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Hormone Replacement Therapy in Postmenopausal Women

Case Study

Ms. P is 48 years old, at average risk for breast cancer, and is complaining of menopause-related hot flashes and insomnia. She is 30 pounds overweight, sedentary, and a social smoker. Ms. C is 40 years old and had breast cancer that was treated successfully with radiation nine years ago. She is a nonsmoker, an avid exerciser, and at her optimal body weight. She is complaining of severe menopausal symptoms, particularly vaginal dryness that is making sexual activity painful. Both women want to know whether hormone replacement therapy (HRT) is warranted.

Clinical Highlights

Several large clinical trials were initiated in the 1990s to obtain scientific data regarding the risks and benefits of HRT. One of the largest trials was conducted by the Women's Health Initiative (WHI). WHI randomly assigned more than 16,000 postmenopausal women 50–79 years of age with an intact uterus to estrogen plus progestin or placebo. The drug arm was halted in 2002 when results revealed that instead of protecting against cardiovascular disease, use of HRT actually increased risks of cardiovascular events, breast cancer, pulmonary emboli, and stroke. However, the study's data and safety monitoring board stopped the trial based on the finding of increased breast cancer risk, supported by the fact that overall health risks exceeded any benefit (Writing Group for the WHI Investigators, 2002).

Specific study findings for the drug arm included a 113% increase in pulmonary emboli, 41% increase in strokes, 29% increase in myocardial infarctions, 22% increase in total cardiovascular events, and 26% increase in breast cancer. A 37% reduction in colorectal cancer and a 24% reduction in fractures also were found. No difference was identified for total mortality. Effects were apparent after an average of five years of follow-up (Grady, 2003; Hays et al., 2003; Monson & Martin, 2001; National Institutes of Health [NIH], 2002; Solomon & Dluhy, 2003; Writing Group for the WHI Investigators, 2002).

Other observational studies have indicated that breast cancer risk may be greater among women using combined estrogen and progestin therapy than estrogen alone (NIH, 2002; O'Meara, Rossing, Daling, & Elmore, 2001). Additional findings have revealed that risk increased with length of use but returned to near-normal levels after therapy was discontinued (NIH; O'Meara et al.; Ross, Paganini-Hill, & Wan, 2000; Schairer et al., 2000). In a study of women diagnosed with breast cancer, prior estrogen users had lower mortality rates than nonusers (Ross et al.). Another study that followed more than 44,000 postmenopausal women who took estrogen for 20 years found that their risk of ovarian cancer was twice as high as nonusers and documented an even higher risk when estrogen was used longer than 20 years (Lacey et al., 2002; Rodriguez, Patel, Callee, Jacob, & Thun, 2001). One study of women with breast cancer who continued estrogen use after their diagnosis reported no increase in recurrence or mortality (O'Meara et al.).

Significant research needs to be conducted to address many unanswered questions. The actual risk increases in the WHI study are small: A 29% increase in the risk of coronary disease and a 26% increase in breast cancer risk actually translate into an additional 4 cases per 1,000 women (Solomon & Dluhy, 2003). Further research will help to clarify the clinical implications of HRT.

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Clinical Problem Solving

Responding to this clinical challenge are Karen Kattwinkel, RN, MA, and Marjorie Knowles, RN, BA, both graduate students in the advanced practice nursing track, and Jeanette Sweeney-Calciano, RN, MSN, an assistant professor, all in the School of Nursing at the University of Medicine and Dentistry of New Jersey in Newark.

What considerations for HRT would you discuss with Ms. P?

J. Sweeney-Calciano: Menopause is a process that occurs as a part of the female life cycle. Consideration of HRT poses many challenges for two million women turning 50 each year (U.S. Department of Health and Human Services, 2001). During initial consultations, postmenopausal patients' symptoms must be reviewed. Assessments should include how severe the symptoms are and the degree to which they are affecting quality of life. Family history of breast cancer is of significance when considering whether to initiate therapy. Educating patients regarding the dynamic nature of symptoms may relieve some associated stress levels and assist patients in coping with their new status as perimenopausal or menopausal women. During patient counseling, patients must be assured that they are a part of the decision-making process. Patients should receive current information about the appropriateness of beginning or continuing HRT.

