Clinical experience with intraoperative floppy-iris syndrome

Results of the 2008 ASCRS member survey

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According to an online survey, most members of the American Society of Cataract and Refractive Surgery believe that tamsulosin makes cataract surgery more difficult (95%) and increases the risks of surgery (77%). Commonly reported complications of intraoperative floppy-iris syndrome (IFIS) were significant iris trauma and posterior capsule rupture, with 52% and 23% of respondents, respectively, reporting these complications at a higher rate than in non-IFIS eyes. There was no single preferred surgical method for managing IFIS; 33% of respondents routinely used multiple strategies. Of respondents with sufficient experience, 90% believe that IFIS is more likely with tamsulosin than with nonspecific α1-antagonists. Ninety-one percent believe that physicians prescribing α1-antagonists should become better educated about IFIS, and 59% would recommend a pretreatment ophthalmic evaluation for patients with cataracts or decreased vision. If they themselves had mildly symptomatic cataracts, 64% of respondents would avoid taking tamsulosin or would have their cataract removed first.


Since intraoperative floppy-iris syndrome (IFIS) was first described in 2005, its association with the systemic α1-adrenergic antagonist tamsulosin (Flomax) has become well established. The clinical manifestations of IFIS complicating cataract surgery are poor preoperative pupil dilation, iris billowing and prolapse, and progressive intraoperative miosis. In one prospective study, 90% of 167 eyes of patients taking tamsulosin exhibited some degree of IFIS during cataract surgery. Tamsulosin is the only systemic α1-antagonist that is selective for the α1A-receptor subtype. This renders it more uroselective, with a reduced incidence of postural hypotension. Intraoperative floppy-iris syndrome has also been reported with nonsubtype-specific α1-adrenergic antagonists such as terazosin (Hytrin), doxazosin (Cardura), and alfuzosin (Uroxatral). Because tamsulosin is the most commonly prescribed medication for benign prostatic hyperplasia (BPH), IFIS has and will continue to confront cataract surgeons on a regular basis.

Several studies confirm that cataract surgical complications increase when IFIS is not anticipated or recognized by the surgeon. The same prospective study of 167 consecutive eyes of tamsulosin patients having cataract surgery showed that when the surgeon was aware of the history of tamsulosin use, surgical risks were reduced by use of a variety of recommended small pupil management strategies. However, because only experienced, high-volume surgeons participated in this multicenter trial, the results may not be representative of the global ophthalmic surgical community. Discontinuing tamsulosin before cataract surgery did not improve the severity of IFIS in the prospective trial. It is well recognized that IFIS can occur up to several years after discontinuation of tamsulosin.

Several important clinical questions surrounding IFIS continue to be debated. Is IFIS seen as frequently with nonspecific α1-antagonists as it is with tamsulosin? What are the most popular and most effective methods for managing IFIS cases? What is the cataract...
surgical complication rate now that most ophthalmologists are aware of IFIS, can anticipate it, and can employ a variety of small pupil management strategies specifically advocated for IFIS? Do patients know to report their past or current history of α1-antagonist use when they are evaluated for cataract surgery? Finally, should patients see an ophthalmologist before initiating chronic systemic α1-antagonist treatment for lower urinary tract symptoms or hypertension? To better understand the current preferences and opinions of practicing cataract surgeons, the Cataract Clinical Committee of the American Society of Cataract and Refractive Surgery (ASCRS) surveyed the global membership about their clinical experience with IFIS.

MATERIALS AND METHODS

In March 2008, a link to an online survey was sent to the approximately 6000 email addresses on file for ASCRS members. The online anonymous survey consisted of 26 multiple choice questions (Appendix) and required fewer than 5 minutes to complete.

RESULTS

Nine hundred fifty-seven (957) members completed the survey. Most respondents (75%) were from the United States, and the entire spectrum of low- to mid- to high-volume surgeons was evenly represented (Figures 1 and 2). Eighteen percent of respondents saw fewer than 6 cases of IFIS per year, 40% saw between 6 and 24 cases, 19% saw between 25 and 36 cases, and 23% saw more than 36 cases. This means that on average, 42% of respondents saw at least 2 IFIS cases per month and 23% saw at least 3 cases per month.

