in the treatment of mild or moderate depression.51 A meta-analysis of 15 trials67 found that St. John’s wort in doses less than 1.2 mg per day produced a 61% improvement in mild to moderate depression, and doses up to 2.7 mg per day produced a 75% improvement.

A 12-week prospective trial68 demonstrated a statistically significant improvement in incidence and severity of psychological, psychosomatic (headaches, palpitations), and vasomotor symptoms in patients 43 to 65 years old with pre- and postmenopausal symptoms. Eighty percent to 90% of women rated their symptoms as “marked” or “moderate” at baseline, which fell to 20% to 30% by the end of the 12 weeks. The majority experienced elimination or significant amelioration of symptoms. Although this study was limited by its small sample size and lack of a control group, the results are encouraging.

Although St. John’s wort has been used to treat mild to moderate depression, overall efficacy cannot be generalized to pre- and postmenopausal women, as few depression studies are limited to menopausal women. In fact, recent studies69 have suggested that St. John’s wort is ineffective in treating major depression. After randomizing and treating 340 patients suffering from major depression, a double-blind placebo-controlled trial failed to demonstrate efficacy in the intervention group. Full response occurred in 31.9% of the placebo-treated patients and 24.8% of control patients, whereas only 23.9% of the intervention group reported response.

Reported adverse events included difficulty breathing, throat constriction, headaches, dizziness, convulsions, rash, and vomiting. Because St. John’s wort contains an inhibitor of monoamine oxidase, interactions with other drugs, including fluoxetine18 and human immunodeficiency virus drugs,86 may occur. Patients should be warned against possible interactions if they use St. John’s wort for menopausal symptoms.

Evening Primrose

Evening primrose (Oenothera biennis), also known as evening star, produces seeds containing gamolenic acid (GLA), a precursor of prostaglandin E1, and is thought by some to relieve vasomotor symptoms. Evening primrose is commonly recommended for mastalgia, premenstrual syndrome, menopausal symptoms, and bladder problems, such as urinary frequency and urgency,14 although scientific evidence has yet to conclusively demonstrate menopausal efficacy. A meta-analysis of clinical trials70 found that only 5 of 7 controlled trials had been properly randomized. To date, only 1 randomized, double-blind, placebo-controlled trial has studied the effects of evening primrose on menopausal symptoms,7,14,71 and it found that evening primrose offered no benefit over placebo in controlling vasomotor symptoms in 56 symptomatic women who received 500 mg of evening primrose oil daily. Furthermore, evening primrose may contain anticoagulant substances, which may cause adverse effects and drug interactions.4,14 Therefore, evening primrose should not be recommended to patients for relief of menopausal symptoms.

Summary

A goal of treatment during menopause is to minimize discomfort from menopausal symptoms, such as hot flashes...
and nights sweats, and promote long-term health. Though MHT is still considered an efficacious short-term treatment for hot flashes, night sweats, and vaginal dryness, many clinicians are now reluctant to use it because of the poor risk-benefit ratio. Moreover, many women cannot or prefer not to be treated with hormonal therapies.72 For these women, a safe and effective alternative is sought in complementary and alternative medicine, and they may self-medicate based on anecdotal reports in lay literature.73 Additionally, it is of concern that many women may not report their use of CAM to their physicians.73 Until additional data are generated, one cannot equate “natural” or complementary therapies with safety or efficacy. Therefore, clinicians must remain abreast of the expanding body of CAM evidence and provide accurate and useful information to help their patients make informed decisions. The federal government is an excellent resource for current and accurate CAM information. The Office on Women’s Health within the Department of Health and Human Services has developed the National Women’s Health Information Center (www.4woman.gov), the largest federal clearinghouse on women’s health information. It provides resources on more than 800 topics, including CAM, and links to the National Center for Complementary and Alternative Medicine website (www.nccam.nih.gov) at the National Institutes of Health. It is through quality research and educational outreach that significant steps can be taken to ensure that the use of CAM to treat menopausal symptoms is effective and, most importantly, safe.

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