

Conversation with the Experts

Toward Optimal Health: Menopause as a Rite of Passage

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TWO THIRDS OF WOMEN may experience some level of vasomotor symptoms, such as hot flashes and night sweats in the years around the menopausal transition, but only a small number will feel discomfort at a level that significantly diminishes their quality of life (QoL).^{1,2} Even so, the focus of scientific research and attention has been directed to the one third of women whose menopause-related complaints are sufficient to warrant medical intervention, chiefly for hot flashes.

The results of the Women's Health Initiative (WHI) in 2002,³ as well as more recent clinical trials, have raised questions about the safety and efficacy of hormone therapy (HT), prompting women to reconsider their use of hormone replacement to alleviate unwanted symptoms. The more recent subanalysis of coronary calcification in the WHI suggests that starting HT earlier in a woman's life may have a protective effect against cardiovascular disease (CVD).⁴ These results, however, did not move the American Heart Association (AHA) to change its recommendation for HT use, following the premise that the benefits of HT do not outweigh the overall risks, given the availability of better medications for cardioprotection.⁵

These trials were conducted to assess prevention of such chronic diseases as heart disease or cognitive decline, and it is difficult to discern a direct impact on menopause-related symptoms because change in vasomotor symptomatology was not directly measured. The findings are a reminder to clinicians that women should be as-

essed for HT use based on symptom status and age rather than risk of heart disease, osteoporosis, or memory status and support the growing interest in and demand for symptom-relieving alternatives.

A number of hormone-based and nonhormone-based approaches have been identified for vasomotor symptom management, with varying degrees of success. Nearly half of women use some type of complementary or alternative medicine (CAM).⁶ Use is influenced by the number of comorbidities and health behaviors, socioeconomic status, symptom intensity, and age but not by menopausal symptoms. Given the number of midlife women who use CAM and the potential for interactions with prescribed medications, healthcare practitioners should inquire about CAM use and be aware of what factors influence the use of different types of CAM.⁷ A discussion of these strategies for symptom management should position clinicians to face the routine and persistent inquiries from women during their menopausal transitions.

With the increasing number of hormonal and nonhormonal treatments available to manage menopausal symptoms, what are the most effective and beneficial remedies for clinicians to recommend?

Before we can address interventions aimed at alleviating menopausal symptoms, let us take a

step back. As clinicians, we should be challenging the larger paradigm—the expectation that menopause must be managed. After all, women face other major reproductive phases. Puberty, for example, is incredibly challenging and fraught with significant physical and psychological changes imposed by fluctuating hormones. This natural phase in every woman's life (menopause) has been medicalized, just as consumer advertising has fostered the need to have a pill to solve any physiological ailment, and women expect to have to manage their menopause rather than accepting it as a stage of life. Furthermore, 30% of women never experience hot flashes. They just seem to slide right through menopause, yet this cohort is rarely studied to see what allows them to transition through the hormonal changes of menopause without significant symptomatology. Why are clinicians not telling women that this is not only possible but a reality for one of three women?

It is disturbing that the current message is that women believe they must consult an expert to get through this phase of life. Worse is the common expectation that there are solutions that will remove all menopausal symptoms—hot flashes, night sweats, vaginal dryness—while revving up the libido.

In cultures that revere age and respect their elders, women appear to experience less stress and anxiety as they pass through menopause. In this country, however, youth is desired over aging (even gracefully), causing a rush to Botulinum toxin (Botox Cosmetic, Allergan Inc., Irvine, CA) and plastic surgery as a way to forestall that harsh, if inevitable, reality. Thus, it is no wonder that American women face menopause and its concomitant symptoms with dread, wanting to eliminate any discomfort even if it means taking HT for the rest of their lives. Clinicians should not be so cavalier, as the long-term consequences of taking HT for some 20, 30, or, 40, years are just beginning to become known.

