

NATURAL ALTERNATIVES FOR HORMONE-REPLACEMENT THERAPY



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By *Jesse Hanley, MD*

Dr. Jesse Hanley, a noted clinician and author, has helped thousands of women discover natural healthcare alternatives during various phases of their lives. Today she is devoting her time to educating practitioners and the public in an effort to assist them in reexamining medical information and to better understand their options. The following is Dr. Hanley's perspective on the controversy surrounding recent news about Hormone-Replacement Therapy (HRT). This summary of recent research is intended to serve as a resource for those in the industry interested in enhancing their knowledge of the science behind natural alternatives to HRT.



Menopause is not a disease. It is a normal and natural life transition. For millennia, women have known what to use in the herbal kingdom to prepare for and to help them to stay strong and healthy during various life cycles. In many Asian and Indonesian cultures, for example, there is not even a word for menopause or hot flash because they do not exist. Their rates of breast cancer are also notably much lower than in North America. It is far too simplistic to attribute credit to tiny amounts of soy consumed in these cultures. Herbalists in these areas have revealed numerous herbal formulas, used and recorded for centuries with great results.

Menopause was once a mystery that modern medicine described only in terms of estrogen deficiency. Pre-Menstrual Syndrome (PMS) was even more elusive until clinicians and researchers began to understand the imbalance between the female hormones, estrogen and progesterone. Eventually the complications that environmental chemicals and stress hormones added to the diagnostic picture could no longer be ignored by even the most austere scientific circles. The symptoms of PMS finally helped us all to focus on the importance of progesterone deficiency and herbal medicine.

For more than 35 years, hormone-replacement therapy (HRT), consisting of either estrogen or a combination of estrogen and the synthetic version of progesterone called progestin, was the preferred medical treatment

for menopausal symptoms, including hot flashes, vaginal dryness, and sometimes moodiness and depression. However, large clinical trials have now conclusively shown that HRT increases the risk of heart disease and some types of cancer. As a result of these studies, there is a growing interest in safe, natural alternatives, such as herbs and antioxidant supplements, to reduce menopausal symptoms.

The Women's Health Initiative Study recently has provided a landmark example demonstrating that assumptions, not facts, provided the basis for much of the information we are all taught about female hormonal balance/imbalance and related life changes. We have now come to learn that there are risks from synthetic female hormones. And the dangers are significant, from increased risk of cancers to heart disease to stroke.

Fortunately, over the past 15 years of integrating nutritional, oriental and herbal medicine with modern medicine, many important, safe and undeniably successful solutions have emerged. The thousands of women I have helped treat for problems relating to reproductive issues, PMS and menopause have clearly benefited from safe, time-tested natural solutions. In fact, PMS and menopause have become conditions relatively easy to treat. Botanicals have assisted women through normal transitions in life gracefully and safely. Today, a woman's life is complicated by

frightening numbers of chemicals in the environment and food chain that interfere with the hormonal balance and adversely affect fertility, PMS and menopause. Nutritional and herbal formulas can effectively relieve the toxic burdens and help restore balance and health.

The Chinese and Aryurvedic physicians have used herbs for more than 3,000 years for assisting women. Many people don't realize that before 1950, numerous herbal formulas, including botanicals for PMS and menopause, were in the Physician's Desk Reference (PDR) — a clinician's medical bible! While the PDR no longer contains any botanical references, I am happy to see the re-emergence of herbal formulas similar to those that were in this highly regarded resource so many years ago.

It is my intent with this review paper to help you to become familiar with the growing literature that is changing the face of the understanding and to acquaint you with the treatments available for women's pre-, peri- and post menopausal conditions.