K. Kattwinkel: Weighing the risks and benefits of HRT is key to making the best healthcare decision (see Figure 1). Symptoms of menopause can be very disabling. Ms. P has cardiovascular and thromboembolic disease risks, namely being overweight, sedentary, and a smoker. The Writing Group for the WHI Investigators (2002) determined that women taking estrogen plus progestin replacement therapy were at increased risk for myocardial infarction, venous thromboemboli, and stroke. This study documented one serious adverse event in every 100 women

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Advantages[a]

- Reduces the risk of osteoporosis
- Relieves hot flashes and night sweats
- Relieves vaginal dryness
- Improves cholesterol levels
- May reduce the risk of heart disease
- May improve mood and psychological well-being
- May prevent the decline of mental abilities with age

Disadvantages

- Estrogen alone without the use of a progestin modestly increases the risk of endometrial cancer.
- Can have unpleasant side effects, such as bloating or breast tenderness
- Hormone therapy may increase the risk of breast cancer while being used; long-term use may pose the greatest risk. When hormones are discontinued, risk gradually returns to near-normal levels.
- May increase the risk of cardiovascular events such as heart attack and stroke initially, but this increased risk appears to decrease over time
- Increases the risk for blood clots
- May raise triglyceride levels and contribute to the occurrence of gallbladder disease

Figure 1. Advantages and Disadvantages of Hormone Replacement Therapy

[a] Data currently are emerging that contrast these advantages.

treated with HRT for five years; however, Ms. P probably would not require treatment for menopausal symptoms for five years or more (Grady, 2003; Hays et al., 2003). Absolute risk was also lower for younger women, which is another factor in Ms. P's favor.

A recent study demonstrated that use of HRT did not improve quality of life (Hays et al., 2003). Although this study was not designed to test the effects of hormones on menopausal symptoms, automatic prescriptions of HRT for such symptoms should be reconsidered. Ms. P should be counseled regarding alternative therapies for menopausal symptoms, such as clonidine or soy. These preparations do not preclude use of HRT. Hot flashes and insomnia are valid indications in the absence of contraindications such as deep vein thrombosis or heart disease (Solomon & Dluhy, 2003).

If Ms. P decides to pursue HRT for her symptoms, she should be referred to the appropriate literature so that she can make an educated decision. She should start with a low-dose preparation and gradually increase the dose until her symptoms are controlled adequately (Grady, 2003). For example, when hormone therapy schedules include cyclic or sequential dosing, estrogen should be administered for 25 or 30 days a month with progestin added for 10–14 days or continuous combined therapy with estrogen and progestin daily.

Estrogen can be supplied as a pill, transdermal patch, vaginal cream or gel, or vaginal ring containing estrogen alone or in combination with progesterone. Locally applied hormone products may not carry the same risks as systemic preparations.

What advice would you give to Ms. C?

M. Knowles: Use of estrogen in women treated for breast cancer currently is not advised (Monson & Martin, 2001; Zibecchi, Greendale, & Ganz, 2003). One of estrogen's primary roles is to promote the growth of cells in the breast, but the safety of using HRT in women with a history of breast cancer is uncertain (NIH, 2002). Ms. C should try alternative therapies for her menopausal symptoms before considering HRT (see Table 1). Zibecchi et al. determined that individualized counseling and support by a nurse practitioner who focuses on alternative treatments for menopausal symptoms improved symptoms and sexual functioning compared to women in the control group.

The need for a detailed history and physical examination is of utmost importance. This should include the use of all prescription as well as nonprescription medications or substances. Some of these products, such as antihistamines, can contribute to her symptoms. Ms. C should be counseled that menopausal symptoms do not always need to be treated with drugs. Commercial products such as Replens® (LDS Consumer Products, Cedar Rapids, IA) can be very effective in decreasing vaginal dryness. The estradiol vaginal ring has been approved for this symptom as well (Zibecchi et al., 2003).

J. Sweeney-Calciano: Because the information about the use of HRT is changing so rapidly, the most current literature should be reviewed before prescribing any interventions.

References

Grady, D. (2003). Postmenopausal hormones—Therapy for symptoms only. *New England Journal of Medicine, 348,* 1835–1837.

Hays, J., Ockene, J., Brunner, R., Kotchen, J., Manson, J., Patterson, R., et al. (2003). Effects of estrogen plus progestin on health-related quality of life. *New England Journal of Medicine, 348,* 1839–1854.

Lacey, J., Mink, P., Lubin, J., Sherman, M., Troisi,

Table 1. Alternatives to Systemic Hormone Replacement Therapy to Help Prevent Postmenopausal Conditions and Relieve Menopausal Symptoms