Rather than assume that menopause is a medical condition that must be managed, one must think of menopause as another transition that all women go through. Such hormonal fluctuations that allow women to be connected to their bodies put them in touch with changing needs. Women do not have to do anything to get through the menopausal transition. It would be wonderful for clinicians to reframe our approach and responses such that women do not feel they must

take something that might increase their risk for breast cancer or stroke or damage their liver just to avoid experiencing any symptoms. Women can be counseled to adjust lifestyle factors to ease bothersome symptoms and consider intervention only if the symptoms significantly impact the QoL. That said, it should be acknowledged that symptoms can be intolerable for some women, and an array of options can be discussed to determine the optimal approach for each woman.

About two thirds of women can expect to face such menopausal symptoms as hot flashes, night sweats, and vaginal dryness, yet clinicians and their patients remain conflicted about whether and when to use HT. How does the use of HT fit in the current paradigm of menopause symptom management?

The vexing question that clinicians should be asking is why so many women are looking for CAM options. The answer may lie in the overwhelming desire of women to have some control over their lives, also, there is very little downside to CAM strategies, such as focused breathing (with a 40% reduction in frequency) to get through a hot flash—no cost, no side effects, and no safety concerns.⁸⁻¹⁰

Although a subset of women may require symptom intervention, many women are seeking medical resolution to their symptoms based on a recurring message that they have problems that need to be medically managed, and they buy into it. Given the 10–15 minutes allotted to patient visits, it is a lot easier for a clinician to pull out a prescription pad than it is to talk to women about these QoL issues, particularly wellness strategies that fall outside the safe zone for most practitioners who are not trained in CAM. This is compounded by the “It takes one to know one” factor, in which exercise tends to be recommended by those who exercise, those who quit smoking tend to be much stronger advocates for smoking cessation, and physicians who have a very healthy diet tend to emphasize good nutrition practices. It would follow that physicians who meditate or go to a yoga class and have had a positive experience or see beneficial effects in their patients are more inclined to recommend these strategies.

A clinician should begin by discussing the way lifestyle habits, such as diet, physical activity, sleep hygiene, and stress can affect

symptoms.^{8,10,11} Interestingly, a clinical study of Asian ginseng's efficacy on hot flashes in women found no difference in frequency of hot flashes but did find improved QoL.¹² Even as their hot flashes continued, the women taking ginseng reported improved mood, more energy, and better sleep quality than their counterparts taking a placebo. The results are more consistent with the historical and traditional uses of ginseng as an adaptogen, that is, a botanical that promotes physiological adjustment during times of stress (i.e., increased hot flashes, irritability, or poor sleep). An adaptogen, such as ginseng, is probably most relevant for women who are having four to six hot flashes daily rather than those who report having twenty or more. Another useful adaptogen, *Rhodiola rosea* (golden root), is more commonly used to lessen cognitive deficits, such as forgetfulness and irritability,¹³ and may work well in women during their menopausal transition. Regardless of hot flashes, these adaptogens promote a feeling of well-being throughout the day. This is consistent with other lifestyle approaches, such as paced breathing, a technique that focuses on deep, abdominal breathing, which when initiated at the start of a hot flash, promotes a sense of relaxation.^{8,9,14,15} The concept of proper breathing illustrates another example of how easily simple remedies can achieve the necessary outcome without clinical intervention. It behooves women's health practitioners to become more familiar with Eastern types of exercise, such as yoga, Tai Chi, and Qi Gong, all of which include a form of paced breathing. For many women, these lifestyle methods are sufficient to get them through the 1 or 2 transitional years in which menopausal symptoms are most bothersome.

Given the need to encourage clinicians to develop a clinical respect for the menopausal transition as a natural part of life, the question remains: Who can or should consider HT, and for how long is its use reasonable?