VIRTUALLY EVERY WOMAN EXPERIENCES MENOPAUSE

- During the phases before, during and after menopause, female hormones fluctuate and decline causing physical symptoms to occur. Some women experience "peri-menopause" symptoms as early as in their thirties and forties, and they often seek out products to alleviate these unpleasant symptoms. Safe options are important as some women may experience symptoms over a long period of time from peri-menopause through post-menopause.
- Menopausal symptoms can be extremely uncomfortable — they can also disrupt sleep and consequently lead to fatigue
- The menopause-related decline in hormones reduces bone density and increases the long-term risk of osteoporosis
- After menopause, a woman's relatively low risk of coronary heart disease increases and equals that of men
- Menopause often affects a woman's self-esteem — to some it is a sign of middle age and the inevitable loss of youth

STUDIES FIND THAT HRT INCREASES THE RISK OF HEART DISEASE AND SOME CANCERS

- In 1942, the U.S. Food and Drug administration approved estrogen for the treatment of menopausal symptoms
- As early as 1975, research showed that estrogen therapy increased the risk of uterine cancer
- In 1990, scientists reported that estrogen therapy also increased the risk of heart disease
- Only about one-third of menopausal women take HRT because of concerns related to side effects or long-term risks, according to the American College of Obstetricians and Gynecologists (ACOG)
- An estimated 30 to 40 percent of women experience abnormal vaginal bleeding during the first year of HRT use, often resulting in a decision to stop HRT, according to ACOG
- Recent, large clinical trials have demonstrated that the perceived benefits of HRT are outweighed by its risks
- The North American Menopause Society reports that more than 30 percent of women use acupuncture, natural estrogen products, herbal supplements, or plant estrogens

STUDY 1:

HEALTH RISKS OF CONVENTIONAL HORMONE-REPLACEMENT THERAPY OUTWEIGH BENEFITS

Design

- 16,608 healthy postmenopausal women, ages 50 to 79 years
- Prescribed estrogen (0.625 mg from horse urine) and progestin (2.5 mg synthetic) or placebo
- Double-blind, placebo-controlled study
- Average of 5.2 years follow-up

Results

- Trial was stopped early because of evidence of increased risk of breast cancer and other adverse health outcomes
- HRT increased the risk of heart disease, stroke, blood clots, and breast cancer (particularly invasive breast cancer)
- HRT decreased the risk of colorectal cancer, endometrial cancer, and hip fracture

Comments

- Researchers troubled by the benefit/risk ratio and recommended that HRT not be “initiated or continued” as a way of preventing heart disease

Writing Group for the Women’s Health Initiative Investigators. Risks and benefits of estrogen plus progestin in healthy postmenopausal women. Principal results from the women’s health initiative randomized controlled trial. *JAMA*. 2002;288:321-333.

According to a physician writing for Harvard Health Publications online (<http://www.health.harvard.edu/page.cfm?name=HRTnews>): “The study’s results (see table below) may seem alarming. But the absolute risk to an individual woman is relatively small. For example, in 10,000 women taking HRT for a year, there will be 7 more heart attacks, 8 more invasive breast cancers, 8 more strokes, and 8 more cases of blood clots in the lungs (pulmonary emboli). At the same time, there will be 6 fewer colorectal cancers and 5 fewer hip fractures. Still, a treatment used in healthy women strictly for prevention shouldn’t carry extra risks.”

After five years, the Women’s Health Initiative (WHI) found increases and decreases in relative risk for several diseases in women who took Prempro. Here are the numbers:

Blood clots in the lungs	113% (increase)
Blood clots in the veins	107% (increase)
Stroke	41% (increase)
Heart disease	29% (increase)
Invasive breast cancer	26% (increase)
Colorectal cancer	37% (decrease)
Hip fractures	34% (decrease)
Spinal fractures	34% (decrease)

STUDY 2:

MAJOR REVIEW OF HRT STUDIES QUESTIONS BENEFITS OF THERAPY

Design

- Data analysis of four major clinical trials using HRT
- Three studies used estrogen/synthetic progestin and one used estrogen only
- More than 20,000 healthy or pre-existing coronary artery disease, menopausal women involved in studies
- Subjects took HRT for an average of about 5 years

Results

- Subjects had a significantly increased risk of breast cancer, stroke, and pulmonary embolism
- Reduced risk of colorectal cancer and fractures of the neck or femur
- No change in risk for heart disease or endometrial cancer

Beral V, Banks E, Reeves G. Evidence from randomised trials on the long-term effects of hormone replacement therapy. *Lancet*. 2002;360:942-944.

