

Dialogues in Menopause Management: Facilitating Counseling about Hormone Therapy

As a second installment to “Dialogues in Menopause Management: Facilitating Counseling about Hormone Therapy” from the March-April issue, here are two more cases that present the potential benefits and risks of hormone therapy (HT) for postmenopausal women. These case scenarios discuss a Caucasian woman at high risk for breast cancer and an African-American woman at high risk for osteoporosis. The series has been presented in three different venues in order to reach the widest possible audience: live (Primary Care Network), Web-based (MedscapeCME.com) and, now, print.*

Case #1: Counseling Women about HT and Breast Cancer Risk

Peter F. Schnatz, DO, FACOG

Teaching Point

To demonstrate to a woman at high risk for breast cancer the potential benefits and risks of using hormone therapy (HT) for menopause symptom relief.

Case History

The third case in our counseling series involves a 55-year-old postmenopausal Caucasian woman who is 4 years beyond menopause and has debilitating vasomotor symptoms. These symptoms were not severe at her last checkup a year ago but are now causing her sleepless nights and exhausted

days. She has previously tried several over-the-counter remedies, including black cohosh, soy and red clover supplements.

The patient’s chart reveals that she reached menopause spontaneously. Her bone density is normal for her age, and her Pap smear and mammogram show no abnormalities. The patient never smoked or used HT in any form. She is in good general health and maintains a healthy routine of exercise and diet.

The patient’s mother was recently diagnosed with breast cancer at age 77. With the patient’s concern about breast cancer, should the clinician suggest a trial course of venlafaxine or other medication used off-label for her menopause symptoms, or should she be counseled on the risks and benefits of HT as the surest therapy for her discomfort?

HT and Breast Cancer

Counseling this woman about HT and breast cancer involves explaining the outcomes of several studies, most notably the Women’s Health Initiative (WHI). After the WHI results on the risks of HT for postmenopausal women were published in 2002, HT use in the US dropped substantially.¹ The incidence of breast cancer also dropped, suggesting a cause-and-effect relationship.² But the cause of this decline in breast cancer remains controversial.

The latest report from the WHI³ confirmed that the increased risk of breast cancer associated with the use of estrogen-progestogen therapy (EPT) dropped soon after discontinuation. The investigators also concluded that this decrease was unrelated to changes in frequency of mammography. It has been noted, however, that the rapid decline in breast cancer rates after discontinuation may not be biologically plausible, because breast cancers normally take several years to develop. Instead, it has been postulated that stopping HT could quickly influence hormone-sensitive tumor growth in much the same ways that tamoxifen and aromatase inhibitors can cause tumor regression in women with metastatic breast cancer after only a few months of treatment.⁴

*This article is a brief synopsis of two cases presented as part of several live and Web-based activities from The North American Menopause Society (NAMS) and Medscape on counseling postmenopausal women about hormone therapy. This article and the entire series are supported by an unrestricted educational grant to Medscape from Wyeth. The material presented here does not necessarily reflect the views of NAMS, Medscape, or Wyeth.

In the original WHI reports,⁵ there was no significant increase in breast cancer until the fifth year in the EPT arm. While there was an overall statistically significant increased risk of 24%, after adjusting for confounders the relative risk was 1.2 (not significant), and for those who had not used HT previously there was no increase in risk. The increased risk at the fifth year raises the question of whether 5 years is the safe window for HT use and, if so, whether that means HT is unsafe after 5 years.

The increased incidence of breast cancer with HT is only seen with longer-term use and the diagnosis of breast cancer appears to increase with EPT use beyond 3 to 5 years. In the WHI, this increased risk in absolute terms was in the rare category, being 4 to 6 additional invasive cancers per 10,000 women per year of EPT use for 5 or more years. Furthermore, the increase in breast cancer risk was significantly related to EPT use before enrollment in the trial. Available evidence suggests that estrogen alone for more than 5 years has little impact on breast cancer risk.⁶

Counseling the Patient

When the patient returns after 4 weeks of trying venlafaxine, she says that her menopausal symptoms have not gotten better. In fact, she is experiencing more hot flashes each day and night. At this point, her stress level is extremely high and she would like to try HT.

