ASCRS White Paper: Clinical review of intraoperative floppy-iris syndrome

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Intraoperative floppy-iris syndrome (IFIS) is associated with the use of systemic α_1-antagonists, and tamsulosin in particular. The incidence and severity of IFIS are variable; however, the syndrome is associated with a higher rate of cataract surgical complications, especially when the condition is not recognized or anticipated. Questioning cataract patients preoperatively about current or previous use of α_1-antagonists is therefore important. Intraoperative floppy-iris syndrome surgical management strategies include pharmacologic measures, the use of high-viscosity ophthalmic viscosurgical devices, and mechanical dilating devices. However, sphincterotomies and pupil stretching are ineffective. Whether used alone or in combination, these small-pupil techniques improve the surgical success rate in these cases. Stopping the α_1-antagonist preoperatively is of questionable value.

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Intraoperative floppy-iris syndrome (IFIS) was first described in 2005 by Chang and Campbell.[1] In addition to a tendency for poor pupil dilation, the authors listed a triad of intraoperative signs that characterized classic IFIS: (1) billowing of a flaccid iris stroma, (2) a propensity for iris prolapse toward the phaco and side-port incisions, and (3) progressive intraoperative pupil constriction.

Chang and Campbell[1] report the strong association of IFIS with the systemic α_1-antagonist tamsulosin (Flomax). A retrospective chart review of all consecutive cataract surgeries performed in Campbell's 2-surgeon practice over a 12-month period (706 eyes in 511 patients) and a separate masked prospective study of 900 consecutive cataract surgeries (741 patients) performed by Chang were used to determine the incidence and common characteristics of IFIS and the percentage of patients who were taking α_1-antagonist medications. In all, 36 eyes in male patients in the 2 studies had IFIS associated with systemic tamsulosin use. These eyes represented approximately 2% to 3% of the entire cataract surgical population from these 2 practices. There was no correlation between IFIS and eye color, diabetes, or pseudoexfoliation.

CAUSES OF INTRAOPERATIVE FLOPPY-IRIS SYNDROME

Tamsulosin is the most commonly prescribed drug for the treatment of lower urinary tract symptoms of benign prostatic hyperplasia (BPH). Its association with IFIS has been confirmed by many additional published studies, but with widely varying rates (S.B. Radomski, MD, et al, "Intraoperative Iris Prolapse During Cataract Surgery in Men Using Alpha-Blockers for Lower Urinary Tract Symptoms Due to Benign Prostatic Hypertrophy," paper presented at the annual meeting of the American Urological Association, Atlanta, Georgia, USA, May 2006. Abstract available at: http://www.urotoday.com/287/conference_reports/bph_medical__hormonal_therapy/aua_2006__abst_1634_intraoperative_iris_prolapse_during_cataract_surgery_in_men_using_alphablockers_for_lower_urinary_tract_symptoms_due_to_benign_prostatic_hypertrophy.html. Accessed September 9, 2008).[2–13] Likely reasons for this variability are the subjectivity of the clinical definition and significant variation in the severity of IFIS in that only some of the 3 classic clinical signs may be present. In addition, retrospective studies typically reviewed operative reports for iris prolapse, which may not have been recorded and from which it would have been difficult to identify milder IFIS cases without iris

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prolapse. Keklikci et al.[12] published the only other masked prospective trial to determine the risk ratios and incidence of IFIS. Twelve (80%) of 15 IFIS patients were taking systemic tamsulosin. Twelve (52%) of 23 patients using tamsulosin showed features of IFIS. The odds ratios (OR) and relative risk (RR) ratios show strong positive correlations between tamsulosin use and IFIS (OR 206.5; 95% confidence interval [CI], 50.9-836.5) (RR 99.3; 95% CI, 30.0-327.8).

The largest prospective study of IFIS management enrolled 167 consecutive eyes in 135 tamsulosin patients presenting for cataract surgery at 10 surgical practices.[8] The following grading system of IFIS was used: mild (iris billowing only), moderate (billowing and intraoperative miosis), and severe (classic triad including iris prolapse). Ninety percent of the eyes enrolled were diagnosed with at least some level of IFIS (17% mild, 30% moderate, and 43% severe). In an online survey conducted by the American Society of Cataract and Refractive Surgery (ASCRS) Cataract Clinical Committee in early 2008,[13] 42% of the 957 respondents reported seeing, on average, at least 2 IFIS cases per month; 23% said they saw at least 3 IFIS cases per month. Excluding those with insufficient experience, nearly one fourth of the respondents felt that IFIS was present to some degree in more than 90% of tamsulosin patients. Seventy percent of respondents saw some degree of IFIS in the majority (>50%) of patients taking tamsulosin, compared with 20% who said the same about nonselective α-blockers.