RESEARCH SUGGESTS THAT BOTANICALS AND ANTIOXIDANTS MAY SAFELY REDUCE MENOPAUSAL SYMPTOMS

Several herbs have traditionally been used to alleviate women’s health problems related to menstruation and menopause. Research conducted over the past 10 years suggests that naturally occurring phytoestrogens (plant estrogens), many of which also function as antioxidants, are the most active components of these herbs. For example, the phytoestrogen genistein has 1,000 times less estrogen activity than the actual hormone. Researchers believe that genistein and similar compounds attach to cellular estrogen receptors, where they provide weak estrogen activity but block the more potent, and potentially hazardous, effect of true estrogen. These estrogen-like substances are found in vegetables, fruits, legumes — all foods that have been safely consumed for many thousands of years.

A variety of studies — cell, animal, and small human trials — have shown that the use of botanical supplements can significantly reduce many menopausal symptoms with few if any side effects. Although large-scale clinical trials have not yet been conducted, the research so far is extremely promising. Due to the subjective quality of many symptoms reported, it has been challenging to objectively analyze study findings. Recently reported health risks of conventional HRT may spur more aggressive research on natural alternatives to ease menopausal symptoms. In fact, the U.S. National Center for Complementary and Alternative Medicine, part of the National Institutes of Health, is currently funding research on several botanicals that have shown promise for easing menopausal symptoms.

Black cohosh, red clover, chasteberry, St. John's wort, soy isoflavones, vitamin E, and wild yam are among the natural remedies that have been used to ease menopausal symptoms. Although these natural substances have shown promise, some professionals want more research-backed evidence before they believe these botanicals should be recommended on a broad scale to women. For example, few controlled human trials have been conducted on antioxidants or botanicals in relieving menopausal symptoms, and many of the perceived benefits have come out of uncontrolled clinical experiences or anecdotal reports.

In addition, these controlled human trials have generally included relatively small numbers of people, and many studies have lacked rigorous controls or sophisticated data analysis. Not surprisingly, the findings of these studies have sometimes been conflicting, and the use of these substances is not always free of side effects (although the side effects tend to be minor or similar to drugs or placebos). Lastly, critics also claim researchers have a limited understanding of how these substances function.

As a result of these limited data, no clear medical consensus has emerged about the use of antioxidants and herbal supplements in reducing menopausal symptoms.

WHERE DO WE GO FROM HERE?

At a recent meeting sponsored by the National Institutes of Health to discuss the future of HRT, scientists said “there was no reason to expect that the other products would not have the same risks as Prempro (combination of estrogen and progestin used in the WHI study)... It is making us re-evaluate the whole area,” Dr. Janet Woodcock, who directs the F.D.A.'s Center for Drug Evaluation and Research, said, “The real question is, ‘Where do we go from here?’”

Researchers at the National Institutes of Health said they must consider whether to sponsor large studies of other therapies for menopause and, if so, which ones to test.

The cost and time required for major clinical trials are major factors. WHI cost \$16 million and was designed as an 8-year trial but was halted after 5 years. In the meantime, Dr. Stephen E. Straus, the director of the National Center for Complementary and Alternative Medicine, said “as many as 20 percent of menopausal women use herbal products, like soy or red clover or black cohosh to relieve symptoms. The risks, and benefits, of these products are unknown,” he said.

“There are no long-term studies — not of safety, not of effectiveness,” Dr. Straus said. Yet large rigorous studies will be a long time coming, he explained, because they require extensive preliminary scientific research before they could be justified. “We are not there yet,” he said.

BLACK COHOSH



The herb black cohosh (*Cimicifuga racemosa*) is native to eastern North America. Historically, Native Americans used it to treat several ailments as well as amenorrhea and menopausal symptoms. Triterpene glycosides, the herb's most active ingredients, are plant estrogens that may exert weak estrogen-like and estrogen-blocking activity in the body.

The following four studies are excerpted from a published review of black cohosh.

