Indian Menopause Society

Guideline Number 9 : February 2011

Alternatives to Hormone Therapy in Managing Menopause

Introduction:

Despite recent encouraging data regarding the safety of traditional hormone replacement therapy (HRT), women and their primary care practitioners continue to be concerned about the purported risks, particularly to the breasts and cardiovascular system. This concern has fuelled continued interest in alternatives to HRT for the management of menopausal symptoms. The choice of treatment remains confusing and the evidence for efficacy and safety for many of these preparations remains limited. Use of complementary and alternative medicine has become part of daily practice as more patients obtain over the counter dietary supplements and herbal products.

The use of non-hormonal therapies for the treatment of menopause was recently reviewed and a Position statement issued by the North American Menopause Society.[1]

Lifestyle Measures

Smoking : Encourage the woman and family to stop smoking and avoid second-hand passive smoke. Prescribe counselling, nicotine replacement or other pharmacotherapy, as indicated in conjunction with behavioral therapy or a formal smoking cessation program.

Exercise : Several randomised controlled trials of middle-aged/menopausal-age women have found that aerobic exercise can result in significant improvements in several common menopause-related symptoms (e.g. mood, health-related quality of life and insomnia) relative to non-exercise comparison groups.

Recommend medically supervised programs for women who have had a recent MI or revascularization procedure.[2]

1. Brisk walking and vigorous exercise are associated with substantial reductions in coronary events and stroke.
2. Physical activity lowers blood pressure, improves the lipid profile, reduces insulin resistance and enhances fibrinolysis. Encourage a minimum of 30 min of moderate-intensity dynamic exercise, e.g., brisk walking, at least 5 days a week, supplemented by an increase in daily lifestyle activities. Optimum results will be obtained with a 5 days per week regimen, with 30 – 40 minutes of aerobic exercise at 70 % of the maximum heart rate (MHR).
3. Exercise reduces central body fat mass while preserving muscle when combined with appropriate nutrition and diet.
4. Any form of aerobic exercise is beneficial – brisk walking, jogging, swimming and cycling – and should be tailored to the individual's preference, age and medical condition.

Weight loss: Encourage gradual weight loss for overweight women through a combination of physical activity and portion control, healthy food choices, and recognition of triggers to overeating. Refer to weight loss support group or formal nutritional counseling when appropriate.[2]

Stress management : Positive coping mechanisms for stress should be advocated (e.g. substitute physical activity for overeating or smoking in response to stressful life situations).

Diet and supplements

1. Encourage a well-balanced and diversified eating pattern that is low in saturated fat and high in fresh fruits and vegetables and fiber.
2. Advocate fats with higher monounsaturated content (e.g. olive oil, canola oil) and soft unsaturated margarine to butter.
3. Encourage seafood and skinless chicken to red meat.
4. Use skim milk and skim milk products or at most 1 % milk instead of products with a higher fat content.
5. Limit the intake of high-cholesterol foods, avoid fast food meals.
6. Consume more than five servings of fruits and vegetables daily.
7. Total dietary fiber intake from food should be 25 – 30 g/day.
8. Diets rich in antioxidant vitamins (i.e. nuts, fruits and vegetables) are preferred over vitamin supplements
9. Limit salt intake to 6 g/day. A reduced salt / reduced saturated fat diet has been shown to reduce blood pressure in clinical trials.
10. Limit alcohol to less than one to two glasses per day

Vitamins and minerals:

Vitamins E and C, and minerals, such as selenium, are present in various supplements.

A statistically significant reduction in hot flush frequency was observed with vitamin E 800 iu/day compared with placebo. In a recent randomised trial of gabapentin versus vitamin E, gabapentin appeared to be effective for the treatment of hot flushes, having a favourable effect on quality of sleep whereas vitamin E had only a marginal effect on vasomotor symptoms.[3]

Vasomotor Symptoms : Refer to Indian Menopause Society Guideline No 1 August 2010

Urogenital Symptoms : Refer to Indian Menopause Society Guideline No 6 February 2011

Osteoporosis

Raloxifene : Refer to Indian Menopause Society Guideline No 7 February 2011

Bisphosphonates: These are synthetic compounds made out of phosphorous and carbon. They inhibit bone resorption and prevent vertebral and non-vertebral fractures. They are the first-line treatment for postmenopausal osteoporosis.[4]

Alendronate is the most commonly used bisphosphonate. It is administered in a weekly oral dose of 35mg for prophylaxis and 70 mg for treatment of Osteoporosis.