Symptom	Interventions
Hot flashes	• Lifestyle changes: Dress and eat to avoid being too warm, sleep in a cool room, and reduce stress. Avoid spicy foods and caffeine. Try deep-breathing and stress-reduction techniques, including meditation and other relaxation methods. • Soy: This contains phytoestrogens, estrogen-like substances derived from a plant source. *Note.* No solid evidence has proven that soy and other sources of phytoestrogens relieve hot flashes. Further, the risks of taking soy, especially in its more concentrated forms (e.g., pills, powders), are not known. Phytoestrogens from soy can be consumed through foods or supplements. Soy food products include tofu, tempeh, soy milk, and soy nuts. These products are more likely to relieve mild hot flashes. • Phytoestrogens: Herbs such as black cohosh, wild yam, dong quai, and valerian root may be taken. • Antidepressants such as venlafaxine, paroxetine, and fluoxetine have been moderately effective in clinical trials.
Vaginal dryness	• Use over-the-counter vaginal lubricants and moisturizers. • Products that release estrogen locally, such as vaginal creams, vaginal suppositories, and a plastic ring (Estring™, Pharmacia, Inc., Kalamazoo, MI), are used for severe dryness. The ring contains a low dose of estrogen and may not protect against osteoporosis. It also must be changed every three months.
Mood swings	• Alter lifestyle behaviors (e.g., get adequate sleep, be physically active). • Practice relaxation exercises. • Take antidepressant or antianxiety drugs.
Insomnia	• Use over-the-counter sleep aids. • Consume milk products, such as 8 oz. of low-fat or fat-free milk or yogurt. • Exercise in the morning or early afternoon. Exercising later in the day may increase wakefulness. • Take a hot shower or bath immediately before going to bed.
Memory problems	• Practice mental exercises. • Alter lifestyle behaviors (e.g., get adequate sleep, be physically active).

Note. Based on information from the National Institutes of Health, 2002.

R., Hartge, P., et al. (2002). Menopausal hormone replacement therapy and risk of ovarian cancer in a prospective study. *JAMA, 288,* 334–341.

Monson, J., & Martin, K. (2001). Postmenopausal hormone replacement therapy. *New England Journal of Medicine, 345,* 34–40.

National Institutes of Health. (2002). *Postmenopausal hormone therapy.* Retrieved July 11, 2003, from http://www.nhlbi.nih.gov/health/women/index.htm

O'Meara, E., Rossing, M., Daling, J., & Elmore, J. (2001). Hormone replacement therapy after a diagnosis of breast cancer in relation to recurrence and mortality. *Journal of the National Cancer Institute, 93,* 754–762.

Rodriguez, C., Patel, A., Callee, E., Jacob, E., & Thun, M. (2001). Estrogen replacement therapy and ovarian cancer mortality in a large prospective study of U.S. women. *JAMA, 285,* 1460–1465.

Ross, R., Paganini-Hill, A., & Wan, P. (2000). Effective hormone replacement therapy on breast cancer risk: Estrogen versus estrogen plus progestin. *Journal of the National Cancer Institute, 92,* 328–332.

Schairer, C., Lubin, J., Troisi, R., Sturgeon, S., Brinton, L., & Hoover, R. (2000). Menopausal estrogen and estrogen-progestin replacement therapy and breast cancer risk. *JAMA, 283,* 485–491.

Solomon, C., & Dluhy, R. (2003). Rethinking postmenopausal hormone therapy. *New England Journal of Medicine, 348,* 579–580.

U.S. Department of Health and Human Services. (2001). *Menopause: One woman's story, every woman's story* [NIH Publication No. 01-3886]. Retrieved July 16, 2003, from http://www.nia.nih.gov/health/pubs/menopause/menopause.pdf

Writing Group for the Women's Health Initiative Investigators. (2002). Risks and benefits of estrogen plus progestin in healthy postmenopausal women: Principal results from the Women's Health Initiative randomized controlled trial. *JAMA, 288,* 321–333.

Zibecchi, L., Greendale, G., & Ganz, P. (2003). Comprehensive menopausal assessment: An approach to managing vasomotor and urogenital symptoms in breast cancer survivors. *Oncology Nursing Forum, 30,* 393–405.

Additional Resources

Brandenburg, S. (2002). Hormone replacement therapy: Questions and controversies. *Primary Care Case Reviews, 5*(1), 2–7.

Chen, C., Weiss, N., Newcomb, P., Barlow, W., & White, E. (2002). Hormone replacement therapy in relation to breast cancer. *JAMA, 287,* 734–741.

Goldsmith, J. (2002). Cutting through the HRT confusion. *American Journal of Nursing, 102*(9), 20.

Grodstein, F., Clarkson, T., & Manson, J. (2003). Understanding the divergent data on postmenopausal hormone therapy. *New England Journal of Medicine, 348,* 645–650.

Laine, C. (2002). Postmenopausal hormone replacement therapy: How could we have been so wrong? *Annals of Internal Medicine, 137,* 290.

Rapp, S.R., Espeland, M.A., Schumaker, S.A., Henderson, V.W., Brunner, R.L., Manson, J.E., et al. (2003). Effect of estrogen plus progestin on global cognitive function in postmenopausal women: The Women's Health Initiative Memory Study: A randomized clinical trial. *JAMA, 289,* 2663–2672.