Estradiol versus venlafaxine for vasomotor symptoms

Estradiol is more effective, but venlafaxine’s effect is robust


Summary. This trial of 339 perimenopausal and postmenopausal women examined the efficacy and tolerability of low-dose oral 17β-estradiol and low-dose, extended-release venlafaxine in relieving vasomotor symptoms (VMS). The women, recruited from the community to Menopause Strategies: Finding Lasting Answers for Symptoms and Health clinical network sites, had at least two bothersome VMS per day. They were randomized to double-blind treatment with low-dose oral 17β-estradiol (0.5 mg/d; n = 97), low-dose extended-release venlafaxine hydrochloride (75 mg/d; n = 96), or placebo (n = 146) for 8 weeks. The primary outcome was mean daily frequency of VMS. Secondary outcomes were VMS severity, bother, and interference with daily life.

Compared with baseline, after 8 weeks, VMS frequency decreased to 3.9 (95% confidence interval [CI], 2.9-4.9) VMS per day (52.9% reduction) in the estradiol group, to 4.4 (95% CI, 3.5-5.3) VMS per day (47.6% reduction) in the venlafaxine group, and to 5.5 (95% CI, 4.7-6.3) VMS per day (28.6% reduction) in the placebo group, with consistent results for secondary outcomes. Treatment satisfaction was highest for estradiol (70.3%; P < .001 vs placebo), lowest for placebo (38.4%), and intermediate for venlafaxine (51.1%; P = .06 vs placebo).

Commentary. This carefully done study shows the significant effect of venlafaxine on VMS, comparable to low-dose estradiol. Although the most significant reduction of VMS occurs with 0.5 mg per day of estradiol, the effect with venlafaxine is robust versus placebo and reassuring for practitioners who often need to give nonhormonal treatment. The inclusion criteria were not as rigid as most VMS studies, in which severe to moderate symptoms are generally defined as seven to nine VMS per day or 50 VMS per week. This study included women with as few as two VMS per day. However, the mean was 8.1 VMS per day, indicating that most of these women qualified as having moderate to severe symptoms. The study was short, but most studies of antidepressants have shown a persistent effect. Extensive studies of desvenlafaxine have shown a rapid and persistent effect in patients who are more symptomatic (12 VMS per day) than those in this study by Joffe and colleagues, with an even greater reduction in VMS.1,2
Increases in blood pressure were seen with venlafaxine. The profile of women developing high blood pressure suggests that those at risk were disproportionally overweight or obese and had higher baseline systolic and diastolic blood pressure.

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References

Screening mammograms: false-positives and their consequences

Short-term anxiety is higher in women with false-positive screening results, who are then more likely to intend to seek future screening


Summary. Using answers from randomly selected Digital Mammographic Imaging Screening Trial (DMIST) quality-of-life sub-study telephone survey participants with positive and negative mammograms, researchers measured the effect of false-positive mammograms on quality of life using personal anxiety, health utility, and attitudes toward future screening as markers. Enrollment and follow-up interviews were obtained for 1,028 women. Women answered the 6-question short form of the Spielberger State-Trait Anxiety Inventory state scale (STAI-6) and the EuroQol EQ-5D instrument with US scoring. Researchers recorded women’s self-report of future intention to undergo mammographic screening and willingness to travel and stay overnight to undergo a hypothetical type of mammography that would identify just as many cancers with half the false-positive results. Anxiety was significantly higher (STAI-6, 35.2 vs 32.7) in women with false-positive mammogram results, and these women were more likely to intend to seek future breast cancer screening (25.7% in false-positive group vs 14.2% in negative group). Health utility scores did not differ, and there were no significant differences between groups after 1 year. Willingness to travel and stay overnight did not change (9.9% vs 10.5% in false-positive vs negative groups). Future screening intention was higher in younger women and women in poorer health. False-positive results were associated with increased short-term anxiety but not long-term anxiety.

Comment. Much controversy surrounded the 2009 release of the US Preventive Services Task Force recommendation for breast cancer screening intervals—Americans began to seriously grapple with the sometimes painful economic realities of our healthcare system. Since then, many studies have been aimed at better understanding the risks and the benefits of existing screening guidelines. The DMIST design was meant to evaluate aspects of this debate, including the personal anxiety involved in false-positive screening mammograms.

