

Ettinger B, Ensrud KE, Wallace R, et al. Effects of ultralow-dose transdermal estradiol on bone mineral density: a randomized clinical trial. *Obstet Gynecol.* 2004;104:443-451.

Q Does ultralow-dose, transdermal estradiol prevent bone loss?

A Yes, but benefits and risks should be weighed for each patient in comparison to other osteoporosis preventives, and the effect on vasomotor symptoms is unknown.

EXPERT COMMENTARY

In this excellent prospective, randomized trial, Ettinger et al seem to have defined the lowest effective dose of transdermal estradiol to preserve bone mineral density in women 60 to 80 years of age. During 2 years of treatment, a daily dose of .014 mg estradiol was more effective than placebo in increasing bone density of both spine and hip. It also caused a significant decrease in markers of bone turnover. And though the estradiol was unopposed, risks of vaginal bleeding and endometrial hyperplasia did not rise.

Too brief to show effect on fractures

The 2 years of study were, understandably, not enough to show a reduction in fractures. Nor does the study show whether this therapy relieves menopausal symptoms, the only other approved indications for estrogen or estrogen-progestin therapy in menopausal women. This, too, is understandable, since the study focused on women well past menopause.

Estrogen's risks: Still much to learn

More important is the fact that the potential risks of estrogen and estrogen-progestin

therapy have not been fully clarified. Although the risk of endometrial hyperplasia

did not increase in 2 years of study, might it rise after 3 or 4 more years? And will the risks of breast cancer, thromboembolic events, or stroke increase with ultralow-dose, transdermal estradiol, as they did with conventional doses of oral conjugated equine estrogen in 1 or both arms of the Women's Health Initiative?



Prescribe for osteoporosis prevention, not menopausal symptoms

Over 2 years, .014 mg daily of transdermal estradiol prevents bone loss without increasing endometrial hyperplasia, but the lack of data on menopausal symptoms limits the drug's applicability.

Ultralow-dose estrogen patches should be prescribed only for prevention of osteoporosis after consideration of other options, such as calcium, vitamin D, raloxifene, and bisphosphonates. Physicians should keep in mind the Food and Drug Administration's directive to prescribe estrogen at the lowest effective dose for the shortest time possible. ■

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FAST TRACK

This study defines the lowest effective dose of transdermal estradiol to preserve BMD in women ages 60 to 80