The frequency with which IFIS occurred with tamsulosin versus with nonspecific α1-antagonists such as terazosin, doxazosin, or alfuzosin is shown in Tables 1 and 2. Excluding those who felt they had insufficient experience to judge, 49% encountered IFIS in most (>75%) tamsulosin patients and 70% encountered IFIS in the majority (>50%) of tamsulosin patients (Table 1). This compares with 9% who encountered IFIS in most (>75%) patients and 20% who encountered IFIS in the majority (>50%) of patients taking other α1-antagonists (Table 1). When asked to compare the relative risk for IFIS with tamsulosin versus with nonspecific α1-antagonists, 21% of respondents did not have enough experience to judge. Of those with sufficient experience, 90% believed that IFIS was more likely to occur with tamsulosin; 65% responded “much more likely” (Table 2).

Excluding respondents with insufficient experience to know, 95% of respondents said they had encountered IFIS in patients with a past history of α1-antagonist use (Table 3). Two-thirds of respondents therefore routinely questioned patients about past α1-antagonist use. Intraoperative floppy-iris syndrome associated with saw palmetto (Serona repens), an over-the-counter alternative therapy for BPH, was seen frequently by only 3% of respondents (Table 4). The same was true for IFIS associated with drugs other than α1-antagonists, although one-third of respondents believed they had seen this at some point (Table 4). Numerous efforts have been made by ophthalmic specialty societies, the U.S. Food and Drug Administration, and the manufacturer of tamsulosin to educate patients about the need to inform their cataract surgeon if they have used or currently take systemic alpha blockers. Eighty-five percent of respondents said that fewer than one-third of patients taking alpha blockers reported it to their cataract surgeon, and 55% said that fewer than 5% of patients taking alpha blockers reported it. Clearly, ophthalmologists cannot rely on patients to report this medication history.
The strategies for managing IFIS preoperatively and intraoperatively are shown in Tables 5 and 6. Preoperatively, only 20% of respondents discontinued tamsulosin before cataract surgery in most patients; 64% did not stop it (Table 5). Twenty-six percent (26%) used topical atropine for most tamsulosin patients; 57% did not (Table 5). Intraoperatively, respondents reported routine use of intracameral \(\alpha\)-agonist injections (38%), iris retractors (23%), viscoadaptive ophthalmic viscosurgical devices (OVDs) (15%), and pupil expansion rings (4%); 18%, 14%, 18%, and 12%, respectively, had tried these strategies but were dissatisfied with them (Table 6). Only 1% of respondents who had used intracameral \(\alpha\)-agonists reported observing systemic hypertensive spikes (8/688) or toxic anterior segment syndrome (TASS) (7/688). There was no clear preferred initial operative strategy for managing IFIS; one third of respondents routinely used multiple methods (Table 7).

Ninety-five percent of respondents reported that cataract surgery was more difficult in tamsulosin patients, and 77% believed there was increased surgical risk in tamsulosin patients compared with patients
who were not taking the drug (Table 8). The most commonly reported complication of IFIS was significant iris trauma; 52% of respondents reported this complication occurring at a higher rate than in non-IFIS patients (Table 9). Posterior capsule rupture in IFIS eyes was reported by 26% of respondents; 23% overall reported that this occurred at a higher rate than in non-IFIS eyes. Thirty percent of respondents had not experienced any surgical complications due to IFIS during the preceding 2 years.

Fifty-nine percent of respondents felt that patients should be referred to an ophthalmologist before starting tamsulosin if there was a history of cataract or decreased vision; 21% believed this should be done even in the absence of such a history (Table 10). For patients about to start nonspecific α1-antagonists, the percentages were 42% and 11%, respectively. Twenty-three percent of respondents reported they would have a mildly symptomatic cataract removed before taking tamsulosin for BPH. Seventeen percent would choose to avoid all systemic α1-antagonists if they were a patient in this situation; 23% would take a nonspecific α1-antagonist instead of tamsulosin (Table 11).

