

Clinicians' FORUM

From time to time, the editors of *Menopause Management* field interesting clinical questions and dilemmas. In this forum, our Editorial Advisory Board members, and guest commentators,* experts in a range of fields related to midlife women's health, tell readers how they handle these situations.

The viewpoints expressed in "Clinicians' Forum" are those of the contributors, and not necessarily those of *Menopause Management* or The North American Menopause Society (NAMS).

Question: A patient enters your office carrying her "brown bag." She empties the contents onto your desk, spilling out more than 15 multi-colored containers of health store herbal, vitamin, hormone/prehormone and "alternative products" in various combinations, permutations and doses. She asks your advice on which, when and how many to take. How do you handle the situation?

Answers:

The popularity of complementary and alternative medicine (CAM) has increased dramatically over the past decade—most notably the use of herbal products. Americans spend more than 19-billion dollars per year on herbal and natural products.¹

A 2004 study published by the Centers for Disease Control and Prevention's National Center for Health Statistics found that 62% of adults in the United States have used some form of CAM in the previous 12 months.² It is reasonable to assume that, more likely than not, your

patients are consuming some form of these products. Certain populations, including women, are more likely to use CAM.² Fifty-five percent of Americans reported that they used CAM in combination with conventional medicine in order to achieve better outcomes.²

Why do patients end up with multiple products, which results in those patients bringing a full "brown bag" or Tupperware container to the office? Consumers will begin alternative therapy believing it will have some immediate effect and, when the desired result is not forthcoming, back they go to the health food store, trying to find the magic bullet, often obtaining the "expert" advice of the store clerk.

The bottom line is that many users equate the term "natural" with being safe. In reality, however, there are associated toxicities and potential interactions with prescription medications. In addition, the very nature of CAM may encourage

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individuals not to seek standard conventional medical intervention.

Below is an overview of the three general areas I cover in discussing alternative therapies with my patients: evaluate, educate and eliminate.

Evaluate

By sharing her current supplement use with her clinician, the patient described in our scenario has exhibited that she trusts that clinician to guide her and is asking for assistance. A major-



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ity of patients never reveal to their healthcare providers that they are consuming herbal products. There are several reasons for this, including embarrassment and fear of a negative response. Women, in particular, report they have never been asked about herbal and natural product use by their healthcare providers.²

I begin with two straightforward questions: “Are you currently taking all of these products?” “What prompted you to buy each of these products?” Common reasons patients seek CAM include the desire for a more holistic approach to care, to feel as if they are actively participating in their treatment plan, because conventional medicine has failed to treat the disease or symptoms, and/or fear of side effects of prescription drugs.³

Based on the patient’s response to your questions, organize the products into categories based on a desired effect. In my women’s health practice these “categories” include a desire for more energy, better memory, better sleep, improved sex drive, decreased hot flashes or alleviation of chronic pain.

Educate

Users of dietary and herbal supplements are unaware of the lack of regulation of these products. They do not understand that these products are not legally required to deliver on the manufacturers’ promises, nor is there quality assurance. Educating the patient about the regulation of dietary supplements and herbal therapies in a clear manner is essential to her understanding

of your subsequent concerns and statements regarding safety and efficacy, and recommendations regarding use.

Regulation of dietary supplements. Under the Dietary Supplement Health and Education Act of 1994, dietary supplements are regulated by the FDA as foods.⁴ Yet, unlike prescription medications, the manufacturers of these supplements are not required to provide proof of their safety or efficacy to the FDA prior to bringing them to market.

I refer my patients to two Web sites for diet and herbal supplements: Consumerlab (www.Consumerlab.com) and US Pharmacopeia (www.usp.org). Consumers should be made aware that these, and other quality-assessment programs, do not verify efficacy. The “seal of approval” on a bottle does not tell the consumer what areas were tested, nor that efficacy is not included in the evaluation.

Eliminate

After careful review and education, I begin the process of eliminating those products that have no proven efficacy or might interact with the patient’s prescription medications. Many times the healthcare provider cannot accurately comment on a supplement with 20+ ingredients or the term “proprietary blend” on the label. If you aren’t knowledgeable about a particular supplement, investigate or tell the patient that while you are unable to make an accurate assessment, the facts regarding regulation of herbal and dietary supplements apply to all.

Through open dialogue with the patient a reasonable assessment can be completed. This should be placed in writing in the patient’s chart and a list given to the patient.

