Intraoperative floppy-iris syndrome (IFIS) is an entity encountered during cataract surgery (phacoemulsification), affecting mainly male patients with a history of benign prostatic hyperplasia being treated with the α-1A adrenergic blocker tamsulosin. Weaker association with other α-1A selective and α-1 nonselective antagonists has been documented. Cases associated with the use of other drugs have also been reported. We present a female patient who had features of IFIS in both eyes during cataract surgery. She had an unremarkable medical history apart from major depressive disorder that was treated with duloxetine. Many reports of IFIS affecting patients of both sexes who were not treated with α-1 antagonists suggest a complex mechanism of the syndrome. The role of other receptors is discussed.

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In 2005, Chang and Campbell \(^1\) first described a syndrome affecting phacoemulsification surgery that was characterized by a billowing iris that flutters as a result of very small intraocular fluid currents, a tendency of spontaneous iris prolapse through the incisions, and progressive intraoperative miosis. The intraoperative floppy-iris syndrome (IFIS) was initially attributed to the use of the α-1A receptor antagonist tamsulosin. Later prospective and retrospective studies and case reports found weaker association of IFIS with other α-antagonists \(^2\)–\(^6\) as well as other medications. \(^7\)–\(^13\)

Duloxetine (Cymbalta and generics) is a serotonin–norepinephrine reuptake inhibitor. It is primarily prescribed for major depressive disorder and generalized anxiety disorder, \(^1\) fibromyalgia, and neuropathic pain. \(^2\) It is also approved across Europe for the management of stress urinary incontinence.

González-Martín-Moro et al. \(^14\) described a case of a highly complicated phacoemulsification with severe IFIS in a patient taking multiple medications including duloxetine. We report the case of a woman who had features of moderate IFIS (according to Chang et al.’s grading \(^15\)) in both eyes during cataract surgery. She had an unremarkable medical history apart from a major depressive disorder being treated with duloxetine. \(^1\)

CASE REPORT

A 46-year-old woman presented in December 2012 reporting blurred vision, most prominent in the right eye. The corrected distance visual acuity (CDVA) was 4/10 in the right eye and 7/10 in the left. Slitlamp examination revealed deep anterior chambers and bilateral posterior cortical cataract, denser in the right eye. Fundoscopy was normal, although both eyes achieved only moderate dilation. The patient had a history of a recently diagnosed major depressive disorder. She had been treated with duloxetine for the previous 3 months at a total daily dose of 90 mg, 30 mg in the morning and 60 mg in the evening. The rest of the medical history was unremarkable. The patient denied previous prescription medication, over-the-counter medicines, herbal medicines, vitamins, and nutritional supplements. There was no family history of eye disease or major medical problems.

A month after presentation, cataract extraction was performed in the right eye. Despite thorough use of mydriatics (phenylephrine, tropicamide, and cyclopentolate) and diclofenac preoperatively, only moderate pupil dilation was achieved. During the surgery, features of moderate IFIS were seen; the iris was floppy and undulated and had a mild tendency to prolapse through the main incision. The
irrigation/aspiration (I/A) parameters were reduced, and the surgery was completed with a combination of dispersive and cohesive ophthalmic viscosurgical devices (OVDs); that is, the soft-shell technique. One month postoperatively, the uncorrected distance visual acuity was 10/10.

Two years later, cataract surgery was performed in the left eye. There had been no change in the medical history in the intervening time; the patient was being treated with only duloxetine at a daily dose of 120 mg. The surgery had the same characteristics as the earlier procedure; that is, moderate pupil dilation despite meticulous preoperative use of mydriatics and floppy iris during surgery, with a mild tendency to prolapse through the main incision. Reducing the I/A parameters as well as proper use of OVDs enabled the surgery to be completed with no complications. One month postoperatively, the CDVA was 10/10.

**DISCUSSION**

The presence of α-1A receptors in both prostate and iris (dilator muscle and arteriolar muscularis) is an explanation of the association between IFIS and tamsulosin use. The direct effect of the drug on iris tissue as well as the histologic changes attributed to chronic use partially explain the abnormal iris behavior. A more complex mechanism is suggested by the weaker association of the syndrome with other α-1A blockers, such as silodosin. Many drugs of different categories have been reported to be responsible for sporadic cases. Figure 1 summarizes the reported drugs, their mechanisms of action, and the receptors affected.

Duloxetine’s main mechanism of action is inhibition of the reuptake of 5-hydroxytryptamine and norepinephrine in the central nervous system. Duloxetine is also a less potent inhibitor of dopamine reuptake. The drug lacks appreciable affinity for muscarinic, histamine, α-1 adrenergic, 5-hydroxytryptamine, dopamine, and opioid receptors. Furthermore, mydriasis is reported to be a side effect of the drug. These findings make the association of the drug with IFIS appear initially paradoxical. Considering the absence of obvious pharmacologic association between duloxetine and the syndrome, González-Martín-Moro et al. avoided using the term association with their patient, who was also being treated for angle closure. Careful observation of the pharmacologic properties shows that tamsulosin, unlike other α-1 inhibitors, has a higher binding affinity for dopamine and 5-hydroxytryptamine receptors. These 2 receptors may also be implicated in the IFIS mechanism. This could explain the higher incidence of IFIS with this α-1A inhibitor than with other α-1A blockers, as well as the association of zuclopenthixol, risperidone, imipramine, quetiapine, and duloxetine with the syndrome.

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