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HerbClip™

FILE: ▪Menopause Symptoms
▪Female Balance™

HC 080752-299

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RE: Small Study Evaluates Herbal Combination for Menopausal Symptoms

Smolinski D, Wolliner D, Orlowski J, et al. A pilot study to examine a combination botanical for the treatment of menopausal symptoms. *J Altern Complement Med.* 2005;11(3):483–489.

Menopause is the natural progression from the reproductive years of women to post-reproduction and the cessation of menses. It is defined as the absence of menses for 12 months. An estimated 50% of women in the United States will be post-menopausal by the year 2015. For some women, menopause occurs without any symptoms. For others, however, the transition into menopause is accompanied by sometimes debilitating symptoms. These include hot flashes, mood changes, depression, cognitive changes ("brain fog" and decreased short-term memory), vaginal dryness, decreased libido, dyspareunia, decreased energy, sleep disturbances, and weight gain. Conventional hormone replacement therapy (HRT), using hormones derived from mare urine (e.g., Premarin®), has recently been shown to cause an increase risk of coronary heart disease (CHD) and stroke.[1, 2] This has prompted many women to seek alternatives. This small, prospective study evaluated a unique combination of herbs to treat menopausal symptoms.

Eight menopausal women (ages 42–63 years, mean 54 ± 6 years) enrolled in this 3-month, non-randomized, non-placebo-controlled study. Included in this study were women experiencing "natural menopause" (no menses for at least 12 months) with moderate severity hot flashes in the previous 3 months as measured on the Menopause Rating Scale. Moderate severity hot flashes was defined on a visual analog scale (VAS), which is a self-assessment of severity on a 1–100 scale (1 = no hot flashes, 100 = worst hot flashes). All women had to rate ≥ 50 on the VAS to participate. Excluded from the clinical trial were women whose menopause was induced by surgery or drugs, the presence of major disease (e.g., heart disease, cancer, renal, or psychiatric disorders); abnormal blood or urine tests showing liver, blood, or renal pathologies; taking prescription drugs or non-prescription remedies; use of complementary and alternative medicine (CAM) therapies for menopause; and allergies to any of the herbs used in the study.

A proprietary formula containing 15 botanicals (Female Balance™, Awareness, Phoenix, AZ) was administered. Volunteers took 2 capsules twice daily, for a total of 2,200 mg/day—300 mg black cohosh (*Actaea racemosa* syn. *Cimicifuga racemosa*) root, 240 mg cramp bark (*Viburnum opulus*), 220 mg partridge berry (*Mitchella repens*), 140 mg valerian root (*Valeriana officinalis*), 140 mg fo-ti (*Polygonatum multiflorum*) seed, 140 mg dandelion root (*Taraxacum officinale*), 140 mg chaste tree (*Vitex agnus-castus*) berry, 140 mg rosemary (*Rosemarinus officinalis*) leaves, 140 mg nigella (*Nigella sativa*), 140 mg Joe Pye (*Eupatorium purpureum*), 100 mg barrenwort (*Epimedium grandiflorum*) leaf, 100 mg chuanxiong (*Ligusticum sinense*) rhizome, 100 mg schizandra (*Schisandra chinensis*) berry, 80 mg peppermint (*Mentha* x *piperita*) leaf, and 80 mg red raspberry (*Rubus idaeus*) leaf.

The primary endpoints measured were the modified Kupperman Index (KI) and daily hot flash scores. KI quantified the subjective severity of 12 symptoms (hot flashes, weight change, insomnia, irritability, depression, low sex drive, fatigue, muscle or joint pain, headache, heart palpitation, vaginal dryness, and forgetfulness) on a scale from 0–3 (0 = no symptoms, 1 = slight, 2 = moderate, 3 = severe). Total KI symptom scores were stratified to reflect severity of menopausal symptoms (15–12 = mild, 21–35 = moderate, and >35 = severe). KI was determined at baseline, and after 1, 2 and 3 months of treatment. Daily hot flashes were recorded in diaries kept by the volunteers during the study, while the frequency and severity of hot flashes were scored on a VAS (frequency of VAS scoring not reported).