Forty percent of respondents felt there is a greater need for patient education about IFIS (7% strongly agree) and 55% believed that more education for ophthalmologists is needed (13% strongly agree) (Table 12). Finally, 91% of respondents believe that more

### Table 5. Preferences for preoperative management of IFIS.

<table>
<thead>
<tr>
<th>Query</th>
<th>Never</th>
<th>Occasionally (&lt;20%)</th>
<th>Sometimes (20-50%)</th>
<th>Usually (&gt;50%)</th>
<th>Routinely</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stop tamsulosin before cataract surgery?</td>
<td>64.2 (614)</td>
<td>11.4 (109)</td>
<td>5.0 (48)</td>
<td>8.6 (82)</td>
<td>10.9 (104)</td>
</tr>
<tr>
<td>Use topical atropine for tamsulosin patients?</td>
<td>56.9 (545)</td>
<td>12.3 (118)</td>
<td>4.8 (46)</td>
<td>7.4 (71)</td>
<td>18.5 (177)</td>
</tr>
</tbody>
</table>

### Table 6. Satisfaction with IFIS management techniques.

<table>
<thead>
<tr>
<th>Query</th>
<th>Have Never Used</th>
<th>Tried but Not Satisfied</th>
<th>Use but Not Always</th>
<th>Use Routinely</th>
</tr>
</thead>
<tbody>
<tr>
<td>Your satisfaction in managing IFIS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With viscoadaptive OVD (Healon5)</td>
<td>46.2 (442)</td>
<td>17.7 (169)</td>
<td>21.6 (207)</td>
<td>14.5 (139)</td>
</tr>
<tr>
<td>With iris retractors?</td>
<td>17.2 (165)</td>
<td>13.7 (131)</td>
<td>46.3 (443)</td>
<td>22.8 (218)</td>
</tr>
<tr>
<td>With pupil expansion rings?</td>
<td>69.9 (669)</td>
<td>11.7 (112)</td>
<td>14.6 (140)</td>
<td>3.8 (36)</td>
</tr>
<tr>
<td>With intracameral epinephrine/phenylephrine?</td>
<td>28.9 (277)</td>
<td>18.2 (174)</td>
<td>14.8 (142)</td>
<td>38.0 (364)</td>
</tr>
</tbody>
</table>

### Table 7. Preferred initial operative strategy for managing IFIS.

<table>
<thead>
<tr>
<th>Query</th>
<th>Topical Atropine</th>
<th>Viscoadaptive OVD (Healon5)</th>
<th>Intracameral Epinephrine/Phenylephrine</th>
<th>Iris Retractors</th>
<th>Pupil Expansion Ring</th>
<th>Other</th>
<th>I Always Employ Multiple Strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Your most favored initial strategy for IFIS?</td>
<td>7.1 (68)</td>
<td>11.0 (105)</td>
<td>19.7 (189)</td>
<td>21.7 (208)</td>
<td>2.3 (22)</td>
<td>5.1 (49)</td>
<td>33.0 (316)</td>
</tr>
</tbody>
</table>

### Table 8. Difficulty of cataract surgery in patients with known history of tamsulosin use.

<table>
<thead>
<tr>
<th>Query</th>
<th>No Different</th>
<th>More Difficult than in Non-IFIS Patients, but Surgical Risks No Higher</th>
<th>More Difficult, with Slightly Increased Surgical Risk</th>
<th>Very Difficult, with Increase in Surgical Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>On average, how difficult is cataract surgery in patients with a known history of taking tamsulosin?</td>
<td>5.1 (49)</td>
<td>17.6 (68)</td>
<td>64.6 (618)</td>
<td>12.7 (122)</td>
</tr>
</tbody>
</table>
education about \(\alpha_1\)-antagonists causing IFIS is needed for prescribing physicians (urology, family practice, internal medicine) (Table 12). Fifty-four percent would strongly agree compared with fewer than 3% who would disagree.

**DISCUSSION**

An online survey alone cannot provide definitive conclusions or recommendations because there are many potential biases in the responses. Nevertheless, there are several clinically relevant implications in the survey results.