Tamsulosin is one of several systemic α_1-adrenergic antagonists commonly prescribed for BPH. The first such medications approved in the United States for BPH were terazosin (Hytrin) and doxazosin (Cardura).[14] This class of drugs improves bladder emptying and reduces urinary frequency by relaxing the smooth muscle in the prostate and bladder neck.[14,15] Because vascular smooth muscle contraction is also mediated by the α_1-adrenoreceptor, terazosin and doxazosin are also prescribed for hypertension and postural hypotension is a potential side effect of systemic α-blockers.

At least 3 human α_1-receptor subtypes have been identified using binding and molecular cloning techniques; they are α_{1A} α_{1B} and α_{1D}.[16,17] Their distribution varies among different human organs, and approximately 70% of the α_1-receptors in the human prostate are of the α_{1A} subtype.[18] Based on animal and in vitro data, tamsulosin has a 20-fold greater affinity for α_{1A} than α_{1B} receptors.[16] For this reason, tamsulosin is more uroselective with fewer cardiovascular side effects than terazosin and doxazosin, which are not subtype selective α_1-blockers.[15,19] Subsequently, a nonsubtype selective α_1-antagonist, alfuzosin (Uroxatral), was approved for BPH and launched in 2003.[20] Like tamsulosin, alfuzosin is a so-called uroselective α_1-antagonist that improves urinary outflow while minimizing vascular side effects such as postural hypotension.[15]

Finally, in October 2008, silodosin (Rapaflo) became the most recent α_1-antagonist approved by the FDA for the treatment of BPH Symptoms.[21] Similar to tamsulosin, silodosin is highly selective for the α_{1A}-receptor subtype.

There are many reports of IFIS occurring in patients taking nonselective α_1-antagonists as well, indicating that IFIS is a potential complication of this entire class of drugs (S.B. Radomski, MD, et al., "Intraoperative Iris Prolapse During Cataract Surgery in Men Using Alpha-Blockers for Lower Urinary Tract Symptoms Due to Benign Prostatic Hypertrophy," paper presented at the annual meeting of the American Urological Association, Atlanta, Georgia, USA, May 2006. Web citation given above).[5–9,17,22–27] Intraoperative floppy-iris syndrome has also been associated with other treatments for BPH, such as finasteride and the herbal BPH remedy saw palmetto (*Serenoa repens*).[28–30] Intraoperative floppy-iris syndrome has been anecdotally reported in association with a variety of other medications, including antipsychotic drugs that may possess some α-antagonistic effects.[31–36] In the ASCRS IFIS survey,[13] 10% of respondents had seen IFIS associated with saw palmetto, while 36% had seen IFIS associated with drugs other than α-blockers. However, fewer than 3% of respondents said they believed that either was a frequent cause of IFIS. Because α_1-antagonists are also prescribed for urinary retention or hypertension in women, it is important to remember that IFIS can arise in either sex.[1,4,37,38] Finally, tamsulosin is often prescribed as a short-term pharmacologic adjunct for the treatment of renal calculi.[39] This is relevant because it appears that tamsulosin can cause IFIS almost immediately. Shah et al.[40] published 1 case of IFIS occurring only 2 days after tamsulosin was started; another case occurring after only 2 weeks of tamsulosin use has been reported.[7]

There are several retrospective and prospective studies suggesting that compared with tamsulosin, IFIS appears to be less frequent or less severe in patients taking nonsubtype selective α_1-antagonists (S.B. Radomski, MD, et al., "Intraoperative Iris Prolapse During Cataract Surgery in Men Using Alpha-Blockers for Lower Urinary Tract Symptoms Due to Benign Prostatic Hypertrophy," paper presented at the annual meeting of the American Urological Association, Atlanta, Georgia, USA, May 2006. Web citation given above).[1,4–9,13,41–43] Campbell's retrospective chart review[1] did not find IFIS in 11 patients (15 eyes) taking nonselective α_1-antagonists, compared

with 63% of the 16 patients taking tamsulosin. In another retrospective chart review of 1298 cataract patients, tamsulosin accounted for only 26% of the α_1-antagonists used but 71% of the cases with intraoperative iris prolapse (Radomski et al. 2006 presentation). Chadha et al.[5] performed a prospective study of 1786 patients having cataract surgery. They found that IFIS occurred in 57% of patients taking tamsulosin but in only 2% of patients taking nonselective α_1-antagonists.

