

FAST FACTS AND CONCEPTS #262
HOT FLASHES IN PALLIATIVE CARE – PART 2

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Background Hot flashes ('flushes') are a common and disabling symptom, particularly when caused by cancer treatment. Assessment of hot flashes was reviewed in *Fast Fact #261*. This *Fast Fact* will cover procedural and pharmacological treatment of hot flashes. Complementary and alternative therapies are reviewed in *Fast Fact #263*.

Pharmacologic Treatments The most well studied populations with cancer treatment-related hot flashes are patients with breast and prostate cancer. Efficacy of pharmacologic treatments seems to be independent of whether the hot flashes are caused by treatment and independent of the patient's sex. The average improvement in hot flashes associated with placebo is around 25% (1), so improvements associated with pharmacologic therapies are typically compared to placebo.

- **Hormonal Therapies:** In general, hormonal therapies are more effective than non-hormonal therapies. Estrogen and progestins are effective in both men and women. Estrogen and progestins are contraindicated in women with a history of breast cancer because of concern for increased risk of recurrence. In men, estrogen therapy is associated with breast tenderness and gynecomastia. Common side effects of progestins include weight gain, nausea and edema. Both estrogen and progestins are associated with some risk of thromboembolic disease and cardiovascular disease. Cyproterone, an antiandrogen (not available in the US), also works in men, but may interfere with androgen deprivation therapy for prostate cancer.
- **Antidepressants:** The mechanism of by which selective serotonin reuptake inhibitors (SSRIs) or serotonin-norepinephrine reuptake inhibitors (SNRIs) reduce hot flashes is thought to be related to the role of serotonin and norepinephrine in thermoregulation. Randomized controlled trials have supported the efficacy of fluoxetine, paroxetine, sertraline, citalopram, escitalopram, venlafaxine and desvenlafaxine. Pooled analysis of 7 trials showed a positive effect greater than placebo as follows: paroxetine (10-25mg) 41%, venlafaxine (75mg) 33%, fluoxetine (20mg) 13%, sertraline (50mg) 3-18% (2). Citalopram (20mg) works about as well as venlafaxine and paroxetine (3).
- Many SSRIs can interfere with the effectiveness of tamoxifen as they inhibit cytochrome P450 enzyme CYP2D6, which is involved in tamoxifen metabolism. Paroxetine and fluoxetine are the strongest CYP2D6 inhibitors, followed, in order of decreasing potency of inhibition, by sertraline, citalopram, and venlafaxine. All SSRIs have similar side effect profiles, including sexual dysfunction, drowsiness, weight gain, insomnia, anxiety, dizziness and headache.
- **Gabapentin:** A pooled analysis of 3 trials showed reduction in hot flashes of 35-38% over placebo at doses of 900-2400 mg/day (2). The mechanism by which gabapentin reduces hot flashes is not clear. Adding an SSRI to gabapentin has not been shown to be additionally effective.
- **Clonidine:** Appears to be marginally, but statistically significantly, better than placebo, with side effects including dry mouth, drowsiness, and constipation (4).

Procedural Pilot data suggest that a stellate-ganglion block may be effective. A small study of 13 patients with a history of breast cancer treated with a stellate-ganglion block (once or twice) showed a decrease in the total number of hot flashes per week, as well as number of very severe hot flashes per week over a three-month period (5). Though standard procedural risks apply, there were no reported adverse effects from the block in this small series.

Summary It is reasonable to use either gabapentin or an SSRI/SNRI as first line treatment. Of the SSRI/SNRI group, venlafaxine and citalopram are among the most effective and have a low risk of interfering with tamoxifen. Paroxetine and fluoxetine should be avoided in patients on tamoxifen.

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