Facial flushing associated with duloxetine use

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Duloxetine hydrochloride, the first selective serotonin- and norepinephrine-reuptake inhibitor, is indicated for the treatment of major depressive disorder and management of neuropathic pain associated with peripheral diabetic neuropathy.1 In clinical trials, the most common adverse effects of duloxetine were nausea, dry mouth, dizziness, constipation, insomnia, and decreased appetite.¹

We present the case of a woman who developed facial flushing after initiation of duloxetine for migraine prophylaxis.

Case report

A 43-year-old nonmenopausal woman was prescribed duloxetine 20 mg daily for migraine prophylaxis after the usual medications for treatment and prevention of migraines were used with little or no success. Magnetic resonance imaging and computed tomography ruled out structural causes of migraines. The patient took 20 mg daily for five days and then decided, on her own, to decrease the dosage after experiencing insomnia, a common adverse effect of duloxetine. She opened the 20-mg capsules and took half of the contents to “create” the 10-mg dose, placing the contents of the opened capsule directly onto her tongue. She did this for two weeks and found the migraines to be significantly reduced in number and intensity. At that time, she began to experience what she described as a hot flash and facial flushing. The flushing was not accompanied by itching and did not spread beyond the face. The flushing occurred one to two hours after administering the 10-mg dose and typically resolved the following day. One week later, the patient noticed that the vessels in her face were more prominent. Concomitant therapies included pindolol for hypertension and duloxetine and botulinum toxin type A injections for migraines. The patient weaned herself off duloxetine. Facial flushing continued for one week after discontinuation of the drug. At a one-month follow-up visit, she stated that the flushing had resolved and not occurred since the original episodes.

Conclusion. A patient treated with duloxetine developed facial flushing, possibly caused by inappropriate administration of the drug.

Index terms: Antidepressants; Botulinum toxin A; Dosage; Duloxetine hydrochloride; Flushing; Migraine; Pindolol; Rational therapy; Toxicity

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As a 43-year-old woman, the patient's flushing and duloxetine therapy.

The only publication found to list flushing as an adverse effect of duloxetine was the prescribing information for Cymbalta, which noted hot flushes in 2 (0.18%) of 1139 patients. In a trial of duloxetine for diabetic peripheral neuropathy, flushing was not reported in duloxetine- or placebo-treated groups. A MEDLINE search found no other studies of duloxetine that listed treatment-related flushing.

Flushing usually affects the face, neck, and upper part of the chest and is characterized by sudden vasodilation with a sensation of heat. The symptoms our patient experienced were consistent with this description. As a 43-year-old woman, the patient may have been perimenopausal. However, discontinuation of the drug eliminated the flushing, and she has not experienced flushing since the initial episodes. We believe the flushing was most likely related to the inappropriate administration of duloxetine. Botulinum toxin type A was not likely to cause this adverse event, as this agent has been used to treat flushing. Pindolol was not likely to be the cause of the flushing, since the patient had been taking the drug for many years and continued to take it after the flushing subsided after discontinuation of duloxetine.

It is unclear why this patient developed flushing. One potential explanation is the patient’s nonadherence to her prescribed duloxetine regimen. The patient stated that she opened the 20-mg capsules and placed half of the contents of each capsule directly onto her tongue to create a 10-mg dose. According to the drug’s prescribing information, “the capsules should be swallowed whole, should not be chewed or crushed, nor should the contents be sprinkled on food or mixed with liquids.” Directly placing the contents of the capsule into the mouth may lead to early dissolution and rapid absorption of the drug, which would not normally occur when the capsules are swallowed whole. Supporting this theory is the fact that the flushing started only after the patient decreased the dose to 10 mg by opening the capsules.

Interestingly, duloxetine is approved for the treatment of major depressive disorder and the management of neuropathic pain associated with peripheral diabetic neuropathy. A MEDLINE search failed to identify any literature describing the use of duloxetine for the treatment or prophylaxis of migraine headache. The use of venlafaxine and selective serotonin-reuptake inhibitors (SSRIs), including fluoxetine and paroxetine, for migraine prophylaxis has been described in numerous studies and case reports. Several studies have investigated the use of SSRIs in combination with tricyclic antidepressants for the prevention of migraine headache. Duloxetine’s use in migraine prophylaxis may be supported by its pharmacologic action of inhibiting the reuptake of serotonin and norepinephrine, similar to the actions of SSRIs and venlafaxine.

Conclusion

A patient treated with duloxetine developed facial flushing, possibly caused by inappropriate administration of the drug.

References