INTRAOPERATIVE FLOPPY IRIS SYNDROME: PATHOPHYSIOLOGY, PREVENTION, AND TREATMENT

BY **Allan J. Flach MD PharmD***

ABSTRACT

Purpose: To extend upon previous reports, observations, and discussions of intraoperative floppy iris syndrome (IFIS) with the goal of providing new insight into the syndrome's pathophysiology, prevention, and treatment.

Methods: Following a review of IFIS and its relationship to autonomic pharmacology, evidence for anatomic changes following exposure of humans and other animals to autonomic drugs is described. The clinical implications for these findings are discussed as they relate to the treatment and prevention of this syndrome.

Results: IFIS has been associated with the use of adrenergic antagonists even after they have been discontinued years prior to surgery. Some investigators believe that this persistence of IFIS reflects anatomic structural change. Evidence from laboratory experiments and human clinical studies using topically applied and systemic autonomic drugs supports the possibility of anatomic changes coexisting with IFIS observed during cataract surgery.

Conclusions: IFIS is a relatively rare syndrome, often associated with the use of systemic α-blockers and conditions that influence dilator muscle tone. Laboratory and clinical evidence supports the possibility of anatomic changes following the use of autonomic drugs. The persistence of IFIS years after cessation of treatment with α-blockers suggests that the potential risks of discontinuing these drugs prior to cataract surgery outweigh potential benefits.

Trans Am Ophthalmol Soc 2009;107:234-241

INTRODUCTION

During 2005, intraoperative floppy iris syndrome (IFIS) and its relationship to the systemic use of α-blockers, in particular tamsulosin HCl (Flomax; Boehringer Ingelheim Pharmaceuticals Inc, Ridgefield, Connecticut), were reported for the first time.[1] Early investigations defined the syndrome its clinical characteristics, incidence, associated surgical outcomes, potential etiologies, and possible treatments. Thereafter, anecdotal reports confirmed the existence of the syndrome and continued to explore other potential treatments and precautions in an effort to minimize surgical complications associated with the syndrome. This report summarizes and extends upon the published reports, observations, and discussions, with the goal of providing an updated ophthalmic clinical pharmacology review of IFIS and its relationship to autonomic pharmacology, as well as potential etiology and suggested methods to prevent and treat the syndrome.

METHODS AND RESULTS

Identification of IFIS requires the recognition of a triad of clinical signs: (1) progressive pupil constriction during surgery, (2) an iris that appears floppy as it billows during normal irrigation and aspiration in the anterior chamber of the operated eye, and (3) a tendency for the iris to prolapse into the phacoemulsification and side port incisions throughout surgery. This triad may or may not be associated with a poorly dilated pupil prior to surgery. Following is a review of why this syndrome is unique, remains poorly understood, and continues to be clinically troublesome for surgeons who encounter it during cataract surgery.

REVIEW OF IFIS STUDIES

Initially, IFIS was observed in association with the α-blocker tamsulosin following retrospective observations made by John R. Campbell, MD (J.R.C.). Soon thereafter, Dr Campbell and David F. Chang, MD (D.F.C.) completed both a retrospective and a prospective study, respectively, to define this syndrome.[1]

The retrospective study involved all the patients undergoing operation in one practice (J.R.C.) by two surgeons during the previous year (2003). A "floppy iris" was recorded in the operative report of 16 of 706 eyes, or 10 of 511 patients. This 2% incidence of "billowing irises" occurred in patients using tamsulosin. In this study, six patients taking tamsulosin did not have IFIS. In addition, some patients were using different systemic α-blockers, and none of them demonstrated a floppy iris.

In the prospective study of 900 consecutive surgical cases in which the surgeon (D.F.C.) was masked as to the patient's medications, 21 of 900 eyes (2%), or 16 of 741 patients (2%), were believed to have IFIS. Among these patients, 15 of 16 were either using tamsulosin or had taken it previously. Not one of the 725 patients without IFIS had been exposed to tamsulosin. Therefore, the incidence of IFIS in these two combined studies, which totaled more than 1,600 eyes and 1,250 patients, is consistently about 2%.[1] Since its original description, IFIS and its association with systemic α_1-adrenergic antagonists, in particular tamsulosin, have been reported worldwide,[2-7] with one study[5] reporting that 90% of 167 eyes of patients taking tamsulosin exhibited some degree of IFIS during cataract surgery.