These are vexing clinical questions with no clear answers because of the conflicting data and the variable needs of individual women. There is nothing more effective than estrogen replacement to remediate hot flashes, because it alleviates vasomotor instability. Clinicians should use the lowest dose for the shortest duration and find the

formulation that works best for the individual patient. Transdermal patch and intranasal delivery of estrogen allows for direct absorption, bypassing the liver, and thereby enabling a lower dose and fewer side effects. But all modes are effective and acceptable to many women.¹⁶

The greatest confusion for many practitioners comes from the emerging area of bioidentical hormones. It is not hard to fathom why women would ask for a hormone (17 beta-estradiol) with which the body is familiar. The furor over bioidenticals heated up over "the Suzanne Somers effect," a fallout of the self-promotion of a Hollywood star whose books, *Ageless* and *The Sexy Years*, hyped her youthful appearance, for which she credited bioidentical hormones. Many women are approaching their doctors for bioidentical hormones because they want to achieve the Somers success are more comfortable taking an estrogen that is produced naturally in the human body. For example, women are asking for such products as Bi-Est (a combination of two estrogens, estriol and estradiol) and Tri-Est (a combination of three estrogens: estriol, estradiol, and estrone), which can be prepared by a compounding pharmacy. Clinicians should help patients understand that bioidentical hormones are manufactured in the laboratory, the only difference being that the molecular structure more closely matches that found naturally in the body. It does not necessarily mean they are safer; in fact, there are few safety data available for these compounded formulations. We should be mindful that many women who develop breast cancer have never taken hormone supplements, which means that they have never been exposed to any hormones other than those in their body. We cannot assume that these products will not increase the risk of breast cancer or stroke simply because they are bioidentical.

According to the North American Menopause Society, custom compounds may provide certain benefits, such as individualized doses and mixtures of products and forms that are not available commercially.¹⁷ They may also pose risks because they have not been approved by the FDA and, therefore, have not been tested for purity, potency, efficacy, or safety.

Clinicians should be aware that prescribing bioidentical hormones does not necessitate the need for salivary testing. Unlike thyroid hormone, which has a specific therapeutic range, HT is given to manage symptoms, and there is no

range for which to aim. The goal is to give only enough to keep the patient comfortable during the 1–2 years of menopausal transition. There is no clinically justifiable reason to test estrogen or progesterone levels, salivary or otherwise, for the basic management of HT during menopause.

In summary, regardless of the source of estrogen and progesterone supplementation, the expert guidelines—lowest dose, shortest duration—should be followed.

For the growing number of women who are turning to botanicals for symptom management, what is the current evidence for black cohosh and soy, the two most heavily researched plant-based remedies/botanicals, which have dominated the literature and received substantial consumer media attention for relief of hot flashes?

Although there have been 14 placebo-controlled clinical trials, the results on black cohosh have been mixed, challenged by the use of different preparations and doses.^{9–11} The very small but growing number of case reports of liver damage may be a warning signal of a problem with black cohosh. At this time, it is unclear if there is a relationship between black cohosh and hepatotoxicity or if hepatotoxicity is due to the presence of other species (e.g., Asian) of black cohosh or other adulterants in products. Because it appears that there may be a rare risk of trouble, however, Canada, Australia, and several European countries have mandated a cautionary statement on black cohosh product labels. Similarly, the U.S. Pharmacopeia now recommends that companies in the United States do the same so that women will be aware that certain symptoms, such as dark urine and abdominal pain, should lead to prompt discontinuation and immediate medical attention.