The secondary endpoint was changes in quality of life (QoL) as determined by the standard SF-36 short-form health survey. The SF-36 short-form was designed for use in clinical practice and research, health policy evaluations, and general population surveys. It assesses 8 health concepts on a 0–100 point scale (lower scores = relatively poorer health status, higher scores = relatively better health): physical functioning, role physical (limitations in role activities due to physical health problems), bodily pain, general health, vitality, social functioning, role emotional (limitations in usual role activities due to emotional problems), and mental health. Adverse events and compliance were captured in weekly telephone calls to volunteers during the first month and biweekly phone calls during the second and third months.

Mean total KI significantly decreased from 30.3 ± 7.5 at baseline to 22.9 ± 8.4 after 3 months of treatment, a 24.4% reduction ($P = 0.0028$). Mean severity and frequency of hot flashes significantly decreased from 68.1 ± 14.3 at baseline to 39.6 ± 9.7 after 3 months of treatment, a 41.9% reduction ($P = 0.0003$). QoL significantly increased in 4 domains: physical function (mean change 6.32 ± 22.64, $P = 0.04$), role physical (mean change 14.21 ± 13.45, $P = 0.01$), general health (mean change 9.47 ± 12.61, $P = 0.02$), and role emotional (mean change 7.53 ± 10.82, $P = 0.03$). One volunteer discontinued treatment due to gastrointestinal disturbances and nausea, but a "direct correlation...to the botanical intervention was not confirmed." No other adverse events were reported.

Conclusion

This study adds to the growing body of evidence that botanicals may offer significant benefit to women experiencing menopausal symptoms and may be safe alternatives to conventional HRT. Previous clinical trials administering soy (*Glycine max*) isoflavones[3, 4],

black cohosh[5, 6], and other herbal formulas[7, 8] all provided significant relief from hot flashes. While the results in this small study are encouraging, a larger, randomized, placebo-controlled trial is needed to verify these findings. A placebo effect cannot be discounted, because the study was not placebo-controlled. Recently, some experts have suggested that the Kupperman Index may be a less sensitive research instrument for evaluation of menopausal symptoms. It would be interesting to see if the same study using the newer Green Index would provide similar results. The large standard deviations noted in the SF-36 short-form results mean that many of the participants experienced either no improvement or a deterioration in symptoms over the 3-month study. Conducting a trial with a larger number of volunteers should decrease the standard deviations detected, and provide more clinically relevant information. The large decrease in frequency and severity of hot flashes in the study is impressive and clinically relevant. Again, however, a larger, more rigorously designed study is needed to verify these results.

—John Neustadt, ND

References

[1]Manson JE, Hsia J, Johnson KC, et al. Estrogen plus Progestin and the Risk of Coronary Heart Disease. *N Engl J Med.* August 7, 2003 2003;349(6):523-534.

[2]Lemaitre RN, Heckbert SR, Psaty BM, Smith NL, Kaplan RC, Longstreth WT, Jr. Hormone replacement therapy and associated risk of stroke in postmenopausal women. *Arch Intern Med.* Sep 23 2002;162(17):1954-1960.

[3]Messina M, Hughes C. Efficacy of soyfoods and soybean isoflavone supplements for alleviating menopausal symptoms is positively related to initial hot flush frequency. *J Med Food.* Spring 2003;6(1):1-11.

[4]Faure ED, Chantre P, Mares P. Effects of a standardized soy extract on hot flushes: a multicenter, double-blind, randomized, placebo-controlled study. *Menopause.* Sep-Oct 2002;9(5):329-334.

[5]Osmers R, Friede M, Liske E, Schnitker J, Freudenstein J, Henneicke-von Zepelin H-H. Efficacy and Safety of Isopropanolic Black Cohosh Extract for Climacteric Symptoms. *Obstet Gynecol.* May 1, 2005 2005;105(5):1074-1083.

[6]Nappi RE, Malavasi B, Brundu B, Facchinetti F. Efficacy of Cimicifuga racemosa on climacteric complaints: a randomized study versus low-dose transdermal estradiol. *Gynecol Endocrinol.* Jan 2005;20(1):30-35.

[7]Sun J. Morning/Evening menopausal formula relieves menopausal symptoms: a pilot study. *J Altern Complement Med.* Jun 2003;9(3):403-409.

[8]Kupfersztain C, Rotem C, Fagot R, Kaplan B. The immediate effect of natural plant extract, Angelica sinensis and Matricaria chamomilla (Climex) for the treatment of hot flushes during menopause. A preliminary report. *Clin Exp Obstet Gynecol.* 2003;30(4):203-206.

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