Q/ Do venlafaxine and gabapentin control hot flashes in women with a history of breast cancer?

**EVIDENCE-BASED ANSWER**

**YES.** Venlafaxine reduces hot flashes more than placebo in women with a history of breast cancer; adverse effects include dry mouth and constipation (strength of recommendation [SOR]: B, randomized clinical trials [RCTs] with heterogeneous outcomes).

Gabapentin also reduces hot flashes more than placebo (SOR: B, a single RCT); adverse effects include dizziness and somnolence (SOR: C, standard reference). After having tried both medications, women tend to prefer venlafaxine (SOR: C, open-label crossover trial).

Treating hot flashes is an off-label use for both drugs.

**Evidence summary**

A double-blind RCT of 191 women who had been treated for breast cancer (two-thirds were taking tamoxifen) and were having at least 14 hot flashes per week randomized the women to one of 4 groups: once-daily extended-release venlafaxine at 37.5, 75, or 150 mg, or placebo. Higher doses of venlafaxine produced greater reductions in hot flash scores from baseline than did the lowest dose or placebo: 150 mg lowered scores by 61% (95% confidence interval [CI], 48%-75%); 75 mg also decreased scores by 61% (95% CI, 50%-68%); 37.5 mg reduced scores by 37% (95% CI, 26%-54%); and placebo lowered scores by 27% (95% CI, 11%-34%).

At the 75- and 150-mg doses, the number needed to treat to reduce the number of hot flashes by 50% was about 3. However, these doses caused dose-dependent adverse effects, including dry mouth, constipation, nausea, and decreased appetite, whereas the lowest dose produced an adverse-effect rate equal to placebo (no statistics supplied for these comparisons).

**Venlafaxine significantly decreased the frequency of hot flashes**

A pair of double-blind RCTs, reported together, evaluated hot flash frequency among 77 breast cancer survivors with at least 7 hot flashes a week who took either extended-release venlafaxine (37.5 or 75 mg daily) or placebo for 6 weeks. Patients then crossed over to take either venlafaxine or placebo for another 6 weeks. Compared with placebo, venlafaxine 37.5 mg reduced the mean daily hot flash frequency by 22% (P<.001); venlafaxine 75 mg reduced it by 14% (P<.013).

In an open-label case series, 40 breast cancer patients with at least 20 hot flashes per week received extended-release venlafaxine 37.5 mg once daily for 8 weeks. Patients reported a 53% reduction in hot flash frequency compared with baseline (P<.001).

**Gabapentin reduces hot flashes at 300 mg tid**

A double-blind RCT of 420 women with breast cancer who had at least 14 hot flashes a week compared the effectiveness of gabapentin at 300 mg tid (3 times a day) to placebo. Gabapentin significantly decreased the frequency of hot flashes (28.3% vs 12.9% reduction; P<.001). Adverse effects included dizziness and somnolence (SOR: C, standard reference) and constipation (SOR: C, randomized clinical trials [RCTs] with heterogeneous outcomes).

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Gabapentin 100 mg tid, 300 mg tid, or placebo for 8 weeks. Investigators found no significant difference between the 100 mg tid dosing and placebo. However, gabapentin at 300 mg tid reduced hot flashes by 44% (an average of 2 fewer per day) compared with placebo (P < .007).

The study didn’t assess adverse effects, but noted that the withdrawal rates were similar between the groups receiving gabapentin and placebo (12%-17%). An authoritative online reference lists the 2 most common adverse effects of gabapentin as dizziness (11%-28%) and somnolence (5.5%-25%).

**Women prefer venlafaxine to gabapentin**

A multicenter, open-label crossover trial involving 66 women with a history of breast cancer who had at least 14 hot flashes per week evaluated patient preference when treated with extended-release venlafaxine 75 mg daily and gabapentin 300 mg tid, each for 1 month. More patients preferred taking venlafaxine than gabapentin (68% vs 32%; P < .01), although both treatments reduced the numbers of hot flashes.

**Recommendations**

In a patient education statement, the American Cancer Society states that women with premature menopause caused by cancer treatment may do well with exercise and relaxation techniques alone. The statement mentions venlafaxine, fluoxetine, and paroxetine as adjunct therapy.

**References**


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**Managing Hypoglycemia in Primary Care**

This supplement on hypoglycemia will help you to:

- Educate patients about their risk of hypoglycemia
- Identify risk factors and behaviors that increase the risk of hypoglycemia in patients
- Compare glucose-lowering agents and the risk of hypoglycemia associated with them

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