In a prospective study of 1968 cataract surgeries, Oshika et al.[6] found the incidence of IFIS to be 43% in patients taking tamsulosin compared with 19% in patients taking naftopidil, a nonselective α_1-antagonist. In another prospective study, Herd[8] found an IFIS incidence of 37% in patients taking doxazosin and 83% in patients taking tamsulosin. None of these prospective trials appears to have been masked. Finally, Blouin et al.[9] retrospectively evaluated 64 patients (92 eyes) who had been taking tamsulosin or alfuzosin at the time of cataract surgery. Intraoperative floppy-iris syndrome was noted in 86% of the tamsulosin patients but in only 15% of the alfuzosin patients ($P < .001$). The adjusted OR of IFIS in patients exposed to tamsulosin compared with those exposed to alfuzosin was 32.15 (95% CI, 2.74-377.11). When asked in the ASCRS survey whether IFIS was more likely with tamsulosin versus nonselective α_1-antagonists, 21% of the respondents said they did not have enough experience to know. Of those who did, 90% said they thought IFIS was more likely with tamsulosin and approximately two thirds said that it was "much more likely."[13] There is insufficient clinical experience with silodosin, the newest α_1-antagonist approved for BHP. Because silodosin is the only α_1-antagonist besides tamsulosin to be selective for the α_{1A}-receptor subtype, it may be just as likely as tamsulosin to cause IFIS.

The 5-α reductase inhibitors, finasteride and dutasteride (Avodart), represent a different class of drugs approved for the treatment of lower urinary tract symptoms of BPH.[14,44] These drugs lower the level of the hormone dihydrotestosterone, with a resulting reduction in prostate size over time.[44] Compared with α_1-antagonists, the onset of improvement in urinary symptoms takes much longer, and these drugs can be associated with reversible sexual adverse effects that appear to lessen over time. The Prostate Cancer Prevention Trial,[45] a large randomized prospective National Cancer Institute–funded study following more than 18 000 men, found that finasteride reduces the risk for prostate cancer by approximately 25% to 30% in men 55 years and older. Recently, new statistical data were reported that further strengthens this conclusion and provides reassurance that finasteride does not increase the risk for more aggressive prostatic malignancies.[46-48] Besides an anecdotal report of IFIS associated with finasteride, there are no studies that indicate a significant risk for IFIS with this drug class.[15,28] Therefore, for patients with cataracts, finasteride is a generic drug that treats BPH symptoms and lowers the risk for prostate cancer without increasing the risk for IFIS. An ongoing clinical trial is evaluating whether dutasteride also reduces the risk for prostate cancer.

PHARMACOLOGY OF INTRAOPERATIVE FLOPPY-IRIS SYNDROME

The precise distribution of α_1-receptor subtypes in the human iris smooth dilator muscle is not known. There is substantial indirect evidence from animal studies that α_1A is the dominant iris adrenoreceptor.[1,17,49–52] Chang and Campbell[1] initially postulated that systemic tamsulosin blocked contraction of the iris dilator smooth muscle and that deficient muscle tone led to poor pupil dilation, iris floppiness, and a propensity to prolapse. A potential factor behind the seemingly stronger association of IFIS with tamsulosin than with the nonselective α_1-antagonists may be that tamsulosin has a much stronger affinity for the α_{1A}-receptor subtype.[41,42,53,54]

Although the pharmacology of tamsulosin and alfuzosin has been well studied in the prostate, Palea et al.[43] recently published the only experimental study of the pharmacological effects on the iris dilator muscle. Tamsulosin was more effective than alfuzosin at blocking adrenergic contraction of the iris dilator muscle in pigmented rabbits. Because α_1-receptor blockade was far less potent in the iris than in the prostate for both drugs, Palea et al. suggest that an additional receptor could be involved in iris dilator muscle contraction. The relatively greater ability of tamsulosin to antagonize iris dilator contraction compared to alfuzosin could be explained by differences in affinity for this unidentified and hypothetical second iris receptor.

