Can nonhormonal treatments relieve hot flushes in breast Ca survivors?

YES A Cochrane Review found clonidine, selective serotonin reuptake inhibitors (SSRIs), selective norepinephrine reuptake inhibitors (SNRIs), gabapentin, and relaxation therapy mildly or moderately effective at reducing hot flushes in this population.

Rada G, Capurro D, Pantoja T, et al. Non-hormonal interventions for hot flushes in women with a history of breast cancer. Cochrane Database Syst Rev. 2010;(9):CD004923. doi: 10.1002/14651858.CD004923.pub2.

EXPERT COMMENTARY
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FAST TRACK

Clonidine, SSRIs, SNRIs, gabapentin, and relaxation therapy reduced the frequency and intensity of hot flushes mildly to moderately

A frequent challenge facing clinicians who manage breast cancer survivors is identifying treatment options to attenuate hot flushes and night sweats without resorting to estrogen, which is contraindicated because it can induce cancer growth.

Variables associated with a high prevalence of hot flushes in this population:

- age at diagnosis (>50 years)
- abrupt discontinuation of estrogen therapy at diagnosis
- induction of premature menopause by therapy (i.e., chemotherapy and surgical or medical ovarian ablation)
- induction of estrogen deficiency symptoms by chemotherapy (e.g., tamoxifen or an aromatase inhibitor).

There are no FDA-approved nonhormonal pharmaceutical options to alleviate bothersome hot flushes that accompany breast cancer treatment and the menopausal transition, whether spontaneous or induced. Moreover, meaningful guidance from

WHAT THIS EVIDENCE MEANS FOR PRACTICE

There are no FDA-approved nonhormonal therapies for hot-flush reduction in breast cancer survivors.

Potentially effective drug therapies include clonidine, SSRIs, SNRIs, and gabapentin. Benefits need to be weighed carefully against side effects, because the reduction in absolute hot flushes is only mild to moderate.

Nonpharmaceutical therapies that are *not* beneficial include homeopathy, magnet therapy, and acupuncture. However, more recent RCT data suggest that, in breast cancer patients, traditional acupuncture (and, in some studies, sham acupuncture) may, in fact, significantly reduce frequency of hot flushes, with a prolonged reduction at 3 to 6 months.[3,4] Relaxation therapy has a modest benefit.

When a patient reports bothersome hot flushes, I recommend that she avoid overheating, use cooling techniques, and try relaxation therapy or acupuncture.

For medical therapy, I usually recommend venlafaxine or gabapentin, both of which have an effect on hot flushes within 2 weeks and both of which are associated with side effects. I start with 37.5 mg of venlafaxine, increasing to 75 mg after 2 weeks, if needed. If using gabapentin, I start with 300 mg, increasing to 600 mg at night and adding 300 mg in the morning or afternoon, if needed, aiming for 900 to 1,800 mg per day.

For vaginal dryness, I recommend vaginal moisturizers (used twice weekly) and lubricants (as needed) for sexual activity. The use of vaginal dilators or topical estrogen therapy is individualized.

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published trials is limited by the small number of enrolled subjects and short duration of study (i.e., ≤12 weeks).

How hot flushes happen

According to Freedman, body temperature is regulated over a range called the thermoneutral zone.[1,2] Reduced or fluctuating ovarian hormones are believed to narrow the thermoregulatory zone such that variations in core body temperature trigger heat loss mechanisms. A narrowed thermoregulatory zone has been associated with increased norepinephrine.

Clonidine, an α-2 adrenergic agonist, decreases norepinephrine and has been found to reduce hot flushes. Other nonhormonal agents that have been found to be at least partially effective in reducing hot flushes include SSRI and SNRI antidepressants, which enhance central serotonin and norepinephrine activity. Gabapentin has also proved to be effective.

Potential adverse events or negative side effects, such as insomnia, weight gain, drowsiness, and sedation, need to be taken into account when evaluating the benefits of pharmaceutical options.

References

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2. Freedman RR. Core body temperature variation in symptomatic and asymptomatic postmenopausal women: brief report. Menopause. 2002;9(6):399–401.
3. Hervik J, Mialand O. Acupuncture for the treatment of hot flashes in breast cancer patients: a randomized, controlled trial. Breast Cancer Res Treat. 2009;116(2):311–316.
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