STUDY 1:

BLACK COHOSH EASES MENOPAUSAL SYMPTOMS

Design

- 80 women with menopausal symptoms
- Double-blind placebo-controlled clinical trial
- 12 weeks duration
- Subjects received 40 mg black cohosh extract, 0.625 conjugated estrogen, or placebos daily
- Changes assessed with two standard tests, the Kupperman Menopause Index and the Hamilton Anxiety Scale

Results

- Women taking black cohosh extract had significant reductions in physical and psychological symptoms, compared with those taking estrogen or placebos, based on scores on the Kupperman Menopause Index and the Hamilton Anxiety Scale

Stoll W. Phytopharmakon influences atrophic vaginal epithelium: double-blind study, *Cimicifuga* vs estrogenic substances. *Therapeuticon*. 1987;1:23-331. Reviewed in: McKenna DJ, Jones K, et al. Black cohosh: Efficacy, safety, and use in clinical and pre-clinical applications. *Alternative Therapies in Health and Medicine*. 2001;7(3):93-100.

STUDY 2:

BLACK COHOSH REDUCES MODERATE MENOPAUSAL SYMPTOMS

Design

- 152 women with moderate menopausal complaints, such as hot flashes or perspiration
- Double-blind, randomized multi-center clinical study
- Subjects ranged in age from 43 to 60 years
- 12 weeks duration
- Dosages were either 20 mg or 40 mg of black cohosh extract daily
- Changes assessed with the Kupperman Menopause Index, Self-Assessment Depression Scale, and other tests

Results

- Significant decrease in scores on the Kupperman Menopause Index and the Self-Assessment Depression Scale with both dosages
- 80 percent of subjects and their physicians rated improvement as good or very good

McKenna DJ, Jones K, et al. Black cohosh: Efficacy, safety, and use in clinical and preclinical applications. *Alternative Therapies in Health and Medicine*. 2001;7(3):93-100.

STUDY 3:

BLACK COHOSH IMPROVES MENOPAUSAL SYMPTOMS AND REDUCES NEED FOR HORMONE TREATMENT

Design

- 50 women with severe menopausal symptoms
- Open trial for six months
- Subjects' estrogen therapy was replaced with 40 mg of black cohosh extract daily
- Hormone injections were given to patients with severe complaints
- Changes assessed with the Kupperman Menopause Index

Results

- 82 percent of subjects reported that black cohosh had beneficial or very beneficial effects
- 56 percent of patients needed no additional hormone injections, and 18 percent needed additional hormone injections
- Scores on the Kupperman Menopause Index declined from an average of 17.6 to 9.2

Petho A. Klimakterische Beschwerden. *Arztliche Praxis*. 1987;47:1551-1553. Reviewed in: McKenna DJ, Jones K, et al. Black cohosh: Efficacy, safety, and use in clinical and preclinical applications. *Alternative Therapies in Health and Medicine*. 2001;7(3):93-100.

STUDY 4:

BLACK COHOSH REDUCES PHYSICAL AND PSYCHOLOGICAL SYMPTOMS IN MENOPAUSAL WOMEN

Design

- 629 women with a variety of physical and psychological menopausal symptoms, including hot flashes, perspiration, headache, irritability, anxiety, and depression
- About one-third of the patients had previously been treated with hormones or other medications
- Open trial conducted at multiple medical centers
- Black cohosh extracts in liquid form, 40 drops, twice daily
- Six to eight weeks duration

Results

- All symptoms resolved in about half of the subjects, with improvements noted in about one-third of others

Foster S. Black Cohosh: *Cimicifuga racemosa*, a literature review. *HerbalGram*. 1999;45:35-50. Reviewed in: McKenna DJ, Jones K, et al. Black cohosh: Efficacy, safety, and use in clinical and preclinical applications. *Alternative Therapies in Health and Medicine*. 2001;7(3):93-100.

RED CLOVER



Red clover (*Trifolium pratense*), a legume, is rich in several isoflavones, including biochanin, formononetin, genistein, daidzein. Biochanin and formononetin are precursors to genistein and daidzein, respectively, and conversion occurs through bacterial cleavage in the gut, a process that influences the absorption of

isoflavones in all people. Red clover also contains coumestrol, another phytoestrogen. Most biomedical

research on isoflavones has focused on genistein and daidzein, and the findings are directly applicable to red clover.