Other drugs in this group are Risedronate, Etidronate and Ibandronate.

Side Effects: Gastric irritation and esophageal ulceration, so women are advised not to lie down for an hour after taking the medication.

Calcitonin : Inhibits bone resorption and regulates calcium metabolism. Calcitonin has been shown to slow bone loss and may improve bone density, but does not decrease fracture risk. This treatment may be most beneficial to those who have a high bone turn over with rapid bone loss. Side effects are flushing, nausea, and dizziness. These can be minimized by taking the drug at bedtime[13]. It is available as nasal spray and injections. The main advantage is that it reduces pain after fractures. It is an expensive drug.

Parathyroid Hormones: This treatment carries the unique potential of activating new bone growth, according to researchers, unlike other available treatments, which mostly retard bone loss. . When low doses of parathyroid hormone are administered intermittently by once-a-day injections, the result is the stimulation of bone-forming cells

(osteoblasts) and an increase in bone mass. In human studies, this approach has consistently resulted in significant increases in trabecular bone (the spongy, inner part of bone) of the spine. Few changes in cortical bone (the outer, more dense part of bone) have been observed.

Complementary therapies

Women perceive complementary therapies to be safer and more natural alternatives to traditional hormone therapies. However, the efficacy and safety of a number of these preparations have not been properly evaluated.

Botanicals: A variety of botanicals are used by women. The evidence from clinical trials of benefit on menopausal symptoms is limited and conflicting. There are no recognised international criteria for the design of clinical trials of alternative therapies as there are for standard medicines and medical devices for endpoints of treatment and safety evaluations. Studies may use different products that are not chemically consistent, making comparison difficult. Also, the stability of individual chemicals may vary and may depend on the type of packaging. Herbs may contain many chemical compounds whose individual and combined effects are unknown.

Phytoestrogens : They comprise mainly plant products including isoflavones (found in soy bean products,chick peas,redclover,beans and peas), lignans (found in whole grains, flaxseed, and vegetable oils,cereal bran,whole cereals,legumes) and coumestans (found in red clover, sunflower seeds, and sprouts).

The role of phytoestrogens has stimulated considerable interest since populations consuming a diet high in isoflavones, such as the Japanese, appear to have lower rates of menopausal vasomotor symptoms, cardiovascular disease, osteoporosis and breast, colon, endometrial and ovarian cancers.A systematic review of 30 randomised trials (lasting at least 12 weeks and involving a total of 2730 participants) for reducing hot flushes and night sweats in peri- or postmenopausal women concluded that isoflavone supplementation may produce a slight to modest reduction in the number of daily flushes in menopausal women and that the benefit may be more apparent in women experiencing a high number of flushes per day. [5]

The effects on Indian women have not been studied. Since there is a high consumption of legumes and cereals, it is possible that the Indian woman may already have high plasma levels of phytoestrogens.[6]

The use of soy and isoflavones may improve lipoprotein profile and reduce cardiovascular risk.[7] Evidence for the beneficial effects of phytoestrogens is increasing, but further studies are needed.

DT56a : A soy-derived preparation, DT56a, has been shown to have an effect on hot flush reduction in a dose ranging study. Clinical and preclinical studies suggest that DT56a has selective estrogen receptor modulator (SERM)-like properties, with agonistic activity on the estrogen receptors in the central nervous system and bone and antagonistic effects on estrogen receptors in the breast and the uterus.[8]

Dehydroepiandrosterone (DHEA): This is believed to have anti-ageing effects. Some studies have shown benefits on the skeleton, cognition, wellbeing, libido and the vagina. There is no evidence that DHEA has any effect on hot flushes. The short-term effects of taking DHEA are still controversial and possible harmful effects of long-term use are, as yet, unknown.[3]

Black cohosh: NAMS has recommended that treatment with black cohosh is "likely to do no harm and may provide relief of hot flashes"; but discourages use of dong quai, evening primrose oil, ginseng, licorice, Chinese herb mixtures, acupuncture, and magnetic therapy.[7] Little is known about the long-term safety of black cohosh. Liver toxicity has been reported, leading to recommendations for caution labels.