To further allay this woman's fear of breast cancer, the clinician explains that current prescribing patterns involve use of the lowest effective dose of estrogen consistent with treatment goals, with a corresponding low dose of progestogen to protect the uterus. These dosages are much lower than those tested and reported on in the WHI.

Since we don't know for sure whether or not HT increases breast

cancer risk, the clinician might explain the risk by presenting a negative hypothesis that "HT does increase breast cancer risk" and propose the worst-case scenario. Most experts agree that a relative risk of about 1.25 (25% increase) is a good estimate of the association between HT and breast cancer; however, patients often misunderstand this "relative risk." When they hear 25% increased risk, what they hear is, "If I'm using HT, and three of my friends are using HT, one of the four of us is going to get breast cancer." Clinically, we know this is not true.

Risk is better understood in absolute terms. For a 51-year-old woman—the average age of women starting HT—the baseline risk of developing breast cancer is about 1 in 50, or 2 in 100, which would be 2% over the remainder of her lifetime. In other words, there is a 98% chance that she would *not* develop breast cancer. Using the relative risk of 1.25, and assuming HT causes breast cancer, the use of HT would result in a 2.5% risk of breast cancer ($1.25 \times 2\% = 2.5\%$). In other words, she would still have a 97.5% chance of *not* developing breast cancer.

With a clearer understanding of the actual risks of HT and breast cancer, along with the fact that evidence cannot prove a cause-and-effect relationship between HT and breast cancer, this patient can now focus her decision on the well-known benefits of HT compared to the small risk.

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Case #2: Counseling Women about HT and Risk of Osteoporosis

Steven R. Goldstein, MD

Teaching Point

To demonstrate to a woman at high risk for osteoporosis the potential benefits and risks of using low-dose estrogen therapy (ET) for menopause symptom relief.

Case History

The fourth (and final) case in the counseling series concerns a 52-year-old postmenopausal African-American woman who presents with severe hot flashes and night sweats. She had a hysterectomy 10 years ago due to fibroids; her ovaries were not removed. The patient's mother was diagnosed with osteoporosis at age 79, so the patient is at high risk for the disease. The woman's paternal aunt had breast cancer at age 67, so the patient is concerned that she will develop the disease as well.

The patient is taking calcium and vitamin D but is not taking any prescription medications. Her physical exam was essentially normal, and her laboratory evaluations, including a mammogram and Pap smear, were normal as well. She maintains a healthy lifestyle, weighs 130 lb, and is 5'8" tall.

The patient's primary concern is how to manage her menopause symptoms, which leave her exhausted during the day and unable to concentrate at work. She is determined not to start HT after hearing media reports about its adverse risk-benefit profile,¹ yet she is desperate to improve her quality of life.

Defining Menopause

From the patient's history and physical examination, the clinician has ascertained that she has recently reached menopause. The decrease in her estrogen levels is the cause of her increased vasomotor symptoms since her last checkup. She is confused because she had a hysterectomy 10 years ago, so why would hot flashes start now?

The clinician explains that even though she had a hysterectomy and her uterus was removed, her ovaries were left intact and continued to make estrogen. As a result, she did not reach menopause at that time. The ovaries recently stopped making estrogen and then the hot flashes started. The patient was counseled that hot flashes are a common response to menopause and the loss of estrogen.

Her speculum pelvic examination revealed that she is also experiencing vaginal discomfort. The clinician explains that this is related to vaginal dryness and lack of lubrication, also caused by the decrease in estrogen at menopause.

It is further explained that even though menopause is normally confirmed after 12 consecutive months

of amenorrhea or after bilateral oophorectomy, this woman had an ovary-sparing hysterectomy 10 years ago,

sity than would be expected at their ages.³ Studies have shown that, in general, African-American women

Research shows that low-dose ET helps secure bone strength and prevent fractures.

and further tests to confirm her menopause status would be prudent.

Low-Dose ET

If the patient's vasomotor symptoms were less severe, the clinician might recommend nonhormonal alternatives to HT, such as gabapentin or antidepressants. But HT is the only treatment proven to quickly and satisfactorily relieve the severe menopause-related symptoms that this woman is experiencing. It is also the only FDA-approved treatment for these conditions,² (including vasomotor symptoms and vaginal dryness) and for preventing osteoporosis.