STUDY 1:

RED CLOVER REDUCES HOT FLUSHES IN MENOPAUSAL WOMEN

Design

- 30 women who had stopped menstruating at least 12 months before the study and were experiencing five or more daily hot flashes
- Subjects ranged in age from 49-65 years
- Double-blind placebo-control trial
- Isoflavone-rich foods as supplements were prohibited
- All subjects received placebos for four weeks, then either 80 mg daily of red clover extract or placebos for 12 weeks
- Patients assessed by changes in the number of daily hot flashes and with the Greene Climacteric Scale Score for 21 menopausal symptoms

Results

- Placebo use resulted in a 16% decline in frequency of hot flashes
- Red clover isoflavones reduced the frequency of hot flashes by an additional 44 percent, compared with the placebo
- Greene Scale showed a trend toward fewer symptoms in the red clover group and more symptoms in the placebo group

Van de Weijer PHM, Barentsen R. Isoflavones from red clover (Promensil®) significantly reduce menopausal hot flush symptoms compared with placebo. *Maturitas*. 2002;42:187-193.

STUDY 2:

RED CLOVER AND SOY ISOFLAVONES ABSORBED SIMILARLY

Design

- Nine men and five women, ages 50-66 years
- Placebo-controlled crossover trial
- Subjects consumed a breakfast cereal enriched with either 30 mg of soy isoflavones or 30 mg red clover isoflavones daily for two weeks. After a two-week washout period, they consumed the other enriched breakfast cereal for two weeks
- Absorption assessments were based on excretion, a standard approach

Results

- Although different individuals varied greatly in their absorption of isoflavones, each individual in the study consistently excreted (and presumably absorbed) approximately the same amount of both soy and red clover isoflavones
- With any particular individual, absorption of the amount of isoflavones from red clover or soy is similar. This means they are likely to have similar effects in the body

Tsunoda N, Pomeroy S, Nestel P. Absorption in humans of isoflavones from soy and red clover is similar. *Journal of Nutrition*. 2002;132:2199-2201.

CHASTEBERRY

The berries of the chaste tree (*Vitex agnus castus*) have been a traditional remedy for relieving symptoms of menopausal symptoms, premenstrual syndrome and cyclic mastalgia (breast pain). Many symptoms of PMS appear related to either elevated estrogen levels or erratic hormone levels, and some of these symptoms are similar to those women experience in menopause. Thus, chasteberry may provide some relief of menopausal symptoms.

STUDY:

CHASTEBERRY REDUCES KEY PMS SYMPTOMS

Design

- 170 women, age 18 and older, who had been diagnosed with PMS
- Double-blind, placebo-controlled trial
- 20 mg of chasteberry extract or placebos daily
- Duration of three menstrual cycles
- Women were assessed for changes in six key symptoms, including irritability, mood alteration, anger, headache, breast fullness, and bloating

Results

- Subjects had improvements in irritability, mood alteration, anger, headache, and breast fullness, but not in bloating
- 52 percent of women taking chasteberry reported that PMS symptoms declined by more than 50 percent. Fewer than half that number of women reported similar benefits with the placebos. Improvements were confirmed by physicians

Schellenberg, R. et al. Treatment for the premenstrual syndrome with agnus castus fruit extract: prospective, randomized, placebo controlled study. *British Medical Journal*. 2001;322:134-137.

WILD YAM

Wild yam (*Disocorea villosa*) is rich in antioxidants and sterols, both of which may interact with estrogen and other hormones. The tuber of this plant has been used historically to treat cramps and dysmenorrhea. A clinical trial showed a marginal but insignificant improvement in menopausal symptoms.

Some research suggests that wild yam may ease some symptoms of estrogen withdrawal, which would be consistent with a benefit during the decline of estrogen production during menopause. It has been hypothesized that some types of yam sterols, which have some chemical similarity to estrogen, might attach to cell receptors, allowing for a very weak estrogen-like effect.