Intraoperative floppy-iris syndrome has been reported with both \(\alpha_{1A}\) specific and nonspecific \(\alpha_1\)-antagonists, as well as with medications outside this drug class.\(^2\)\(^\text{-}^\text{7}\) However, this survey supports growing evidence that IFIS is much more strongly associated with tamsulosin.\(^2\)\(^\text{-}^\text{7}\)\(^\text{9}\) Excluding those who report insufficient experience, more respondents saw at least some signs of IFIS in the majority of tamsulosin patients (70% of respondents) than in the majority of nonspecific \(\alpha_1\)-blocker patients (20% of respondents). Ninety percent felt that IFIS was more common with tamsulosin than with nonspecific \(\alpha_1\)-antagonists (with nearly two thirds believing that it is much more common). It is therefore appropriate to consider whether phakic patients should be started on nonspecific \(\alpha_1\)-antagonists first for the treatment of lower urinary tract symptoms if other prescribing factors are equal. Of the nonspecific \(\alpha_1\)-antagonists, alfuzosin is clinically uroselective, with significantly less tendency to cause postural hypotension than terazosin or doxazosin.\(^7\)\(^\text{10}\)\(^\text{11}\)

In a retrospective study, Blouin et al.\(^6\) reported that 86% of patients on tamsulosin had IFIS compared with 15% of patients on alfuzosin (\(P < .001\)). Palea et al.\(^9\) performed the first laboratory study of \(\alpha_1\)-antagonist pharmacology in isolated iris dilator muscle strips from pigmented rabbits. They found that tamsulosin was a much stronger antagonist of iris dilator muscle contraction than alfuzosin. In addition, based on the comparative findings with isolated prostatic smooth muscle blockade, they hypothesized that an additional receptor besides the \(\alpha_1\) receptor might be involved in iris dilator muscle contraction. This might explain the much stronger tendency for tamsulosin to block iris dilator muscle contraction in their experimental model and to cause clinical IFIS compared with alfuzosin.

A second clinical issue relates to the best surgical strategy to manage IFIS in patients taking systemic \(\alpha_1\)-antagonists. Our survey shows that surgeons are using a variety of methods with no single method favored by a clear majority. The following percentages of respondents indicated that they routinely or occasionally used the following strategies for cataract surgery: discontinuing the \(\alpha_1\)-antagonist antagonist preoperatively (36%), preoperative topical atropine (43%), viscoadaptive OVD (36%), iris retractors

<table>
<thead>
<tr>
<th>Query</th>
<th>Not Necessary</th>
<th>Only If History of Cataracts/Decreased Vision</th>
<th>Yes, Routinely</th>
</tr>
</thead>
<tbody>
<tr>
<td>Should prescribing MDs refer patients to an ophthalmologist</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior to starting tamsulosin?</td>
<td>41.5 (397)</td>
<td>37.8 (362)</td>
<td>20.7 (198)</td>
</tr>
<tr>
<td>Prior to starting alpha blockers other than tamsulosin?</td>
<td>57.7 (552)</td>
<td>31.3 (300)</td>
<td>11.0 (105)</td>
</tr>
</tbody>
</table>
Table 11. Preferences for self-management.

<table>
<thead>
<tr>
<th>Query</th>
<th>No, Would Take Nonspecific Alpha Blocker Instead</th>
<th>No, Would Avoid All Alpha Blockers If Possible</th>
<th>Yes, Would Do So If Recommended</th>
<th>Yes, but Would Have Cataract Surgery Performed First</th>
</tr>
</thead>
<tbody>
<tr>
<td>Would you take tamsulosin if you had BPH and mildly symptomatic cataracts?*</td>
<td>17.3 (166)</td>
<td>23.2 (222)</td>
<td>36.1 (345)</td>
<td>23.4 (224)</td>
</tr>
</tbody>
</table>

*Females asked to answer as males.
recommend it for patients who might and cataract surgery based on how many of the respondents (64%) would manage or treat themselves differently if they were faced with BPH and mildly symptomatic cataracts. Overall, 91% of respondents believed that urologists and primary care physicians should be better educated about IFIS; fewer than 3% disagreed. That the majority of ophthalmologists would recommend a pretreatment eye evaluation for patients with cataracts or decreased vision should be emphasized as part of that education. Based on the results of this survey, the ASCRS Cataract Clinical Committee plans to initiate a campaign, in partnership with the American Academy of Ophthalmology and the appropriate non-ophthalmic specialty societies, to better educate pharmacists and prescribing physicians about IFIS caused by tamsulosin and other α1-antagonists.