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Caring for women across the menopause transition presents some special challenges. These include staying up to date in a rapidly changing medical and scientific landscape, and addressing a broad range of physical and emotional issues in a complex social context. Another frequent subject in the consulting room is the many claims about a variety of products promoted to treat the multiple ills attributed to “hormones.” And yes, women regularly present with bags full of such remedies, asking for guidance.

What to do when confronted with multicolored containers, Xeroxed materials from a wide range of books available about managing menopause, or print from the ever-expanding destinations attainable from a launch on Google? The answer is quite simply: No different from usual care.

Take a history and be clear on the patient’s personal medical issues, her specific concerns and symptoms. Find out what she has tried and what she is currently taking. Listen and be respectful. Then, tell her what you know.

For me, the generalities include the following:

- Over-the-counter (OTC) products are not FDA-regulated or quality-controlled;
- Such products have rarely been tested for efficacy or safety;
- There are evidence-based lifestyle and prescription interventions to help manage a variety of menopausal ailments;
- Sometimes anticipatory guidance, education and reassurance are sufficient to address a menopausal woman’s concerns.

But then there are the specifics and, of course, each ingredient and each formulation has its own potential benefits and harms. The black cohosh story is instructive. This Native-American herb has been used therapeutically for centuries. A monograph for black cohosh appeared in the first “US Pharmacopeia” (USP) in 1820.¹ It is an ingredient in all of the several OTC menopause products in my local pharmacy. The 2004 NAMS position statement, “Treatment of Menopause-Associated Vasomotor Symptoms,”² presents the available data on black cohosh’s effectiveness. Those data are inconsistent. The associated statement on safety is, “There are no known reports of serious adverse effects or drug interactions

with black cohosh. Moderate side effects are rare and include gastrointestinal upset.”²

NAMS supported the use of the German standardized product in its consumer-oriented “Menonote”[®] on hot flashes, and so, I might add, have I. However, studies of the efficacy of this herb continue to be contradictory,³ and now, for the past 4 years, concerns about its safety have been accumulating in the form of case reports about serious liver toxicity. These became numerous enough that there were cautionary statements from regulatory agencies in Canada, Australia and the European Union. This year, USP determined that a warning statement that black cohosh can “affect the liver” would be required on products that qualify for a US label.¹

The association between black cohosh and hepatitis is rare and not proven. But the above sequence illustrates some of the pitfalls of dealing with unregulated therapies. It doesn’t speak to all the various formulations available, some of which have been marketed under the same name over time, or that safety data exist

for only 1 year, to name two additional issues relevant for this single ingredient in many OTC products aimed at the menopausal woman.

So, back to the question at hand: What can be said to our patients about any of the literally dozens (maybe hundreds!!!) of possibilities available to them to treat symptoms they think might be caused by menopause? It is difficult to find good evidence to support the effectiveness of many OTC products—they cost money and they could be unsafe.

So, if women really want to try something available without a prescription to help with a particular complaint, they should try a single product, give it time and monitor their response.

Finally, the use of herbal and dietary supplements is another area in women’s health and menopausal medicine that screams for more research.



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—Martha K. Richardson, MD

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The patient described in this scenario is becoming more and more common. If a woman lives long enough she is sure to become menopausal, and approximately 90% of menopausal women experience hot flashes and/or night sweats. Despite the fact that hormonal therapy (HT) has been identified as the single best treatment option for vasomotor symptoms, the Women's Health Initiative (WHI) has resulted in many women fearing the use of such therapy. Many women, for example, have bought into the belief that herbal therapies or "bioidentical hormones" are safer alternatives, despite a lack of evidence. The FDA has acknowledged that the safety and enhanced efficacy of bioidentical hormones, as claimed by many pharmaceuticals and compounders, is not supported by the medical literature.¹ Despite this, many patients, like our patient described above, are looking for alternatives that they believe are safer and effective.

The term "complementary and alternative medicine" has been coined to describe a class of therapies that are used in conjunction with (ie, complementary) or in place of (ie, alternative) conventional medications.² Herbal therapies and various oral products have become common alternative therapies for treating menopausal symptoms. In one study, as many as 46% of patients used CAM, and many of these women had not seen a healthcare provider about their symptoms.³

The controversy generated by the WHI has left women with severe symptoms in a state of confusion. Because studies consistently show that a placebo has some effect on vasomotor symptoms, many wonder whether alternative products could act in the same way, potentially opening the door to abuse of a vulnerable population. While HT is the most effective, and is safe in most patients, many women have been led to believe that hormones are overly harmful and that the risks outweigh the benefits.