Gruenwald J, Brendler T, Jaenicke C. *PDR for Herbal Medicines*, First Edition. Montvale, New Jersey: Medical Economics Company. 1998:609-610. Mills S, Bone K. *Principles and Practice of Phytotherapy: Modern Herbal Medicine*. Edinburgh: Churchill Livingstone. 2000:46.

ST. JOHN'S WORT



Depression and anxiety are common psychological features of menopause. Considerable research, including recent clinical trials, have found St. John's wort (*Hypericum perforatum* L.) to be at least as effective as prescription antidepressant medications in the treatment of mild to moderate depression. It also has the advantage of producing fewer side effects than antidepressant drugs. However, the herb does not appear to have any clear clinical benefits in the treatment of severe (major) depression.

The benefits of St. John's wort may be related to its complex chemical constituents rather than to any single ingredient. Most studies have used an extract containing either 0.3 percent hypericin or 3 percent hyperforin, either of which serves as a marker for the herb's overall potency.

Some cautions are warranted for St. John's wort. Recent research has shown that St. John's wort may enhance liver detoxification processes, including the breakdown of pharmaceutical drugs. St. John's wort can decrease blood concentrations of certain drugs, including cyclosporin, chemotherapeutic agents, HIV protease inhibitors, and reverse transcriptase inhibitors. The herb may also increase photosensitivity in some people, but this side effect was not noted in recent clinical trials.

STUDY 1:

ST. JOHN'S WORT REDUCES SYMPTOMS OF PMS

Design

- 19 women, aged 18-50 with premenstrual syndrome, including anxiety, irritability, depression, mood swings, insomnia, headache, aches and pains, tender breasts, and food cravings
- Open, uncontrolled, observational pilot study
- St. John's wort extract, 300 mg three times daily
- Duration of two complete menstrual cycles
- Primary assessment based on the Daily Symptom Report, a checklist of 17 premenstrual symptoms; secondary assessments based on the Hospital Anxiety and Depression Scale and the Social Adjustment Scale

Results

- Significant reductions in all outcome measures
- More than two-thirds of the subjects had at least a 50 percent reduction in symptom severity by the end of the trial
- Virtually all symptoms improved, with the greatest improvements in anxiety, depression, nervous tension, confusion, crying and insomnia
- These results provide the basis for further investigating of St. John's Wort in a placebo-controlled trial

Stevinson C, Ernst E. A pilot study of *Hypericum perforatum* for the treatment of premenstrual syndrome. *British Journal of Obstetrics and Gynaecology*. 2000;107:870-876.

STUDY 2:

ST. JOHN'S WORT EQUALLY EFFECTIVE TO PROZAC; FEWER SIDE-EFFECTS

Design

- 240 women and men with mild to moderate depression
- Average ages were 46 (St. John's wort group) and 47 (Prozac group)
- Double-blind trial
- 500 mg daily of St. John's wort extract or 20 mg Prozac
- Duration of six weeks
- Assessments with the Hamilton Depression Scale and the Clinical Global Impression

Results

- Scores on the Hamilton Depression Scale declined by approximately 12 percent in both the herb and drug groups
- The Clinical Global Impression found St. John's wort to be significantly better than Prozac, with about one-third more patients responding to the herb than to the drug

Comments

- One-fourth of patients taking Prozac reported side effects, including agitation, gastrointestinal problems, vomiting, dizziness, and erectile dysfunction. Fourteen percent of the patients taking St. John's wort complained of side effects, the most common being gastrointestinal disturbance

Schrader E. Equivalence of St. John's wort extract (Ze 117) and fluoxetine: a randomized controlled study in mild-moderate depression. *International Clinical Psychopharmacology*. 2000;15:61-68.

STUDY 3:

ST. JOHN'S WORT AS EFFECTIVE AS ZOLOFT

Design

- 30 women and men with mild to moderate depression (20 subjects completed the study)
- Average age of 45 years
- Double-blind trial
- 600 mg of St. John's wort extract or 50 mg Zoloft daily for one week, followed by increased amounts (900 mg, 75 mg respectively) for six weeks
- Duration of seven weeks
- Assessments with the Hamilton Depression Scale and the Clinical Global Impression Scale

Results

- Substantial improvements noted in patients taking St. John's wort after two weeks
- After six weeks, symptoms reduced by an average of 47 percent among people taking St. John's wort and 40 percent among those taking Zoloft

Brenner R, Azbel V, Madhusoodanan S, et al. Comparison of an extract of hypericum (LI 160) and sertraline in the treatment of depression: a double-blind, randomized pilot study. *Clinical Therapeutics*. 2000;22:411-419.