A German study used optical coherence tomography to measure the cross-sectional iris thickness in 58 eyes of patients taking tamsulosin before cataract surgery. Total iris thickness was reduced when compared with that in 41 control eyes evaluated by a masked examiner, and IFIS was subsequently noted in all tamsulosin eyes during cataract surgery despite the drug being stopped 2 weeks earlier (V. Reichenberger, et al., "Atrophie des Musculus dilatator pupillae durch selektive alpha1A-Adrenozeptorantagonisten zur Behandlung der benigen Prostatahyperplasie. [Reduced Iris Thickness on Therapy with Selective

Alpha1A-adrenergic Receptor Antagonist Tamsulosin as a Cause for IFIS]," poster presented at the 104th Annual Meeting of the Deutsche Ophthalmologische Gesellschaft, Berlin, Germany, September 2006. Abstract available at: http://www.egms.de/en/meetings/dog2006/06dog644.shtml. Accessed September 9, 2008).

There is only 1 report of iris pathology in patients taking tamsulosin. The histological thickness of the iris dilator muscle was normal in 16 cadaver eyes from tamsulosin patients when compared with that in controls (T. Kim, MD, et al., "The Effect of α_1-Adrenergic Receptor Antagonist Tamsulosin (Flomax) on Iris Smooth Dilator Muscle Anatomy," poster presented at the ASCRS Symposium on Cataract, IOL and Refractive Surgery, San Francisco, California, USA, March 2006. Abstract available at: http://stream.expoplanner.com/ascrs2006/handouts/076414_powerpointtamsulosin.ppt#10. Accessed September 9, 2008).

INTRAOPERATIVE FLOPPY-IRIS SYNDROME MANAGEMENT STRATEGIES

Several approaches to manage the troublesome iris behavior in IFIS have been proposed. These include a variety of pharmacologic strategies, the use of bimanual microincision phacoemulsification, the use of highly viscous or viscoadaptive ophthalmic viscosurgical devices (OVDs) in conjunction with low-flow fluidic parameters, and the placement of mechanical dilating devices.[1,4,7,11–13,26,55–64]

Certain general surgical principles should be observed in IFIS cases. Appropriately sized incisions should be carefully constructed with an entry that is anterior to the iris root. Hydrodissection must be performed very gently to avoid iris prolapse. Consideration should be given to decreasing irrigation and aspiration flow rates if possible and to directing irrigation currents away from the pupillary margin. Bimanual microincision phacoemulsification may reduce the tendency toward iris prolapse due to the tighter incisions, but it does not prevent this from occurring with severe IFIS.[1] Finally, as initially reported by Chang and Campbell,[1] partial-thickness sphincterotomies and mechanical pupil stretching are ineffective for IFIS and may exacerbate the condition.

Pharmacologic Measures

The serum half-life of tamsulosin is approximately 48 to 72 hours. Although it would seem logical, the utility of stopping tamsulosin preoperatively remains controversial and of unproven benefit.[1,7,13,17,65,66] In their initial description of IFIS, Chang and Campbell[1] reported its occurrence in patients who had stopped tamsulosin for more than 1 year. This unexpected finding was subsequently confirmed by others.[4,7,37,67] In the ASCRS survey,[13] 73% reported encountering IFIS in patients with a history of taking α_1-antagonists and roughly one half of the respondents therefore routinely inquire about previous use of these drugs. In a small clinical study, tamsulosin was detectable in aqueous humor samples from 3 of 5 patients who had discontinued the drug for 7 to 28 days before cataract surgery, suggesting a very prolonged drug-receptor binding time.[3,68]

In the prospective trial of cataract surgery in 167 consecutive eyes of tamsulosin patients,[7] the drug was stopped preoperatively in 32 cases (19%). This resulted in a larger pupil diameter at the beginning of surgery (mean diameter 6.9 $\pm$ 1.5 mm in stopped cases versus 6.0 $\pm$ 1.2 mm in nonstopped cases; $P < .001$) but did not result in a statistical improvement in IFIS severity. The risk for causing acute urinary retention by stopping tamsulosin is also unknown but is believed by some to be quite small.[17,66] Overall, it appears that stopping tamsulosin preoperatively is of unpredictable value and does not reliably prevent IFIS or reduce its severity. In the 2008 ASCRS survey,[13] 11% of surgeons said they routinely stopped tamsulosin before cataract surgery, while 64% said they never do.