In conclusion, according to a large online survey, 95% of ASCRS respondents currently believe that tamsulosin makes cataract surgery more difficult and 77% believe that it increases the risks of surgery. Twenty-three percent reported an increased rate of posterior capsule rupture in eyes with IFIS during the previous 2 years. Of those respondents with enough experience to judge, 90% believed that IFIS was more likely to occur with tamsulosin than with nonspecific α1-antagonists. We believe these findings explain the strong consensus that physicians prescribing α1-antagonists should become better educated about IFIS and why a majority of ophthalmologists would recommend a pretreatment ophthalmic evaluation for patients with cataracts or decreased vision. Because nearly two-thirds of the respondents would avoid taking tamsulosin if they had a mildly symptomatic cataract or would have their cataract removed first, it is reasonable that they would want their patients to have the same options. This important information should be conveyed to pharmacists and prescribing physicians, who might consider referring patients with cataracts or decreased vision for an ophthalmic evaluation before starting long-term treatment with α1-antagonists in general and with tamsulosin in particular.

REFERENCES


APPENDIX

ASCRS 2008 IFIS QUESTIONNAIRE

1. Annual cataract volume

( ) < 100 cases ( ) 100–300 cases
( ) 300–500 cases ( ) > 500 cases

2. Your location

( ) United States ( ) Canada ( ) Europe
( ) Latin/South America/Mexico ( ) Africa
( ) Australia/Asia

3. Number of intraoperative floppy iris (IFIS) cases that you see per year

( ) < 6
( ) 6–24
( ) 25–36
( ) 36

4. In your experience, how many patients taking tamsulosin have IFIS to any degree?

( ) Almost all (>90%)
( ) Most (75–90%)
( ) Majority (50–75%)
( ) Many (25–50%)
( ) Minority (10–25%)
( ) Very few (<10%)
( ) Not enough experience to know
5. In your experience, how many patients taking nonspecific alpha blockers (terazosin, doxazosin, alfuzosin) have IFIS to any degree?
   ( ) Almost all (>90%)
   ( ) Most (75–90%)
   ( ) Majority (50–75%)
   ( ) Many (25–50%)
   ( ) Minority (10–25%)
   ( ) Very few (<10%)
   ( ) Not enough experience to know

6. Is IFIS more likely with tamsulosin or the nonspecific alpha blockers?
   ( ) Much more likely with tamsulosin
   ( ) Somewhat more likely with tamsulosin
   ( ) Equally likely
   ( ) Somewhat more likely with nonspecific alpha blockers
   ( ) Much more likely with nonspecific alphablokers
   ( ) Not enough experience to know

7. Have you encountered IFIS in patients with a PAST history of alpha blocker use
   ( ) Never
   ( ) Yes—but rare so I don't routinely ask about alpha blocker history
   ( ) Yes—and I always ask about alpha blocker history
   ( ) Not sure or not enough experience to know

8. Have you encountered IFIS with saw palmetto?
   ( ) Yes—but uncommon
   ( ) Yes—frequently
   ( ) No
   ( ) Not sure or not enough experience to know

9. Have you encountered IFIS with drugs other than alpha blockers?
   ( ) Yes—but uncommon
   ( ) Yes—frequently
   ( ) No
   ( ) Not sure or not enough experience to know

10. How many patients taking alpha blockers know to report this to the ophthalmologist?
    ( ) Never happens
    ( ) Small minority (<5%)
    ( ) Some do (5–33%)
    ( ) Many do (33–66%)
    ( ) Majority do (66–95%)
    ( ) Everyone does (>95%)

11. Do you stop tamsulosin prior to cataract surgery?
    ( ) Never
    ( ) Occasionally (<20%)
    ( ) Sometimes (20–50%)
    ( ) Usually (>50%)
    ( ) Routinely