STUDY 4:

ST. JOHN'S WORT EQUIVALENT TO IMIPRAMINE

Design

- 263 women and men with moderate depression
- Average age ranged from 43 to 48 years in the study groups
- Double-blind, placebo-controlled trial in multiple medical centers
- 1050 mg of St. John's wort extract, 100 mg imipramine (a tricyclic antidepressant), or placebos daily
- Duration of eight weeks
- Assessments with the Hamilton Depression Scale, the Clinical Global Impression Scale and other clinical tests

Results

- St. John's wort was superior to placebo in improving the patients' mental and physical well being
- St. John's wort was at least as effective as imipramine in treating moderate depression
- The safety profile of St. John's wort was similar to placebo and better than imipramine

Philipp M, Kohnen R, Hiller K-O. Hypericum extract versus imipramine or placebo in patients with moderate depression: randomized multicentre study of treatment for eight weeks. *British Medical Journal*. 1999;319:1534-1539.

STUDY 5:

ST. JOHN'S WORT INEFFECTIVE IN SEVERE DEPRESSION

Design

- 360 women and men diagnosed with severe depression
- Placebo-controlled study
- St. John's wort extract; 900-1500 mg daily, Zoloft, 50-100 mg daily; or placebo
- Duration of 26 weeks
- Assessments based on scores on the Hamilton Depression Scale and other tests

Results

- Neither Zoloft nor St. John's wort were as effective as placebo
- Zoloft led to slightly better improvements compared with St. John's wort

Comments

- Severe depression is difficult to treat regardless of therapy

Hypericum Depression Trial Study Group. Effect of Hypericum perforatum (St. John's wort) in major depressive disorder. A randomized controlled trial. *JAMA*. 2002;287:1807-1814.

SOY ISOFLAVONES



Soybeans are rich in several phytoestrogens, including the isoflavones genistein, daidzein and glycitein. Several studies have found that these isoflavones can ease menopausal symptoms, particularly hot flashes.

STUDY 1:

SOY ISOFLAVONE SUPPLEMENTS REDUCE KEY MENOPAUSAL SYMPTOMS

Design

- 80 women who had been experiencing menopausal symptoms for at least a year and had not been receiving hormone therapy for at least 12 months

- Subjects ranged in age from 45-55 years
- 100 mg of total daily isoflavone supplements containing 23.3 mg of genistein, 6.2 mg of daidzein, and 3.8 mg of glycitein given three times per day, or placebos; for four months
- Double-blind, placebo-controlled trial
- Assessments based on the Kupperman Menopause Index to track 11 symptoms, including hot flashes, nervousness, weakness, depression, headache, insomnia, and vertigo

Results

- Compared to placebo, women taking the isoflavone supplements for four months had significantly lower menopausal symptoms, with improvements in all measured symptoms
- Women taking the isoflavone supplements had significant declines in total cholesterol and the “bad” low-density lipoprotein form of cholesterol
- No changes occurred among women taking placebos

Comments

- The researchers noted that isoflavones may be a safe alternative to HRT. They also noted that estrogens can increase the risk of endometrial cancer, and progestin may have side effects as well

Han KK, Soares JM, Haidar MA, et al. Benefits of soy isoflavone therapeutic regimen on menopausal symptoms. *Obstetrics & Gynecology*. 2002;99:389-394.