Because the patient does not need progesterone for endometrial protection, unopposed low-dose ET would be appropriate, and can be expected to be safer than doses studied in the WHI.

Another of the patient's risk factors is osteoporosis.

Osteoporosis Risk

The patient's family history of osteoporosis is a concern for her. Everyone loses bone strength as they age, but because her mother has osteoporosis, this patient is at higher risk for the disease. She might already have significant bone loss, and is thus more likely to suffer a bone fracture.

This woman works out and eats a healthy diet, which her mother did not do. The clinician explains that healthy living certainly helps lower her risk of osteoporosis, but female children of women who have osteoporosis have lower bone mineral den-

have a lower risk of osteoporosis than white women. However, this woman's strong family history and her thinness probably trump this benefit.

Treatment Plan

A discussion of the potential risks associated with estrogen follows. The good news is that the patient is young. Initiating ET at the age of 52 and when the patient is newly menopausal is safer than starting several years after menopause.⁴

A major finding of the WHI was that many of the reported risks—including breast cancer and stroke—were associated with the use of added progesterone. Because this woman has had a hysterectomy, she does not need progesterone, and may be prescribed estrogen alone.

The patient's concern about breast cancer does not have as strong a basis as she may perceive, as she has a second-degree relative (aunt) with the disease, not a first-degree relative (mother, sister, daughter), which would have increased her risk. Again, not needing progesterone, and taking the lowest effective dose of ET for the shortest period of time consistent with the treatment plan, further minimizes her risk. Regular clinical breast exams and mammograms are another safety net.^{5,6}

ET for 2 to 3 years would more than likely relieve this woman's hot flashes and night sweats, as well as lower her risk of osteoporosis while she takes the medication. Research shows that low-dose ET helps secure

bone strength and prevent fractures. Adequate calcium and vitamin D are also encouraged for her bone health.^{7,8}

Counseling the Patient

The patient is now just about convinced that ET is the treatment for her. The clinician orders more tests, including follicle-stimulating hormone and serum estradiol to confirm that menopause has been reached, dual-energy x-ray absorptiometry to get a baseline measurement of her bone density, and vitamin D level to rule out any nutritional deficiency. Once these results are in, the patient can begin ET. She is encouraged to schedule regular checkups to monitor her progress and adjust her treatment plan, if necessary, to ensure optimal relief. ■

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Disclosure: Dr. Goldstein reports: Advisory board—Boehringer Ingelheim, Eli Lilly, GlaxoSmithKline, Merck, Novartis, Novo Nordisk, Pfizer, Procter & Gamble, Upsher-Smith, Wyeth. Consultant—Ackrad Labs, Cook Ob/Gyn. Director—SonoSite. Speaker's bureau—Eli Lilly, Procter & Gamble, Wyeth.

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From the Editor

(continued from page 12)

prescribe HT for prolonged periods with the sole indication being prevention or slowing of skin aging.

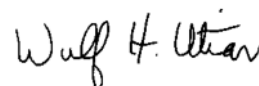
But what about topical use of estrogens? Covering large areas of skin, even with very low-dose products, would still result in unacceptably high systemic levels through transdermal absorption. This represents a challenge and a potential windfall for the developer of a product that works locally without absorption or without systemic effect.

Conclusions

Never forget the skin when you perform your annual evaluation of your menopausal patients. Ask about symptoms of skin dryness, pruritus and lack of wound healing, as well as cosmetic concerns. Do a complete skin examination to exclude suspicious lesions, and refer to the dermatologist as necessary. Remember, the skin can be your first indicator of a potentially serious systemic illness. Consider the growth-promoting effects of estrogen on the stratum corneum, fibroblasts, collagen

and elastic fibers as a potential benefit when balancing pros and cons for indicated HT. Above all, counsel about sun protection, avoidance of skin-drying agents, use of occlusive moisturizers and the potential role of topical retinoids.

Like Sherlock Holmes, be observant—your patient's skin quality will tell you much about her state of health and frame of mind!



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Suggested Reading

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