12. Do you use preoperative topical atropine for tamsulosin patients?
    ( ) Never
    ( ) Occasionally (<20%)
    ( ) Sometimes (20–50%)
    ( ) Usually (>50%)
    ( ) Routinely

13. Your satisfaction with viscoadaptive OVD (Healon 5) for managing IFIS
    ( ) Never have used
    ( ) Tried but not satisfied
    ( ) Use but not always
    ( ) Use routinely

14. Your satisfaction with iris retractors for managing IFIS
    ( ) Never have used
    ( ) Tried but not satisfied
    ( ) Use but not always
    ( ) Use routinely

15. Your satisfaction with pupil expansion rings for managing IFIS
    ( ) Never have used
    ( ) Tried but not satisfied
    ( ) Use but not always
    ( ) Use routinely

16. Your satisfaction with intracameral epinephrine or phenylephrine for managing IFIS
    ( ) Never have used
    ( ) Tried but not satisfied
    ( ) Use but not always
    ( ) Use routinely

17. Have you experienced complications with intracameral epinephrine or phenylephrine?
    ( ) Have never used
    ( ) Have used, but no complications
    ( ) Excessive corneal edema
    ( ) TASS or excessive inflammation
    ( ) Systemic hypertensive spike
18. Your most favored initial strategy for managing IFIS:
   ( ) Topical atropine
   ( ) Viscoadaptive OVD (Healon5) + lowered fluidics
   ( ) Intracameral epinephrine or phenylephrine
   ( ) Iris retractors
   ( ) Pupil expansion ring
   ( ) Other

   ( ) I always employ multiple strategies

19. On average, how difficult is cataract surgery in patients with a known history of taking tamsulosin?
   ( ) No different than non-IFIS patients
   ( ) More difficult than non-IFIS patients, but surgical risks no higher
   ( ) More difficult, with slightly increased surgical risk
   ( ) Very difficult, with increase in surgical risk

20. Have you had cataract surgical complications in IFIS patients during the past 2 years? (can check more than one response)
   ( ) No personal experience with IFIS
   ( ) No complications
   ( ) Yes—posterior capsule rupture (higher rate than non-IFIS pts)
   ( ) Yes—posterior capsule rupture (same or lower rate than non-IFIS pts)
   ( ) Yes—significant iris damage (higher rate than non-IFIS pts)
   ( ) Yes—significant iris damage (same or lower rate than non-IFIS pts)
   ( ) Yes—other (higher rate than non-IFIS pts)
   ( ) Yes—other (same or lower rate than non-IFIS pts)

21. Should prescribing doctors refer patients to an ophthalmologist prior to starting tamsulosin?
   ( ) Not necessary
   ( ) Only if (+) history of cataract or decreased VA
   ( ) Yes, routinely

22. Should prescribing doctors refer patients to an ophthalmologist prior to starting alpha blockers other than tamsulosin?
   ( ) Not necessary
   ( ) Only if (+) history of cataract or decreased VA
   ( ) Yes, routinely

23. Would you take tamsulosin if you had BPH and mildly symptomatic cataracts? If female, please answer as though male.
   ( ) No—would take a nonspecific alpha blocker instead
   ( ) No—would avoid all alpha blockers if possible
   ( ) Yes—would do so if recommended
   ( ) Yes—but would have cataract surgery performed first

24. Manufacturer patient education and regulatory authority labeling (eg, FDA) regarding IFIS are adequate.
   ( ) Strongly agree
   ( ) Agree
   ( ) No opinion
   ( ) Disagree
   ( ) Strongly disagree

25. Should ASCRS provide more education to ophthalmologists on IFIS?
   ( ) Strongly agree—should have much more
   ( ) Agree—there should be more
   ( ) No opinion
   ( ) Disagree—most necessary information already adequate
   ( ) Strongly disagree—already more than enough

26. Education for nonophthalmic MDs (urology, family practice, internal medicine) about IFIS should be greater.
   ( ) Strongly agree
   ( ) Agree
   ( ) No opinion
   ( ) Disagree
   ( ) Strongly disagree