Intracameral injection of α_1-agonist drugs has been advocated as a means to directly stimulate the iris dilator smooth muscle receptors.[11,12,26,55,59,61] Gurbaxani and Packard,[55] Manvikar and Allen,[56] and Allen and Packard[57] first reported success with managing IFIS by using intracameral phenylephrine, which is not available in the United States. Shugar[58] was the first to report the efficacy of intracameral epinephrine in tamsulosin patients. It is advisable to avoid preserved solutions and to use a diluted mixture; for example, 1:1000 bisulfite-free epinephrine mixed 1:3 or 1:4 with fortified balanced salt solution (BSS Plus) or plain BSS to buffer the acidic pH.[59] Intracameral phenylephrine or epinephrine may further dilate the pupil in some, but not all, eyes with IFIS. In addition, these agents frequently restore iris rigidity by increasing the dilator smooth muscle tone, which can markedly reduce the tendency for iris prolapse and billowing. The risk for triggering a hypertensive episode with intracameral α-agonists is unknown but has been reported.[36] In the ASCRS survey,[13] only 1% of respondents who had used intracameral α-agonists reported observing systemic hypertensive spikes (8/688) or toxic anterior segment syndrome (7/688).

Masket[7] first advocated the use of preoperative atropine drops to maximize cycloplegia in eyes at risk for IFIS. Although this approach is helpful in some eyes, the prospective tamsulosin trial found that preoperative atropine was the least reliable single small-pupil

management strategy for IFIS.[7,59,60] Although it generally produced the largest preoperative pupil (mean diameter 7.2 mm), 58% of the 19 eyes receiving topical atropine required additional measures such as iris retractors to manage the iris. Masket and Belani[61] also had success combining topical atropine with intracameral epinephrine in a small uncontrolled clinical trial. No study, however, has evaluated whether this combination is better than using an intracameral agonist alone.

Ophthalmic Viscosurgical Device Strategies

As initially advocated by Osher and Koch,[7] Healon5 (sodium hyaluronate 2.3%) is a maximally cohesive OVD that excels in its viscomydriatic ability. Because of its high viscosity, Healon5 is also uniquely able to block the iris from prolapsing to the incisions. However, low aspiration flow and vacuum settings (eg, $\leq$25 cc/min and $\leq$200 to 250 mm Hg, respectively) are necessary to prolong its presence in the anterior chamber as long as possible. If the pupil constricts during phacoemulsification, Healon5 can be reinjected repeatedly. Compared with using mechanical expansion devices, the Healon5 method is more dependent on proper phacoemulsification technique and fluidic parameters. This strategy is therefore less suitable if high vacuum settings are desired for denser nuclei or if the surgeon is inexperienced with its use.

Other OVDs can be used instead of or in combination with Healon5. Arshinoff[62] suggests placing a dispersive OVD such as Viscoat (sodium hyaluronate 3.0%–chondroitin sulfate 4.0%) peripherally, followed by injecting Healon5 centrally to create what he calls the IFIS ultimate soft-shell technique. Modi found that DisCoVisc (hyaluronic acid 1.6%–chondroitin sulfate 4.0%) remained in the eye longer and was better than Healon5 for IFIS when high flow and vacuum fluidic parameters were used (S. Modi, MD, FRCSC, "DisCoVisc for IFIS," Cataract & Refractive Surgery Today, September 2006, page 57. Available at: http://www.crstoday.com/PDF%20Articles/0906/CRST0906_09.pdf. Accessed September 9, 2008).

