

Clinically Effective, Evidence-Based, Non-HRT/BHRT Treatment Options for Perimenopause

by Todd A. Born, ND

As health-care practitioners, we see the following scenario play out in our practice a few times a week: 48-year-old female presents with chief concerns of hot flashes, night sweats, irritability, xerosis, dry eyes, vaginal atrophy, dyspareunia, sleep dysfunction, mood swings, an irregular menstrual cycle, and memory concerns.

You run some blood chemistries, and everything is unremarkable besides decreasing estrogen and progesterone, with an increase in FSH. This woman clearly is in the throes of perimenopause. She's hesitant to start hormone or biological hormone replacement therapy because of what she has heard and read online about side effects and risks of prolonged hormone replacement.

You begin to comb the Rolodex of treatment options that actually work and have a very low side effect profile and minimal if any long-term risks, but you can't think of any that work quite as well as hormones.

This article will discuss the definition of menopause, clinical signs and symptoms, long-term consequences of estrogen deficiency, conventional treatments, and finally, evidence-based, nonhormonal approaches.

The average onset of perimenopause in the US is at the age of 47.5 years. The average duration of perimenopause is 4 years, with the median age of 12 months of amenorrhea occurring at 51.4 years of age.¹ An article in February 2015 in *JAMA* looking at 3302 women showed that vasomotor symptoms lasted for more than 7 years in more than half the women, and persisted for 4.5 years after the final menstrual period.²

The most common symptoms that women experience are hot flashes, night sweats, sleep disturbances, vaginal dryness, and mood changes. Less common, but still prevalent, are recent onset depression, arthralgias, memory loss, breast pain and menstrual migraines.³

The long-term consequences of estrogen deficiency include osteopenia/osteoporosis, dementia (but only in those who have artificially induced premature menopause), dyslipidemia, and cardiovascular diseases.⁴⁻⁹

Although the evidence varies for the risks of prolonged (>5 years) use of hormone replacement therapy (HRT), at this time the preponderance of data indicate that HRT, particularly unopposed estrogens, should not be used long term.¹⁰ The risks and consequences include endometrial hyperplasia, coronary heart disease (CHD), stroke, venous thromboembolism (VTE), and breast cancer.^{11,12}

There is a major misconception amongst many health-care providers and the general public that bioidentical hormone replacement therapy (BHRT) is safer than HRT. Albeit this makes sense logically, particularly to integrative health-care practitioners, in that one would want to use a hormone with the same molecular structure as a hormone that is endogenously produced, versus one that is completely synthetic, but both carry similar risk profiles, except for medroxyprogesterone acetate (MPA).¹³⁻¹⁶ It is believed that MPA increases the risk of breast cancer, while this has not yet been seen in bioidentical use of progesterone.¹⁷⁻¹⁹

More and more clinicians, as well as more and more patients, are looking into safe and effective alternatives as a first-line intervention to alleviate menopausal symptoms. Let's take a look at what natural agents have some of the strongest human efficacy, while also carrying a strong safety profile, even in the long term.

- Patented extract from *Humulus lupulus*, high in prenylflavonoids, particularly 8-prenylnaringenin (8-PN).
 - A 2006 double-blind, randomized, placebo-controlled trial in 67 menopausal women given the extract for 12 weeks significantly reduced hot flashes over placebo.²⁰
 - A 2010 double-blind, placebo-controlled crossover study in 36 menopausal women followed for 16 weeks showed improvement in most menopausal complaints.²¹
- Combination of three Korean herbs: *Cynanchum wilfordii*, *Phlomis umbrosa*, and *Angelica gigas* Nakai.
 - Human trials have shown increase in bone mass, while relieving menopausal symptoms.
 - In a 2005 prospective RCT, 48 perimenopausal women were given the extract twice a day, or placebo, for 12 months. By the end of the study, it was shown that the group that took the extract had improved bone density, increased human growth hormone, and improved triglycerides. At the 3-month mark, 57% reported improvements in hot flashes, dyspareunia, sleep disorders, and fatigue. Only 17% of the control group reported improvements.²²

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- - A 2012, phase II double-blind, placebo-controlled safety study in 64 pre-, peri-, and postmenopausal women followed for 12 weeks showed that “the constituting symptoms of vasomotor, paresthesia, insomnia, nervousness, melancholia, vertigo, fatigue and rheumatic pain were significantly improved in the EstroG-100 group in comparison with the placebo group ($p < 0.05$). Statistically significant improvement in vaginal dryness in the EstroG-100 group was also observed compared with that of the placebo group ($p < 0.05$). In conclusion, EstroG-100 significantly improved the menopausal symptoms of pre-, peri-, and post-menopausal women without weight gain or any serious side effects.”²³
 - Patented grapeseed extract high in proanthocyanidins.
 - A 2014, randomized, double-blind, placebo-controlled pilot study enrolled 96 women aged 40 to 60, who had at least one menopausal symptom. They were given 100 mg/day, 200 mg/day, or placebo for 8 weeks. It was shown that in

the 200 mg/day group, hot flashes reduced, anxiety improved, systolic and diastolic blood pressures decreased, and in both 100 mg and 200 mg group, lean muscle mass increased.²⁴

- Although not a human trial, in 1999, rabbits fed a high-cholesterol diet and that developed atherosclerotic lesions had these lesions significantly reduced when adding in the grapeseed extract to their diets.²⁵

Conclusion

The variability of what women will experience through the menopausal transition is vast, but given that most experience at least one of the aforementioned symptoms, with an average duration of 4 years, it makes sense that we have a duty as clinicians to alleviate their symptoms as much as possible, as safely and effectively as possible. One can see that this can be done without going straight to hormone replacement therapies, although this intervention may be needed for certain individuals.

We have a responsibility to use tools in our toolbox that work and have human data to support efficacy. Here, I have shown that these natural therapeutics do exist.

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Notes

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