STUDY 2:

ISOFLAVONES REDUCE HOT FLASHES IN MENOPAUSAL WOMEN

Design

- 104 post-menopausal women experiencing at least seven moderate to severe hot flashes daily including night sweats; 79 subjects completed the study
- Subjects ranged in age from 45-62 years
- Double-blind, placebo-controlled trial at multiple medical centers
- 60 grams soy protein (containing 76 mg of isoflavones) or 60 grams of milk protein (placebo) added daily to diet for 12 weeks
- Menopausal symptoms assessed by Kupperman Menopause Index
- Wilcoxon test used to measure number of daily hot flashes

Results

- After 12 weeks, women consuming the isoflavone-rich soy protein had 45 percent fewer hot flashes, compared with a 30 percent reduction in the placebo group
- Kupperman Menopausal Index symptoms were not affected by soy isoflavones

Albertazzi P, Pansini F, Bonaccorsi G, et al., The effect of dietary soy supplementation on hot flushes. *Obstetrics & Gynecology*. 1998;91:6-11.

VITAMIN E

Anecdotal medical reports on the use of vitamin E in easing menopausal symptoms date back more than 50 years. Some scientific research suggests a potential benefit in reducing hot flashes. However, vitamin E may play a more important role in reducing the risk of heart disease, which increases after menopause.

STUDY 1:

VITAMIN E HAS MODEST EFFECT IN REDUCING HOT FLASHES

Design

- 105 women who had been treated for breast cancer and for whom HRT was contraindicated
- Subjects aged 18 years and older, with at least 14 hot flashes per week for at least one month
- Placebo-controlled, double-blind crossover trial
- Subjects received 800 IU of vitamin E daily, then an identical-appearing placebo, or vice versa
- Duration of four weeks
- Assessment based on patient diaries of hot flash frequency and severity

Results

- Vitamin E supplementation led to a reduction of one hot flash daily

Comment

- Supplementation was for only one month, and a longer duration may have yielded more positive results

Barton DL, Loprinzi CL, Quella SK, et al. Prospective evaluation of vitamin E for hot flashes in breast cancer survivors. *Journal of Clinical Oncology*. 1998;16:495-500.

STUDY 2:

VITAMIN E LINKED TO LOWER RISK OF HEART DISEASE IN WOMEN

Design

- 87,245 female nurses
- Ages 34 to 59 years at the start of the study
- Prospective epidemiological study
- Diet and supplements assessed, and health tracked for eight years

Results

- Women who took vitamin E supplements for more than two years had a 41 percent lower risk of heart disease

Stampfer MJ, Hennekens CH, Manson JE, et al. Vitamin consumption and the risk of coronary disease in women. *New England Journal of Medicine*. 1993; 328:1444-1449.

STUDY 3:

VITAMIN E SUPPLEMENTS REDUCE RISK OF HEART DISEASE

Design

- 2,002 women and men with heart disease
- Average age of 61 years
- Double-blind, placebo-controlled trial
- Subjects were given 400 or 800 IU of natural-source vitamin E or placebos
- Average duration of 17 months

Results

- 77 percent reduction in nonfatal heart attacks

Comments

- A slight increase in fatal heart attacks in the vitamin E group was attributed to patients who did not take their assigned supplements

Stephens NG, Parsons A, Schofield PM, et al. Randomized controlled trial of vitamin E in patients with coronary disease: Cambridge heart antioxidant study (CHAOS). *Lancet*. 1996;347:781-786.

SCIENTIFIC WEB SITES ON NATURAL ALTERNATIVES TO HRT

http://www.acog.org/from_home/publications/misc/pb028.htm

<http://nccam.nih.gov/htdig/search.html>

http://www.ahpa.org/02_09_Feature.pdf

<http://www.herbalgram.org>

About Jesse Hanley, MD

Dr. Hanley is a women's health expert and recently retired as Medical Director of the Malibu Health Center and Malibu Health & Rehabilitation. She lectures to physicians as well as the public on numerous women's health issues. She also co-authored the book, *What Your Doctor May Not Tell You About Premenopause* published by Warner Books. Her most recent book, *Tired of Being Tired* was just published in paperback. Dr. Hanley entered medical school at the University of Illinois, Chicago, inspired by her own recovery from chronic illness with natural methods. During medical school she simultaneously began her study of oriental medicine and acupuncture at UCLA Medical School, integrating both models along the way with her in-depth nutrition knowledge. Dr. Hanley may be contacted at drhanley@jessehanley.com or 310/457-5806.