Mechanical Pupil Expansion Devices

Iris retractors and pupil expansion rings mechanically dilate the pupil, prevent it from constricting, and restrain the iris from prolapsing.[64,69–72] Both the 5S Pupil Ring (Morcher GmbH, distributed by FCI Ophthalmics, Inc.) and the Perfect Pupil (Milvella Ltd.) are disposable grooved plastic rings that are threaded along the pupillary margin using a metal injector.[70] An opening in the ring is aligned with the incision to provide access for the phaco tip. In contrast, a preloaded disposable plastic injector is used to insert the Graether silicone pupil expansion ring (Eagle Vision).[71] All of these rings are more difficult to position if the pupil is less than 4.0 mm wide or if the anterior chamber is shallow. A foldable and disposable square expansion device was developed by Malyugin (MicroSurgical Technology).[64] Made of 5-0 polypropylene, this flexible device is also folded and injected into the anterior chamber with a disposable injector system. Its 4 circular coils engage the pupil edge to expand it to a 6.0 mm diameter, and it is the easiest pupil device to insert and remove. An excessively large pupil diameter will prevent all these rings from properly engaging the pupillary margin.

Iris retractors are currently the most popular mechanical strategy used for pupil expansion in IFIS.[4,7,13] Disposable retractors are manufactured with 6-0 nylon (Alcon Laboratories), while reusable retractors are made of 4-0 polypropylene (Katena Products, FCI, and Oasis Medical). Being of the same size and rigidity as an IOL haptic, the latter are more easily manipulated and can be repeatedly autoclaved, making them more cost effective to use. As first recommended by Oetting and Omphroy,[72] placement of the hooks in a diamond configuration has several advantages. The subincisional retractor is inserted through a separate paracentesis track that is beneath and separate from the phaco incision. This retractor maximizes exposure immediately in front of the phaco tip and pulls the iris posteriorly behind it. The nasal retractor also facilitates placement of a chopper. If the pupil is fibrotic (eg, due to chronic miotic use or posterior synechias), overstretching it with iris retractors can cause bleeding, sphincter tears, and permanent mydriasis. This typically does not occur with the IFIS pupil, which is so elastic that it readily springs back to physiologic size despite being maximally stretched.[1] Should iris retractors have to be inserted after the capsulotomy and hydrodissection, it is useful to lift the pupil margin with a manipulating hook or with an OVD to avoid snagging the capsulorhexis edge with the retractor.

Combining Intraoperative Floppy-Iris Syndrome Strategies

There is a wide range of IFIS severity, which can vary between patients and even between eyes of the same patient.[2,4,5,7,10,37,41,56,63,67] Because of this individual variability, it is difficult to conclude whether a single IFIS management technique is superior to another without a randomized prospective trial or a bilateral eye study. There was no clear preference for any single surgical technique in the ASCRS IFIS survey (Tables 1 and 2).[13] In declining order of frequency, strategies most often used on a routine basis

Table 1. Satisfaction with different IFIS management techniques of 957 respondents to the 2008 ASCRS survey.[13]

Your Satisfaction for Managing IFIS…	Number (%)			
	Have Never Used	Tried, But Not Satisfied	Use, But Not Always	Use Routinely
With viscoadaptive OVD (Healon5)?	442 (46.2)	169 (17.7)	207 (21.6)	139 (14.5)
With iris retractors?	165 (17.2)	131 (13.7)	443 (46.3)	218 (22.8)
With pupil expansion rings?	669 (69.9)	112 (11.7)	140 (14.6)	36 (3.8)
With intracameral epinephrine or phenylephrine?	277 (28.9)	174 (18.2)	142 (14.8)	364 (38.0)

IFIS = intraoperative floppy-iris syndrome; OVD = ophthalmic viscosurgical device

were intracameral α-agonists (38%), iris retractors (23%), preoperative atropine (19%), Healon5 (15%), and pupil expansion rings (4%). However, 69% of respondents reported using iris retractors at least some of the time.

Unfortunately, there is no reliable way to predict the severity of IFIS in advance. In the prospective multicenter study,[7] IFIS severity scores did not differ according to eye color and were not reduced by stopping tamsulosin preoperatively. Other studies have failed to find a correlation between the severity of IFIS and the patient's age or duration of tamsulosin intake.[2,12] Poor preoperative dilation is a strong predictor of severe IFIS. Billowing of the iris during an initial injection of lidocaine into the anterior chamber also indicates that IFIS may ensue. As stated earlier, several studies suggest that IFIS severity is generally greater with tamsulosin than with nonselective α_1-antagonists such as alfuzosin, doxazosin, or terazosin.