Because herbal products are considered "natural," many patients believe they are safer. This, however, is not a justifiable assumption; for example, poison ivy, arsenic and hemlock are all naturally occurring. Arsenic, in fact, has been found in herbal preparations.⁴ Herbals and dietary supplements are not considered medications in the US. Furthermore, there are no required approval, regulatory or safety standards⁵ as long as the label states that 1) there has been no FDA testing of the product, and 2) the product is not intended to treat, diagnose or prevent illness. Because the producers of these products are successful in marketing and sales, and since there are no regulatory restrictions, there is little motivation to begin scientific studies. While many herbal therapies are likely safe and benign, the major problem is a lack of well-designed studies to assess the extent of product safety, efficacy, potency and sterility. In 2001 the FDA performed a limited survey of 29 compounded products.⁶ Of these, 10 (34%) failed at least one quality test and 24% failed for potency; of those failing, some were as low as 59% of the expected potency.

Because well-designed studies on this topic are rare, data are limited mostly to case reports. A concern, therefore, is that many side effects, complications and interactions may not be identified or recognized. When the literature is reviewed, the following generalizations can be ascertained. Although most interactions are not serious, some can be life-threatening. St John's wort, for example, has been noted to have serious potential interactions with cyclosporin, digoxin, protease inhibitors, antidepressants and anticoagulants. There has also been concern about ginkgo and ginseng, but these are not as well-documented.⁷ Other herbals that can have varying degrees of medicinal interactions include agnus castus, black cohosh, dong quai, soya and red clover. The medications that could potentially interact with herbals include antidepressants, hormonals or antiestrogens, benzodiazepines, opiates, thyroxin, antihypertensives, antidiabetics, antineoplastics, anticoagulants and anesthetic agents. Herbal products may also cause inhibitory or additive effects with traditional medications or hormones.⁷ Black cohosh,

for example, may decrease the response to estrogen, and at times can cause an additive effect.⁸ Therefore, black cohosh should be avoided when estrogen-sensitive tumors are present. Because



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many patients do not talk to their providers about herbal therapies, it is important that we initiate discussion of the topic with our patients. Even if you do not consider yourself an expert, identifying the concomitant use is important, and patients can be directed to a variety of resources to identify risks.^{5,7,8}

With this background, in a situation like the one described here, the following is a reasonable approach:

1. Spend time educating the patient about the lack of data to confirm efficacy and long-term safety of herbal and many alternative therapies.
2. If applicable, let the patient know, in a sensitive and non-threatening way, that you do not want herbal sales persons to take advantage of her as a part of a vulnerable population.
3. Support the patient who has decided on herbal use. It is important that patients do not feel that we get some secondary gain from discouraging their use. Supporting these patients will also make it more likely that they will come to us (their clinicians) with questions or concerns.
4. If patients decide to use herbals or alternative therapies, it is important that they know there are potential unknown risks and that many studies show no significant benefit to their use.
5. Make sure there are no major contraindications in regard to other medications or procedures the patient may be anticipating.

At a minimum, this patient needs to narrow her spectrum of products from the “shot-gun” approach. If she chooses to continue herbal therapy, she should choose one product for each indication.

There are many reasons that some women are drawn to herbal and alternative therapies. These include the desire to have control of one’s

own health maintenance, frustrations with traditional medicine, a shortage of providers and fear of traditional medications. The fear of medications likely stems from research data that can often be misunderstood or misrepresented in the media. While we are serving as patient advocates as we bring informed consent, the information patients hear may be scaring them. A lack of information about herbal therapy may be less threatening to patients but may leave them more vulnerable. As providers and advocates we need to do the best we can to educate patients regarding the data that are available, and help them make informed decisions.

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I have seen “this woman” in my office many times. I first fight the urge to let my head drop down onto my desk in frustration. I then sincerely thank her for bringing in all the bottles of supplements and vitamins, as I believe all patients should bring in both prescription and non-prescription bottles and boxes at each office visit. So many times, patients are not taking what we think they are, and what we have prescribed might very well not have been properly dispensed

by the pharmacist. (For example, I have seen the birth control vaginal ring Nuvaring being dispensed in place of the local estrogen Estrinring vaginal ring, and estrogen-only generic patches being dispensed instead of estrogen-progestin patches to women needing progestin therapy.)