Evening primrose oil: This is rich in gamma-linolenic and linolenic acid. Even though it is widely used by women, there is no evidence for its efficacy in the menopause. One small randomised placebo-controlled trial has shown it to be ineffective for treating hot flushes.[2]

Indian Herbs: Indian herbs for use in menopause are generally dietary herbs like turmeric, ginger, fenugreek, linseed, cumin, fennel, saffron, and cinnamon.

Chinese herbs:

Dong quai (*Angelica sinensis*) is a perennial plant native to southwest China that is commonly used in traditional Chinese medicine. Interactions with warfarin, increasing the risk of bleeding and photosensitisation, have been reported. A recent trial has examined the efficacy of another Chinese herb, Danggui Buxue Tang, on a variety of vasomotor symptoms. Benefit over placebo was found only for mild hot flushes.[7]

Ginseng:

Ginseng is a perennial herb native to Korea and China that is used extensively in eastern Asia. Used for vasomotor symptoms. Case reports have associated ginseng with postmenopausal bleeding and mastalgia; interactions have been observed with warfarin (leading to a reduced international normalised ratio), **Red clover and Chinese ginseng** are dietary supplements for which evidence is currently still lacking has some question about the quality and purity of supplements on the market.[2]

St. John's Wort (*Hypericum perforatum*) is best used, if indicated, for mild-to-moderate depression[17] and has both serotonergic and dopaminergic effects(. SSRI-type effect). If efficacious, effects should be seen within 3 weeks and side effects within 2 weeks. St. John's wort should not be used concomitantly with cytochrome P450-inducing liver enzyme drugs and should be discontinued before surgery. In a recent randomised placebo-controlled trial, women on St John's wort reported improved menopause-specific quality of life and a non significant improvement in hot flushes.[9]

Other Herbs *-Ginkgo biloba*, hops, sage leaf, liquorice and valerian root are popular, but there is no good evidence for their use. Kava kava (*Piper methysticum*), which was previously widely used for anxiety can cause liver damage.[2]

Other complementary interventions: include acupressure, acupuncture, ayurveda osteopathy, hypnotherapy, and Reiki. Further research is needed to understand their possible effects.

Reflexology - aims to relieve stress or treat health conditions through the application of pressure to specific points or areas of the feet, hands and ears. There have been few studies of the use of reflexology for menopausal complaints. One randomised trial published so far shows a reduction in symptoms.[10]

Magnetism: There is no known mechanism of action for magnet therapies for the treatment of hot flushes. There is no evidence of benefit at present.[10]

Homeopathy: Data from case histories, observational studies and a small number of randomised trials are encouraging, but more research is needed. Larger randomised trials are required to confirm these effects.[10]

Stellate ganglion blockade - involves local anaesthetic injection into the stellate ganglion, recently emerged as a new technique against hot flushes and sweating, refractory to other treatments or where HRT is contraindicated, such as in women with breast cancer. Preliminary studies report encouraging efficacy with minimal complications.[11]

Conclusion

A woman with menopausal symptoms may choose not to use conventional HRT, or there may be contra-indications to HRT. Clinicians should be aware of the range of options available and be able to discuss their advantages and disadvantages and specific risk factors in a balanced, evidence-based manner, based on symptom severity, quality of life and the risks of the condition itself.

The efficacy of alternative preparations, continues to be lower than with traditional HRT (maximally 50–60% symptom reduction compared with 80–90% with traditional HRT). There are increasing data for SNRIs and their metabolites. New techniques such as stellate ganglion blockade are showing promise for refractory symptoms. While the initial data are encouraging, further scrutiny is warranted with well-designed, prospective, randomised controlled trials in order to confirm both efficacy and long-term safety. Ultimately, it is hoped that some of these products will have sufficiently robust data, thus providing and women alternatives to HRT that are safe, efficacious and licensed for the indication.

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