Understanding this variability and being proficient with multiple management approaches allow surgeons to use a staged approach for eyes with IFIS.[56] The various strategies mentioned have complementary advantages and can be combined. In the ASCRS survey,[13] one third of respondents said they routinely use multiple strategies for IFIS cases (Table 2). Pharmacologic measures alone may be adequate for mild to moderate IFIS cases. Whether they expand the pupil, intracameral α-agonists may prevent or reduce iris billowing and prolapse by increasing the iris dilator muscle tone. The surgeon's experience and the presence of other surgical risk factors will determine with how large an intraoperative pupil the surgeon is comfortable. If the pupil diameter is inadequate, a viscoadaptive OVD can further expand it for the capsulorhexis or nuclear removal. Finally, iris retractors and pupil expansion devices should provide reliable surgical exposure in even the most severe IFIS cases. They can be considered for severe IFIS or when other surgical comorbidities (eg, dense nuclei, pseudoexfoliation, or weak zonules) are present. They may also be preferable for less experienced surgeons or when a high-vacuum phaco technique is favored.

SURGICAL RISK IN INTRAOPERATIVE FLOPPY-IRIS SYNDROME

Especially before its initial description, IFIS was associated with an increased rate of surgical complications. Problems resulting from unexpected iris prolapse and miosis included iris trauma, iris aspiration by the phaco or irrigation/aspiration tip, iridodialysis, hyphema, posterior capsule rupture, and vitreous loss.[1,4,7,9,73] Intraoperative floppy-iris syndrome with iris prolapse complicating trabeculectomy has also been reported.[74,75] An interesting case report of recurrent choroidal detachments suggests that tamsulosin might also affect the α_1-receptors in the choroid.[76]

Chang and Campbell[1] found a 12% rate of posterior capsule rupture and vitreous loss in a retrospective series of IFIS cases. Furthermore, 4 tamsulosin patients who had had cataract surgery in the contralateral nonstudy eye elsewhere were included in the retrospective and prospective arms of the study. Posterior capsule rupture and vitreous loss occurred in 2 of the 4 contralateral nonstudy eyes. Other

Table 2. Preferred initial operative strategy for managing IFIS of 957 respondents to the 2008 ASCRS survey.[13]

Most Favored Initial Strategy for IFIS	Number (%)
Topical atropine	68 (7.1)
Viscoadaptive OVD (Healon5)	105 (11.0)
Intracameral epinephrine or phenylephrine	189 (19.7)
Iris retractors	208 (21.7)
Pupil expansion ring	22 (2.3)
Other	49 (5.1)
Always use multiple strategies	316 (33.0)

IFIS = intraoperative floppy-iris syndrome; OVD = ophthalmic viscosurgical device

retrospective studies document a higher rate of posterior capsule rupture associated with unrecognized IFIS or tamsulosin use. Nguyen et al.[4] conducted a national retrospective survey in the United Kingdom and found a 7% rate of posterior capsule rupture in more than 600 cases of IFIS reported. A Canadian retrospective trial[9] had a 15% incidence of major complications when IFIS was present. A retrospective review of resident cataract surgery in patients taking tamsulosin at the Massachusetts Eye and Ear Infirmary from 2001 to 2006 showed a statistically significant increase in posterior capsule rupture (22%) compared with the rate in age-matched controls (P. Joseph, MD, et al., "Intraoperative Floppy-Iris Syndrome Associated with Tamsulosin in a Residents' Cataract Outcomes Database," poster presented at the annual meeting of the Association for Research in Vision and Ophthalmology, Fort Lauderdale, Florida, April 2006). However, during the 2-year period immediately before the first description of IFIS, 71% (5/7) of the eyes in tamsulosin patients had vitreous loss.

A prospective multicenter trial was conducted in 2005[7] to determine the incidence of surgical complications when the cataract surgeon, forewarned by a history of α_1-antagonist use, could anticipate IFIS and use alternative methods of small-pupil management. At their discretion, the surgeons selected 1 of 4 methods for managing the pupil; that is, iris retractors, a pupil expansion ring, a viscoadaptive OVD (Healon5) with low aspiration parameters, or preoperative topical atropine. A second strategy could be used if the primary method by itself was ineffective. The use of intracameral epinephrine had not been reported by the time the study was initiated and was therefore not included as a surgical option. In this study, the Healon5 method was the most common primary strategy used (60%) followed by iris retractors (31%), preoperative atropine (5%), and pupil expansion rings (4%). Of 167 consecutive eyes in 135 patients taking tamsulosin, there was only 1 case of posterior capsule rupture and vitreous loss (incidence 0.6%). The most common complications were mild to moderate iris transillumination defects, which were noted in 16% of eyes, all of which were asymptomatic.