Annual mammograms are associated with a higher rate of false positives than biennial screening, but the latter results in a small but real increased risk of late-stage cancer diagnosis. Is reducing that increased risk of late-stage cancer diagnosis worth the personal anxiety associated with the false-positive mammograms? This study begins to shed some reassuring light on the topic in finding that the anxiety produced is temporary. Other studies have further shown that the anxiety seems to be specific to the diagnosis of breast cancer and is not generalized anxiety.
In this case, our role as providers seems to have three parts: First, we need to decrease the negative aspects of this anxiety. Studies have suggested that short follow-up intervals help, as does a same-day reading of the report by a radiologist. Second, we need to maximize the positive aspects of the anxiety. Most studies suggest that patients with false-positive mammograms are more likely to return for their next screening appointment than those with negative mammograms. These patients also seem to be more aware of changes in their breasts. Finally, we need to anticipate their anxiety and better educate our patients about the risks and benefits of mammograms in order to minimize the effect of that dreaded phone call.

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References

Delivering depression care in obstetrics and gynecology clinics

Collaborative care integrating mental health specialists reduced depressive symptoms more than usual in obstetrics and gynecology care


Summary. In primary care settings, collaborative care for depression is effective; however, whether this model would also work in obstetrics and gynecology clinics, which are the sole source of healthcare for many women, is not known. Investigators randomized 205 women (mean age, 39 y; 44% nonwhite; 40% with private insurance) seen at two urban obstetrics and gynecology clinics who screened positive for depression to receive usual care (including written material about depression) with or without collaborative care provided in the clinic (evidence-based psychotherapy, active management of follow-up, and antidepressant medication as needed). Participants were followed for 18 months.

Compared with women in the usual-care group, those in the collaborative-care group had greater reductions in depressive symptoms and were more likely to attend mental health visits, receive adequate antidepressants, and to report greater satisfaction with care.

Comment. These results suggest that the mental health collaborative-care model can be extended from primary care settings to obstetrics and gynecology clinics. Though the approach might not be feasible for smaller offices, many larger clinics that serve women at high risk for
depression could benefit. Furthermore, the cost of this strategy balances favorably against the cost of untreated depression and its long-term impacts on women and their families.

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**Menopause Editor’s picks from June 2014**

NAMS spotlights selections from the most recent issue of the Society’s official journal, *Menopause*, chosen by its editor in chief, Isaac Schiff, MD.

**Phase 3 randomized controlled study of gastroretentive gabapentin for the treatment of moderate-to-severe hot flashes in menopause.**
JoAnn V. Pinkerton, MD, Risa Kagan, MD, David Portman, MD, Rekha Sathyanarayana, BS, and Michael Sweeney, MD, for the Breeze 3 Investigators.

♦ **Cognitive-behavior therapy for menopausal symptoms (hot flushes and night sweats): moderators and mediators of treatment effects.**
Sam Norton, PhD, Joseph Chilcot, PhD, and Myra S. Hunter, PhD.

♦ **A standardized exercise intervention differentially affects premenopausal and postmenopausal African-American women.**
Jan Kretzschmar, BS, Dianne M. Babbitt, MS, Keith M. Diaz, PhD, Deborah L. Fearheller, PhD, Kathleen M. Sturgeon, PhD, Amanda M. Perkins, PhD, Praveen Veerabhadrapa, PhD, Sheara T. Williamson, PhD, Chenyi Ling, BS, Hojun Lee, MS, Heather Grimm, MS, Sunny R. Thakkar, MS, Deborah L. Crabbe, MD, Mohammed A. Kashem, MD, and Michael D. Brown, PhD.
The level of evidence indicated for each study is based on a grading system that evaluates the scientific rigor of the study design, as developed by the US Preventive Services Task Force. A synopsis of the levels is presented below.

- **Level I**: Properly randomized, controlled trial.
- **Level II-1**: Well-designed controlled trial but without randomization.
- **Level II-2**: Well-designed cohort or case-control analytic study.
- **Level II-3**: Multiple time series with or without the intervention (eg, cross-sectional and uncontrolled investigational studies).
- **Level III**: Meta-analyses; reports from expert committees; descriptive studies and case reports.

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