

beats of inducible ankle clonus, frequent myoclonic jerking and tonic spasm of the right side of his orbicularis oris muscle. His abdomen was tense, but non-tender, with normal bowel sounds. An electrocardiogram showed sinus tachycardia with a baseline tremor, but no other abnormality.

Therapy with dexamphetamine and venlafaxine was ceased, and cyproheptadine (8 mg doses up to a total of 32 mg over three hours) was given. The patient had a stepwise reduction in heart rate, with complete resolution of his symptoms, and was discharged the next morning. Dexamphetamine therapy was restarted three days later and citalopram therapy was commenced one week after discharge. Two weeks after discharge, he reported similar symptoms, and ceased citalopram. Three days later he was still agitated, with nausea, diarrhoea and teeth clenching. There was no rigidity, tremor or diaphoresis, and his heart rate was 76 bpm. He was given two 8 mg doses of cyproheptadine and was asymptomatic two days later.

Some of this patient's symptoms could be attributed to noradrenaline excess. However, the combination of neuromuscular and autonomic features is more consistent with serotonin toxicity. The fact the symptoms resolved after administration of cyproheptadine (a 5-HT₂-receptor antagonist) supports this hypothesis. There is no theoretical reason why the interaction of citalopram (a pure SSRI) and dexamphetamine should cause catecholamine excess, and again the more likely explanation is serotonin toxicity.

Dexamphetamine causes psychostimulation and increased peripheral sympathomimetic activity. Centrally it causes presynaptic release of serotonin,¹ and dopamine and catecholamine release.² Venlafaxine and its metabolite, *O*-desmethylvenlafaxine, inhibit both neuronal 5-HT reuptake and noradrenaline reuptake,³ whereas citalopram, an SSRI, has little effect on noradrenaline reuptake.⁴ The combination of serotonin reuptake blockade and either presynaptic release of serotonin or monoamine oxidase inhibition by dexamphetamine will cause increased serotonin levels in the central nervous system, and is the likely mechanism of toxicity in this patient. This is consistent with the mechanism for other reports of serotonin toxicity.⁵

Increased awareness and cautious monitoring is advised when using a combination of dexamphetamine and either venlafaxine or an SSRI. This is particularly important in people using amphetamines recreationally and in children taking dexamphetamine for attention deficit hyperactivity disorder.

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Venlafaxine and bilateral acute angle closure glaucoma

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TO THE EDITOR: We report a case of bilateral acute angle closure glaucoma associated with venlafaxine.

A 45-year-old woman with a history of bipolar affective disorder and borderline personality traits was admitted with increasing depression and suicidal ideation. She was taking sodium valproate (1500 mg/day) and slow-release lithium (450 mg/day). She had also taken dothiepin (50 mg nightly) for seven days, but this therapy was ceased on admission. Her only previous ophthalmological history was hypermetropia, and she had been taking low-potency neuroleptic medications and selective serotonin reuptake inhibitors in the past with no significant adverse effects.

She was treated with chlorpromazine (up to 150 mg daily), and venlafaxine therapy (extended release, 75 mg/day) was commenced.

After three days of taking venlafaxine, she developed left retro-orbital pain associated with nausea and vomiting, with subsequent swelling and drooping of the left upper lid and a dilated and fixed pupil. The eye was congested and visual acuity was reduced to counting fingers. She was diagnosed with acute angle closure glaucoma, treated with timolol, and transferred to a tertiary referral hospital. During this period, she sustained an injury to her right eye following an assault by a third party. A computed tomography scan revealed a right blow-out fracture with inferior rectus muscle entrapment.

On admission, intraocular pressures were 16 mmHg in the right and 50 mmHg in the left eye, and gonioscopy revealed closed

angles (grade 1–2). Ninety minutes after being given intravenous mannitol, topical apraclonidine hydrochloride, latanoprost and pilocarpine eye drops, the intraocular pressure dropped to 35 mmHg in the left eye. Initial laser iridotomy was unsuccessful because of a hazy cornea. Laser iridotomy was repeated several times after topical steroid therapy until it was successful. The right orbital floor fracture was repaired with a Medpor implant (Porex Surgical Products Group, Atlanta, Georgia).

Eight days after starting venlafaxine therapy, she developed similar symptoms in her right eye, despite prophylactic treatment with pilocarpine eye drops four times a day. Venlafaxine was discontinued, and three days later a successful right laser iridotomy was performed. Her visual acuity was 6/5 in her right and 6/18 in her left eye. After eight weeks she was receiving no ophthalmic treatment and her intraocular pressures were well controlled.

In a MEDLINE search, we found no published reports of venlafaxine associated with acute angle closure glaucoma. The manufacturers report it as a rare adverse event (fewer than 1/1000; data on file; Wyeth-Ayerst laboratories). There has been one previous report of increased intraocular pressures in two patients with known narrow-angle glaucoma who began taking venlafaxine.² Glaucoma has also been reported with paroxetine.³⁻⁴ Our patient had no associated family history of glaucoma, but her eyes were predisposed to angle closure glaucoma owing to hypermetropia.

Patients with acute angle closure glaucoma usually have a structural defect that produces a narrow drainage angle, and thus moderate dilation of the pupil may precipitate an attack. Drugs like tricyclic antidepressants cause mydriasis and may cause the narrow angles to close as a result of anticholinergic effects. Venlafaxine, however, is a serotonin and noradrenaline reuptake inhibitor without anticholinergic activity. This fact and the time course suggest that a combination drug interaction may have occurred in this patient, perhaps by the hepatic inhibition of chlorpromazine metabolism by venlafaxine, increasing anticholinergic activity, or by a direct effect of venlafaxine on the eye unrelated to mydriasis.

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