One important criticism is that only high-volume cataract surgeons participated in the study, which therefore may not accurately represent the clinical experience in a typical community. The 2008 ASCRS IFIS survey[13] suggests that this criticism may be valid. Respondents were asked to report complications in IFIS eyes during the preceding 2 years, when recognition of its association with α_1-antagonists should have been widespread. Most respondents (95%) reported that tamsulosin increases the difficulty of cataract surgery, with 77% believing that it increases the risk for complications compared with non-tamsulosin cases. The most common complication was significant iris damage, with 52% of respondents reporting that it occurs at a higher rate than in non-IFIS eyes. Twenty-three percent of respondents reported posterior capsule rupture at a higher rate than in non-IFIS eyes. Thirty percent of respondents reported no complications in IFIS eyes during the preceding 2 years.

Undoubtedly because of the surgical risks associated with IFIS, 21% of respondents said they thought that prescribing doctors should routinely refer all patients to an ophthalmologist before tamsulosin is started. Another 38% said only patients with cataracts or decreased vision should be referred. The remaining 41% thought that a pretreatment examination was not necessary. For nonselective α_1-antagonists, the corresponding percentages were 11%, 31%, and 58%, respectively. Another question asked whether the respondent would take tamsulosin if he or she had BPH and a mildly symptomatic cataract. Nearly two thirds would not, instead electing to have cataract surgery first (24%), taking a nonselective α_1-antagonist instead (17%), or avoiding α_1-antagonists entirely (23%).

DISCUSSION

The incidence of BPH is approximately 50% in men older than 50 years and 90% in men older than 85 years.[17] The number of men with BPH who present for cataract surgery will certainly increase as the population ages. Because of its uroselectivity, the α_1A subtype selective antagonist, tamsulosin, is the most popular pharmacologic treatment for BPH, and it is also the most common cause of IFIS. The recently approved α_1-antagonist silodosin is also selective for the α_{1A}-receptor subtype. Because it is pharmacologically more similar to tamsulosin than the other nonselective α_1-antagonist, ophthalmologists should be particulary vigilant about the possibility of IFIS with this drug. Especially if it is unexpected or unrecognized, IFIS is associated with an increased rate of cataract surgical complications. Stopping the drug preoperatively is of uncertain benefit, and the popular technique of pupil stretching is ineffective and counterproductive. Although several alternative methods of small-pupil management reduce the risk for complications, phacoemulsification in eyes with IFIS is generally more difficult and surgeons must approach these cases with caution.

Because the patient's medication history can forewarn the cataract surgeon about the likelihood of IFIS, educating ophthalmologists, prescribing doctors, and patients about IFIS continues to be important. The

ASCRS first issued a global advisory alert regarding tamsulosin in January 2005. Following multiple individual physician reports later that year, the United States Food and Drug Administration instituted a labeling warning about α_1-antagonists and cataract surgery in 2005. The ASCRS, American Academy of Ophthalmology (AAO), and American Urological Association issued a joint press release in 2006 highlighting the need for patients taking systemic α_1-antagonists to inform their ophthalmologist before cataract surgery. Soon after, this message was incorporated into the direct-to-consumer advertisements for Flomax. It is advisable for cataract surgeons to ask about current or prior use of α_1-antagonists when taking a mediation history preoperatively.

Finally, following publication of the ASCRS IFIS survey results, ASCRS and the AAO issued a joint educational update statement in July 2008 that was disseminated by the American College of Physicians and the American Academy of Family Physicians to their 125 000 members and 93 000 members, respectively. For patients with known cataracts, prescribing physicians were asked to consider involving the cataract surgeon before initiating nonemergent, chronic tamsulosin or α_1-antagonist treatment. The need for this effort was underscored by a survey from the United Kingdom that was published at the same time as this educational update.[77] This survey reported that 96.8% (62/64) of referring primary care physicians were not aware of the association between tamsulosin and IFIS and approximately four fifths of those physicians prescribed more than 5 tamsulosin prescriptions per month.

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