Intraoperative floppy-iris syndrome and use of chronic oral tricyclic antidepressant

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We report a case of complete intraoperative floppy-iris syndrome associated with longstanding use clomipramine, an oral tricyclic antidepressant, in a female patient and discuss the role of receptor affinities.

Financial Disclosure: None of the authors has a financial or proprietary interest in any material or method mentioned.

JCRS Online Case Reports 2016; 4:74–75 Crown Copyright © 2016 Published by Elsevier Inc. on behalf of ASCRS and ESCRS.

Intraoperative floppy-iris syndrome (IFIS) was first described by Chang and Campbell1 and is characterized by a triad of poor iris dilation with progressive intraoperative constriction and a billowing, flaccid iris stroma with a propensity to prolapse toward the phacoemulsification and side-port incisions.1,2 The syndrome is associated with α1A-antagonists, particularly tamsulosin, although IFIS has been described with other α-blockers (eg, doxazosin).3 The β-blocker labetalol, which possesses α-blocking properties, has also been associated with IFIS.4 Intraoperative floppy-iris syndrome has been reported with antipsychotic5–8 and antidepressant9 use, likely reflecting their diverse receptor-blocking properties. Intraoperative floppy-iris syndrome is associated with a higher rate of surgical complications, with an incidence of 15% if not preempted.1,2 Early identification allows for the use of ophthalmic viscosurgical devices, mechanical iris dilation, and pharmacologic measures to minimize intraoperative risk.2 To our knowledge, this is the first reported case of complete IFIS associated with longstanding clomipramine (tricyclic antidepressant [TCA]) use and the first reported case in a female patient.

CASE REPORT

A 63-year-old woman was listed for small-incision cataract extraction in the left eye following a 6-month history of blurred vision with a moderate nuclear sclerotic cataract evident on examination. No other ocular history was noted. She had been taking oral clomipramine, 75 mg, at night for the past 8 years, as well as oral simvastatin, 20 mg, at night. No other α-blocker or over-the-counter or herbal supplements were used.

The preoperative corrected distance visual acuity (CDVA) (logMAR) was 0.6 in the left eye and 0.2 in the right eye. The refractive error in the left eye was +1.0 diopter (D). The preoperative biometry of the 2 eyes is shown in Table 1.

A standard superior approach with topical and intracameral local anesthetic agents was adopted using a Stellaris phacoemulsification machine (Bausch & Lomb) and a 2.2 mm superior clear corneal incision. Intraoperatively, the patient displayed the classic signs of IFIS—a poorly dilated, flaccid, billowing, prolapsing iris with progressive intraoperative constriction. The IFIS was managed with a standard intracameral adrenaline-enriched balanced salt solution.

No postoperative complications were noted, and no additional measures were required. At 3 weeks, the CDVA in the left eye was 0.2 with a postoperative refraction of −0.5 −0.5 × 18 and the patient was happy with the postoperative vision.

DISCUSSION

Three α-receptors (α1A, α1B, α1D) have been described in the human iris. Intraoperative floppy-iris syndrome is reported to occur secondary to α1A-receptor blockade, as occurs with antagonists, most notably tamsulosin prescribed for benign prostatic hypertrophy (BPH) and systemic antihypertensives such as doxazosin.1–3 However, IFIS may represent a multimodal dynamic process that involves other iris-dilator pathways including nitric oxide, endothelin-A, angiotensin, sympathetic,
parasympathetic, serotonergic, and peptidergic signalling.\textsuperscript{10,11} This may explain the recent association between select antipsychotics \textsuperscript{5,8} and antidepressants \textsuperscript{9,12} with IFIS given their affinities to multiple receptor types.

Clomipramine is a tricyclic antidepressant indicated for use in depression and phobic and obsessive states.\textsuperscript{13} It acts primarily as a serotonin reuptake inhibitor but also has affinity for noradrenergic, muscarinic, histaminergic (H1), and $\alpha_1$-adrenergic receptors, where it has antagonistic effects.\textsuperscript{14} Other TCAs, including imipramine\textsuperscript{9} and mianserin,\textsuperscript{12} have been reported to cause IFIS. Both imipramine and mianserin have similar $\alpha_1$-adrenergic receptor affinities to clomipramine.\textsuperscript{14} The length of TCA use and cessation of use prior to surgery does not seem to correlate with the development of IFIS.\textsuperscript{9} The $\alpha_1$-adrenergic receptor blockade properties with the possible contribution of other receptor blockade are also the proposed mechanisms by which select antipsychotics induce IFIS.\textsuperscript{5,8}

It is well known that IFIS occurs commonly with tamulosin and other $\alpha_1$-receptor antagonists used mainly for BPH treatment in the male population.\textsuperscript{1,2} The association between TCAs\textsuperscript{9,12} and antipsychotics\textsuperscript{5,8} with IFIS has significant implications for clinical practice given their prevalent use in the general population, especially antidepressant use in female patients.\textsuperscript{15} As well as the well-described $\alpha_1$-blockers associated with IFIS (ie, tamulosin and doxazosin),\textsuperscript{1,3} ophthalmologists should be alert to and elucidate from the patient’s history the use of TCAs or antipsychotics. Use of TCAs or antipsychotics should highlight the possible risk for IFIS and the need for preventive measures to reduce intraoperative complications. Future studies should investigate in greater detail the strength of association between antidepressants, antipsychotics, and IFIS in male and female patients.

### Table 1. Preoperative biometry in the 2 eyes.

| Measurement                       | Left Eye | Right Eye |
|----------------------------------|----------|-----------|
| Axial length (mm)                | 24.0     | 24.0      |
| K1 (flat keratometry) (D)        | 44.0 \( @ \) 11 | 43.6 \( @ \) 172 |
| K2 (steep keratometry) (D)       | 44.8 \( @ \) 101 | 44.4 \( @ \) 82 |
| Anterior chamber depth (mm)      | 3.49     | 3.40      |

K = keratometry

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