I also have educated women who tell me they are taking “1,000-mg vitamin D” when they are really taking 1,000 mg of calcium and not the 1,000 international units (IU) of vitamin D₃ (cholecalciferol) that I routinely recommend. I then go on to tally the exact number of IUs of vitamin D that she is taking. Ironically, I have found that many of the women taking the largest number of herbs and supplements are not on any vitamin D at all, and are actually quite deficient. Newer recommendations for vitamin D are at least 1,000 IU, and go up to even 2,000 IU, in contrast with the 400 IU that is deemed “100%” of the daily requirement. Based on the widespread vitamin D deficiency, I liberally check 25-OH vitamin D levels. The evidence continues to mount regarding protean health benefits of vitamin D.¹ I also examine each bottle, looking for both a lot number and an expiration date, and tell the patient to be very wary of those substances without this mark or ability to trace. I also refer patients to my book’s chapter on nutritional supplements and alternative therapies in “Women’s Health: Your Body, Your Hormones, Your Choices.”²

Once I have gained her trust and confidence that I am both open and knowledgeable about vitamins and supplements, I briefly tell her about my experience with the L-tryptophan-induced eosinophilia myalgia syndrome epidemic.³ While a “natural” amino acid, L-tryptophan was not being manufactured “naturally” and the manufacturing process led to several deaths. I gently explain that if something is not a food or a drug, it is quite simply “unregulated”. I offer the www.consumerlab.com site as one that, for a small fee, will release information about substances that have been tested for purity. I explain that just because something is “natural” does not mean it is something that should be ingested (eg, manure).

I do try to be exceedingly patient with these women as many of them have been driven to take

unregulated supplements and concoctions because we, the medical profession and research establishment, have failed too many symptomatic menopausal women in this post-WHI era. We have failed them because we have not always put the rare risks of menopausal HT in perspective in the context of other therapies.⁴ This, coupled with the pervasive anti-big pharma sentiment amongst consumers, has made it ripe for purveyors of “alternative” therapies to target symptomatic midlife women.

I always emphasize lifestyle management, including diet, exercise and judicious use of supplements, particularly vitamin D. I then go on to offer individualized therapy that may include the use of menopausal HT or other indicated pharmacotherapies. By utilizing a stepwise, individualized and compassionate approach, I find that women are much more likely to embrace evidence-based, regulated therapies versus unregulated herbs and supplements.

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Unfortunately, this is a common issue, particularly for a patient who is afraid of medication, or is trying to treat herself, or both. These patients need to be treated carefully as they often have significant symptoms and are very afraid of prescriptions. I first review the decision process that led the patient to decide to take these supplements. I also review the ingredients for possible harmful elements or those that may interact with other medications the patient is taking. I also assess how the patient is feeling on these supplements.

Next, after examining the patient, I make an individualized assessment of her needs and her possible risks. I explain that medical decisions concerning medication are based on scientific evidence, and try to review, in simple terms, the evidence (often nonexistent) for the use of the supplements.¹ In some cases I feel that supplements may be acting as a benign placebo, and I have no objection to their use. However, the financial investment is, in many instances, considerable and I feel ethically obligated to point this out to the patient. In some cases the supplements are indicated, such as calcium and vitamin D, or there may not be options available that suit the patient's needs. I then review the advantages of regulated versus unregulated products. If FDA-approved products are available I feel obligated to offer them and review the risks and benefits associated with these products. One of the main advantages is the considerable literature on side effects, dose and efficacy, which is not available for most supplements. There is also quality control for purity and dosage accuracy, and mandatory reporting of adverse events, and surveys of some have shown inconsistencies.² This is not true of many supplements and unregulated drugs. For instance, makers of so-called "bioidentical" custom-compounded hormones

claim that there have never been any reports of adverse events, but such reporting is not mandatory as these drugs are not regulated. In some cases the patient may have been influenced by misleading claims about supplements, which translates into a lost opportunity to offer effective treatment.

Osteoporosis is an example of a problem that surfaces frequently; patients take an OTC progesterone cream because of claims that this supplement protects against osteoporosis, but these claims are not backed by science.

Part of the problem with respect to menopause is the fear of hormones for treatment of menopausal symptoms, a problem engendered by the reports from the WHI.³ In fact, the risks are

very small and severe symptoms usually last only 2–5 years. I usually try to work with the patient in this regard as trust is an important issue. Some patients will agree to pare down their supplements and eventually follow a more reasonable regimen.

Lastly, some patients are suffering from an obsessive-compulsive disorder, and this issue needs to be addressed before adequate treatment can be initiated and the patient can remain compliant. There is often resistance so trust should be established first.

In conclusion, the physician and patient should work together to find the most effective and safe treatment for a symptom or medical condition. This will improve compliance and start the patient on the road to understanding the steps that need to be taken to achieve a healthier life.

—Michelle P. Warren, MD

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