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Venlafaxine Hydrochloride and Chronic Pain

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CLINICAL TRIALS of tricyclic antidepressants have shown efficacy for both chronic headaches and neuropathic pain.[1] The tricyclic antidepressants useful for chronic pain block the neuronal reuptake of both serotonin and norepinephrine. Serotonin-selective reuptake-inhibitor antidepressants have shown little or no efficacy when compared with placebo or tricyclic antidepressant use for neuropathic pain.[2] Unfortunately, the use of these drugs for chronic pain is limited by numerous side effects such as sedation, cognitive impairment, orthostatic hypotension, cardiac conduction abnormalities, dry mouth, and constipation. Many of these effects are due to the affinity of tricyclic antidepressants for the muscarinic-cholinergic, histaminic, and α_1-adrenergic receptors. Venlafaxine hydrochloride is a new antidepressant medication that, like the tricyclic antidepressants, inhibits the neuronal reuptake of both serotonin and norepinephrine.[3] Venlafaxine does not bind to muscarinic-cholinergic, histaminic, and α_1-adrenergic receptor sites, making its side effect profile substantially different from and theoretically more benign than that of the tricyclic antidepressants.

We report our initial open-label experience with venlafaxine in treating patients with chronic pain, primarily headache and neuropathic pain. Pain relief was rated by combining a patient's rating of efficacy with the clinician's global impression after a minimum of four weeks of therapy. If a patient completed less than four weeks of treatment, efficacy was rated at the end of treatment. An 80% or greater reduction in pain severity was interpreted as complete pain relief, a 50% to 79% reduction as moderate pain relief, 20% to 49% as mild pain relief, and less than 20% reduction in pain as no pain relief.

Summary of Cases

Table 1 summarizes the cases of the first 12 patients we treated with venlafaxine. All of them had had inadequate pain relief or intolerable side effects with the use of at least one antidepressant. These patients completed at least two weeks of therapy with venlafaxine. One case was not included in the results because the patient had severe nausea after taking only two doses. Otherwise, the data were collected over a seven-month period after patients were examined for chronic pain or headache.

The eight women and four men had an average age of 54 years and an average pain duration of 7.7 years. Four patients had headache, seven had neuropathic pain, and one had atypical facial pain. Patients had tried an average of 2.6 different antidepressants before taking venlafaxine. Patients 6 and 10 were on concurrent opioid therapy with transdermal fentanyl citrate patches. Patients 5 and 9 did not complete four weeks of therapy. Patient 5 had complete relief of chronic daily headache for two weeks, but when pain began to return, she elected to discontinue venlafaxine instead of adjusting the dose. Patient 9 was taking several medications—mexiletine hydrochloride, carbamazepine, and valproate sodium—for pain due to a posterior fossa arteriovenous malformation after a stroke. With the start of venlafaxine therapy, an increased blood pressure required the cessation of fludrocortisone acetate used for the control of orthostatic hypotension. The patient experienced persistent drowsiness and unsteady gait after three weeks of therapy, and venlafaxine was discontinued. In the other ten patients, pain relief was rated as moderate in seven and mild in three at total daily dosages from 18.75 to 250 mg per day (average, 99 mg per day). The most common side effect was nausea, which was made manageable by starting therapy at 18.75 mg per day. Patient 10 had moderate relief of peripheral neuropathic pain at a dose of 37.5 mg per day but later reduced the dose to 18.75 mg per day because of subjective hyperthermia and impotence, with only a slight diminution of pain relief. Patient 12 later required a dose reduction from 75 mg twice a day to 37.5 mg twice a day because of worsened hypertension. She became normotensive without a loss of pain control. Based on these results, ven-

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TABLE 1.—*Patients Treated With Venlafaxine Hydrochloride (HCl)*

Patient	Age, yr	Sex	Diagnosis	Duration, yr	Antidepressant Drug Trials	Venlafaxine HCl Dosage, mg/d	Dose Response
1	30	Female	Reflex dystrophy	1	Desipramine HCl	75, 2×	Mild relief
2	42	Female	Migraine	10	Nortriptyline HCl, amitriptyline HCl	37.5	Moderate relief
3	44	Male	Intercostal neuralgia	9	Amitriptyline, fluoxetine, nortriptyline	125, 2×	Moderate relief
4	45	Female	Atypical facial pain	11	Desipramine, imipramine HCl, doxepin HCl, nortriptyline	37.5	Moderate relief
5	47	Female	Mixed headache	18	Nortriptyline, amitriptyline, paroxetine	75, 4×	Complete relief
6	50	Female	Multiple sclerosis	5	Amitriptyline	37.5	Mild relief
7	52	Female	Mixed headache	15	Amitriptyline, fluoxetine, sertraline, paroxetine	75	Moderate relief
8	53	Male	Peripheral neuropathy	3	Amitriptyline, fluoxetine	50, 4×	Moderate relief
9	65	Male	Poststroke pain	5	Amitriptyline, desipramine	37.5	Moderate relief
10	70	Male	Peripheral neuropathy	6	Desipramine, amitriptyline, doxepin	37.5	Moderate relief
11	71	Female	Mixed headache	2	Nortriptyline, paroxetine	37.5	Mild relief
12	74	Female	Postzoster pain	7	Desipramine, amitriptyline, imipramine, sertraline	75, 2×	Moderate relief

lafaxine provided substantial relief in patients who were refractory to treatment with other antidepressants.

Conclusion

Venlafaxine appears to be a useful addition to the list of antidepressants with efficacy in pain management. Like other antidepressants, side effects are minimized by starting at the lowest possible dose. Increased blood pressure and nausea seen with venlafaxine are uncommon with the use of tricyclic antidepressants, and antidepressant-like cognitive impairment and anticholinergic side effects were uncommon with the use of venlafaxine. This open-label experience supports the need for controlled, randomized clinical trials of venlafaxine for chronic pain.

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