

In the aftermath of the WHI, consider estrogen patient by patient

➡ The Women's Health Initiative wrought a sea change in attitudes toward menopausal estrogen therapy. According to Isaac Schiff, MD, estrogen is still the best option in some patients. Here's what he says about individualizing therapy.

Janelle Yates

Senior Editor, OBG MANAGEMENT

CASE Vasomotor symptoms and a request for relief

A 54-year-old woman with a family history of osteoporosis visits your office complaining of mild vasomotor symptoms. She reports that it has been 3 years since her last menstrual period. She also points out that she has type 2 diabetes.

Is she a good candidate for estrogen therapy?

How would you manage her vasomotor symptoms?

In the 8 years since initial publication of the Women's Health Initiative (WHI), ideas about when to use estrogen—and whom to treat—have evolved considerably. Today, we know that hormone therapy remains an appropriate and effective option in properly selected cases, said Isaac Schiff, MD, one of two experts selected to deliver the Morton and Diane Stenchever Lecture at the ACOG Annual Clinical Meeting last month in San Francisco. Along with JoAnn E. Manson, MD, DrPH, Dr. Schiff spoke on “Hormone therapy in the post-WHI era.”

Dr. Schiff is chief of the Vincent Obstetrics and Gynecology Service at Massachusetts General Hospital in Boston and the Joe Vincent Meigs Professor of Gynecology at Harvard Medical School.

Symptoms are the main requisite for estrogen

Estrogen remains the most effective therapy for vasomotor flushes and vaginal atrophy, Dr. Schiff said.

The most important requirement for its use?

The patient must have bothersome symptoms.

Menopausal status is also key—estrogen is appropriate only in recently menopausal women. In a woman who has never used estrogen and who is more than 10 years past the menopausal transition, vasomotor flushes are not very common. If vaginal atrophy is a problem, however, local estrogen therapy may be an option.

Estrogen is not recommended for prevention of cardiovascular events or osteoporosis, but it is appropriate for the patient who is bothered by moderate or severe vasomotor flushes or urogenital symptoms—provided it is prescribed at the lowest effective dosage and for a short duration.

Indication #1: Alleviating the vasomotor flush

Among the nonhormonal options many women use for relief of vasomotor flushes are complementary and alternative preparations

IN THIS ARTICLE

Estrogen is not first-line therapy for osteoporosis
page 2a

such as black cohosh, dong quai, red clover, and ginseng, but research into these therapies has revealed that they yield mixed results, with herbal remedies usually having an effect similar to that of placebo, Dr. Schiff said.

“But if it works, so be it,” he added.

Selective serotonin reuptake inhibitors (SSRIs) and other antidepressants have been somewhat effective, he noted. In particular, paroxetine (Paxil) and venlafaxine (Effexor) have outperformed placebo—though paroxetine should be avoided in women who are taking tamoxifen because it diminishes the efficacy of tamoxifen.^{1,2} Paroxetine and venlafaxine are not FDA-approved for hot flashes, he noted.

The gold standard for relief of vasomotor flushes is estrogen, said Dr. Schiff. Although the efficacy of estrogen in regard to vasomotor flushes appears to increase with the dosage, progestin has an additive effect. Therefore, when both estrogen and a progestin are prescribed, the estrogen dosage can be kept at a lower range, Dr. Schiff said.

Among the options are transdermal estrogen gel, cream, and a patch; and oral estrogen. Because observational studies have shown that venous thromboembolic events are four times more likely when oral estrogen is used, compared with transdermal formulations, the latter could be considered, said Dr. Schiff.³

There is no evidence that compounded bioidentical formulations of estrogen are any safer than their manufactured counterparts, he noted.

Indication #2: Urogenital atrophy

Research has demonstrated that local estrogen therapy thickens the vaginal wall and stimulates glycogen formation, thereby increasing lactic acid and lowering the pH level, which may reduce vaginal infections.⁴

Because vaginal atrophy can significantly impair a woman's quality of life, estrogen therapy may be warranted, said Dr. Schiff. The good news is that local estrogen appears to be amply effective and lacks many of the risks inherent in oral administration.

More good news: Regular sexual activity has a positive effect on vaginal lubrication and elasticity and promotes natural maintenance of urogenital health. For that reason, any woman being treated with estrogen for urogenital issues should have the dosage reassessed once therapy has allowed her to resume or increase sexual activity, Dr. Schiff noted.

If a patient wants to avoid hormonal therapy for urogenital atrophy, a number of other options are available, such as the polycarbophil-based vaginal moisturizer Replens, which has been shown to increase vaginal moisture and fluid volume and lower the vaginal pH level. It is not quite as effective as estrogen, Dr. Schiff noted, but does provide some relief.^{5,6}

Estrogen is not first-line therapy for osteoporosis

One of the principal findings of the WHI is that estrogen reduces the risk of fracture. Dr. Schiff noted, however, that estrogen should not be prescribed for that indication, as a host of other medications are available that lack the risks of estrogen therapy. Those medications include alendronate and the other bisphosphonates; raloxifene; and zoledronic acid.

What's the bottom line?

There is no single “right” answer to the question of when estrogen therapy is appropriate. Each case should be individualized, Dr. Schiff said. If a patient is healthy, recently menopausal, and bothered by moderate or severe vasomotor flushes or urogenital symptoms, then estrogen is one option that should be presented, along with its benefits and risks. Ultimately, it is the patient, in partnership with her physician, who must decide for or against estrogen therapy.

CASE RESOLVED

This patient may not require estrogen, although it is certainly an option. Although she is young,



Any woman being treated with estrogen for urogenital issues should have the dosage reassessed once therapy has allowed her to resume or increase sexual activity

symptomatic, and recently menopausal, her vasomotor symptoms are mild. Because her symptoms are not severe, time alone may be sufficient “treatment,” or she may want to try a simple lifestyle adjustment such as the wearing of layers of clothing that can be removed when a vasomotor flush occurs.

If vaginal atrophy is a problem, local estrogen or a topical vaginal agent such as Replens may provide relief. 🚫

References

1. Soares CN, Joffe H, Viguera AC, et al. Paroxetine versus placebo for women in midlife after hormone therapy discontinuation. *Am J Med.* 2008;121(2):159–162.e1.
2. Cheema D, Coomarasamy A, El-Toukhy T. Nonhormonal therapy of postmenopausal vasomotor symptoms: a structured evidence-based review. *Arch Gynecol Obstet.* 2007;276(5):463–469.
3. Canonico M, Plu-Bureau G, Lowe GDO, Scarabin PY. Hormone replacement therapy and risk of venous thromboembolism in postmenopausal women: systematic review and meta-analysis. *BMJ.* 2008;336(7655):1227–1231.
4. Archer DF. Efficacy and tolerability of local estrogen therapy for urogenital atrophy. *Menopause.* 2010;17(1):194–203.
5. Bygdeman M, Swahn ML. Replens versus dienoestrol cream in the symptomatic treatment of vaginal atrophy in postmenopausal women. *Maturitas.* 1996;23(3):259–263.
6. Nachtigall LE. Comparative study: Replens versus local estrogen in menopausal women. *Fertil Steril.* 1994;61(1):178–180.