The longest clinical trial, the Herbal Alternatives for Menopause (HALT) study, that lasted 12 months, failed to show any benefit in reducing hot flashes among those women taking black cohosh.¹⁸ There were some confounding variables in the study, however, including the cessation of the WHI, which affected some women who were included in both studies. Additionally, independent analysis of the combination formula that was used in one treatment arm of HALT failed to find three herbs that were purported to be in the preparation. Black cohosh appears effective for some women in early menopause who exhibit severe symptoms.¹⁹

Botanicals are optimally used in the way that herbalists administer them—by blending a selection of herbs that fit the patient based on individual presentation and symptoms. Historically, black cohosh was considered an anti-inflammatory agent, used to treat arthritis and aches and pains as well as depression. Fifty years ago, its role in menopause surfaced in Germany, but this is a relatively new use in the United States for this indigenous North American herb. Current research suggests that black cohosh affects neurotransmitters, supporting its possible effectiveness as an antidepressant. Therefore, black cohosh may be most effective for women who complain of musculoskeletal aches and pains or a depressed mood and poor sleep. Definitive studies and safety data are still needed, however.

The use of selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) has been suggested as a viable intervention for menopausal symptoms. Is it appropriate to use SSRIs or SNRIs to treat women in menopausal transition who have QoL issues or specific symptoms, such as depressed mood or hot flashes?

Women can struggle with QoL issues just as readily at age 35 as at age 65, meaning symptoms are not necessarily related to menopause. Essentially, anything and everything that does not feel right has been linked to hormonal fluctuations. We must be careful not to make every emotion or physical symptom experienced by women between the ages of 45 and 60 a menopause-related problem. After all, it is a period of life during which a great many stresses and responsibilities exist within the context of daily living. Although there is modest evidence of efficacy of SSRI/SNRIs, generalizability is limited.^{8,20} Given the adverse effects and cost, these therapies may be most useful for highly symptomatic women who cannot take estrogen.

From WHI findings, we know that there are woman's health risks after 5 years on continuous HT, but are there benefits for any woman to stay on HT indefinitely?

Women should consider the fact that taking a naturally imposed hormone break, as occurs during pregnancy or nursing, may offer protection against breast cancer. Although long-term HT is

not advisable, clinicians can only present the facts as they understand them to insistent patients. There is a small minority of women who may suffer with hot flashes and night sweats for up to 15 years after menopause. These women may need to use HT for a significant length of time. For most women, however, the symptoms that prompted medical intervention will taper off within 1–2 years, eliminating the need for HT. Not knowing the length of time hot flashes will remain severe is another reason for limited duration prescribing of any course of therapy (be it HT or botanicals) for easing unmanageable symptoms during menopause.

The data on soy remain controversial and elusive. However, it is popular and convenient. How much must be taken to achieve a reduction in hot flashes?

Recent studies show that reduction in hot flashes is significantly related to baseline hot flash rate and the dose and ratio of isoflavones studied.^{8,21} Even more than this, the effectiveness of soy for hot flashes may be related to women being equol converters. When nonfermented soy is eaten, the isoflavone daidzein must first be converted to daidzein and then to equol, which is the most potent form of phytoestrogen derived from soy. This conversion is dependent on the type of intestinal microflora present, however, and only a third of people in the Western hemisphere appear able to make this conversion, compared with the majority of women who live in the East.²² This geographical variability, even more than a placebo effect, may be sufficient to explain the differences in study results from different populations.

Including soy in the diet is not an issue, but there are no conclusive data that suggest a safe upper limit for these isoflavones once removed from food. Therefore, it is judicious for clinicians to caution patients to limit their intake of isolated isoflavone to 40–80 mg/day, with 100 mg as the upper limit.^{8,19,21} Women who are at high risk for or who have breast cancer are probably best advised to avoid taking isolated isoflavone supplements.²³

Beyond black cohosh and soy, what value might other popular botanicals offer for women in the menopausal transition?

Red clover is another isoflavone-rich botanical, with a broader array of isoflavones than soy. Clin-

ical trials for hot flashes are mixed, but the data support its safety.⁸ St. John's wort alone and in combination with black cohosh has also been shown to reduce hot flashes.⁸ St. John's wort is now in a phase II clinical trial at the National Cancer Institute (NCI) for women with breast cancer who are experiencing hot flashes. Other herbs that appear useful include hops, damiana, valerian, and maca.^{1,8,9,24}

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