

# Palliation of vasomotor instability (“hot flashes”) using pregabalin

**V**asomotor instability (“hot flashes”) is a common problem in postmenopausal women, breast cancer patients, and prostate cancer patients. Hot flashes have been controlled by various non-estrogenic measures, including environmental control (eg, fan cooling); vitamin E; a proprietary combination of ergotamine, belladonna alkaloids, and phenobarbital (formerly marketed as Bellergal-S); venlafaxine (Effexor) and other antidepressants; progestins; and gabapentin. In particular, treatment with gabapentin has led to a 31%–66% reduction in hot flash scores in breast cancer patients with hormone-related vasomotor instability.<sup>1–3</sup>

Recently, pregabalin (Lyrica), a gamma-aminobutyric acid (GABA) analog related to gabapentin, has been approved for the management of postherpetic neuralgia, partial-onset seizures, and neuropathic pain associated with diabetic peripheral neuropathy. Because of the chemical similarity of pregabalin to gabapentin, and because of the widespread use of gabapentin in patients with cancer and various pain or neuropathic syndromes, we evaluated the efficacy of pregabalin in breast or prostate cancer patients experiencing treatment-related hot flashes.

## Methods

Patients were eligible for this open-label, non-placebo-controlled trial if they had breast or prostate cancer, were receiving some type of hormonal therapy, and had been experiencing hot flashes after initiating hormonal therapy. Patients were considered for pregabalin therapy if they had some type of pain for

which pregabalin might be therapeutic, had hot flashes that were refractory to environmental changes, and desired therapy for their vasomotor symptoms. Voluntary informed consent was given for receiving pregabalin.

Patients were initially prescribed pregabalin 50 mg orally once daily. If there was no response and no toxicity, doses were escalated to 50 mg orally twice daily and, if still needed and tolerated, 50 mg orally 3 times daily. By comparison, the recommended starting dose for pregabalin’s approved indications is 150 mg/d.<sup>4</sup>

Patients underwent semi-structured interviews to determine the frequency and severity of their vasomotor symptoms before treatment with pregabalin and after 4 weeks of treatment with the drug. The number of hot flashes per day and their severity were estimated by the patients. A hot flash score was determined by multiplying the severity of the patient’s symptoms (mild = 1, moderate = 2, severe = 3) by the number of hot flashes per day. The presence and severity of other symptoms were also recorded by patients. Side effects of pregabalin were reviewed with the patients every 4 weeks.

## Results

Twelve patients were given prescriptions for pregabalin; however, only eight patients actually took the medication. The remaining patients elected not to receive pregabalin due to fear of its potential side effects, which were explained during the informed consent process. Of the eight patients who actually took at least one dose of pregabalin, six were women with breast cancer and two were men with prostate cancer. Their ages ranged from 53 to 81 years,

with a median of 63 years. Hormonal therapy associated with hot flashes was anastrozole (Arimidex) in five patients with breast cancer, tamoxifen in one breast cancer patient, and leuprolide in the two prostate cancer patients.

Six of the eight patients (75%) obtained some relief from their vasomotor symptoms after treatment with pregabalin. The benefit was rated as slight by one patient, good by one patient, and excellent by four patients. The doses associated with good or excellent effectiveness were 50 mg/d in two patients, 100 mg/d in two patients, and 150 mg/d in one patient.

The number of hot flashes before treatment with pregabalin ranged from 2 to 21, with a mean of 9.6 and a median of 9 (Table 1). After treatment with pregabalin, the mean number of hot flashes had declined by 53% and the median number of hot flashes, by 78%.

The median pretreatment hot flash score was 24 (Table 1). Post treatment, the mean hot flash score fell by 65% and the median hot flash score, by 90%. Six of eight patients obtained a 50% or greater reduction in their hot flash score.

Other hormonal treatment-related symptoms also improved with pregabalin therapy. Five of seven patients (71%) with sweats reported improvement, four of six patients (67%) with insomnia experienced improvement, two of three patients (67%) with anxiety reported feeling less anxious, and one of three patients (33%) with depression stated feeling less depressed after treatment with pregabalin. Benefit was reported as early as 1 week after starting pregabalin and persisted for up to 6 months.

Adverse events due to pregabalin were also reported. Four patients (50%)

**TABLE 1**

Effect of pregabalin on the frequency of hot flashes and hot flash score

	Before treatment	After treatment	Response
Hot flashes/day			
Range	2–21	0–16	–
Mean	9.6	4.5	53%
Median	9	2	78%
Hot flash score*			
Range	4–72	0–32	–
Mean	24.8	8.6	65%
Median	24	2.5	90%
50% reduction	–	6/8	75%

\* Severity (1 = mild, 2 = moderate, 3 = severe) × number of hot flashes per day

complained of drowsiness; two patients (25%) had altered mentation; and one patient (12%) experienced dizziness, lethargy, constipation, and flatulence. Two of the patients (25%) discontinued the drug due to altered mentation, and one patient (12%) stopped taking it because of drowsiness. The doses associated with discontinuation of the drug were 50 mg/d in one patient and 150 mg/d in two patients.

## Discussion

The data collected in this small, uncontrolled pilot study suggest that low doses (50–150 mg/d) of pregabalin may

be effective in controlling hot flashes in many patients with breast or prostate cancer who are receiving hormonal therapy. The dose-limiting side effects of the drug were predominantly neurologic, including drowsiness and altered mentation, and were severe enough sometimes to result in discontinuation of the medication, even at low doses.

Since the doses used by these cancer patients were generally lower than those used for pregabalin's approved indications in non-cancer patients, we feel that the side effects of pregabalin might be considered to be worse by cancer patients than by non-cancer patients, perhaps as a result of disease or other treatments. It is also possible these patients were anticipating having side effects from pregabalin therapy, having learned about them during the informed consent process.

The reduction in hormonal therapy-related vasomotor instability seen with pregabalin is similar to that reported in cancer patients receiving gabapentin<sup>1–3</sup> and may be a beneficial class effect of all GABA analogs. A randomized, prospective, double-blinded trial of pregabalin versus gabapentin or placebo is warranted based upon this pilot study.

Owing to the small number of patients in this study, comparisons of the effectiveness of pregabalin with that of gabapentin or other treatments of hot flashes are not possible. Pregabalin appears, however, to be another promising option available for controlling hot flashes in breast or prostate cancer patients undergoing hormonal therapy. Further studies of pregabalin are warranted to determine the role it might have in controlling this tormenting symptom in patients with cancer.

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