Although there are other possible etiologies for iris prolapse or intraoperative miosis during cataract surgery, the combined presence of all of three clinical features that define the syndrome makes it unique. In addition to the triad of defining characteristics, occasionally the pupil dilates poorly prior to surgery when the syndrome is present. However, the preoperative and early intraoperative

*Presenter.
Bold type indicates AOS member.
From the Department of Ophthalmology, University of California, San Francisco (UCSF) Medical Center.

suboptimal mydriasis is quite variable. In fact, the surgeon frequently develops a false sense of safety as the capsulorrhexis is easily completed early during the cataract surgery. In this circumstance, unfortunately, it is not until phacoemulsification is under way that the syndrome becomes manifest. Commonly used methods of enhancing surgical exposure of the lens when confronted with a miotic pupil during phacoemulsification, such as pupil stretching and small sphincterotomies, are ineffective techniques in this setting. Furthermore, inserting iris hooks or pupil expanders following completion of the capsulorrhexis can easily tear the anterior capsulorrhexis edge, destroying the integrity of the curvilinear capsulorrhexis. Therefore, it is not surprising that this syndrome, even if recognized in a timely fashion, appears to be associated with an increased incidence of posterior capsule rupture and vitreous loss.[1,4-7]

Although IFIS has been most recently described as associated with systemic α-blocker ingestion, it is premature to conclude that alpha blockade is the only underlying cause of this syndrome and that it is the only mechanism by which this triad of signs can occur. Investigators have suggested that the existing clinical studies would be strengthened by including additional clinical data, such as more complete and detailed descriptions of coexistent diseases and drug doses, coupled with more careful collecting of drug data. Furthermore, a greater understanding of the α-blockers and other drugs used prior to surgery of the reported cases is indicated.[8]

RELATED AUTONOMIC PHARMACOLOGY

Systemic α-blockers are used to treat the urinary symptoms of benign prostatic hypertrophy (BPH). These agents relax smooth muscle in the prostate and bladder. More than 80% of patients with BPH in the United States use tamsulosin because of the belief it is associated with less postural hypotension than other treatments. However, this potential benefit is not well documented. BPH and its associated lower urinary tract symptoms involve the prostate, urethra, bladder, and spinal cord. The α_{1A}- and α_{1D}-receptors predominate in all of these organs, but all three α_1-adrenergic receptor subtypes are present. Therefore, α-blockers are useful in ameliorating symptoms associated with BPH, and this alpha blockade can influence iris behavior. Although most reports of IFIS describe men, urologists occasionally attempt to treat urinary retention problems in women with these same α-blockers.[9] Therefore, reports of women demonstrating IFIS, as well as men, should be anticipated.

At least 9 adrenergic receptors (α_1- and α_2-receptors and their subtypes) have been identified using molecular pharmacology. These subtypes (3 of which are α_1-receptors) are distinguished by their pharmacology, structure, interactions with second messenger systems, and anatomic location at the nerve terminal synaptic area.[10]

Four α_1-blockers that are in use in the United States have the following relative receptor binding affinities:

1. Tamsulosin (Flomax): alpha 1a = alpha 1d > alpha 1b
2. Terazosin (Hytrin): alpha 1a = alpha 1d = alpha 1b
3. Doxazosin (Cardura): alpha 1a = alpha 1d = alpha 1b
4. Alfuzosin (Uroxatral): alpha 1a = alpha 1d = alpha 1b

Therefore, while all of these adrenergic antagonists are α_1-blockers, tamsulosin differs, having a greater degree of specificity for the α_{1A}-receptor in its binding affinities compared to the other three α-antagonists.[11] This may be clinically important because a retrospective study reports that 86% of the patients using tamsulosin had IFIS compared with 15% of those using alfuzosin ($P < .001$).[6] In addition, tamsulosin appeared to be a more potent antagonist of iris dilator muscle contraction in pigmented rabbits compared to alfuzosin in at least one laboratory investigation.[12] This study also revealed potentially different receptors in prostate compared to iris within these rabbits. The investigators propose a theory to explain observed differences between different α-antagonists. Although in most animal studies, α_{1A}-receptors are reported to be the predominant subtype in the iris dilator muscle,[9,13,14] it has been recognized for more than four decades that extrapolating results from rabbit studies to humans can be misleading owing to other differences between receptors in the iris of different animal species.[15]

DISCUSSION

There is a wide range of severity of IFIS reported within the literature. Mild cases have minimal billowing of the iris and dilate well, which permits any of the recommended treatment techniques to be successful in controlling the undesirable iris behavior during the surgery. However, severe cases demonstrating marked iris billowing, extensive and repetitive iris prolapse, and marked intraoperative miosis require use of iris retractors, hooks, or expanders to complete the surgery comfortably.[1-7] Naturally, this great variability in severity of IFIS, and its unpredictability, even within one patient, make comparisons between individual cases and reports of different treatments and their relative effectiveness difficult. Therefore, because of the existing evidence in the literature, decisions concerning the optimum preventative measures and treatments are difficult to make and definitive studies of the prevention and treatment of the syndrome are difficult to design.

Simply discontinuing use of an α-blocker treatment regimen prior to surgery is usually not an effective remedy, because IFIS has been associated with the use of adrenergic antagonists even after they have been discontinued years prior to the surgery.[1,5] Some believe that the persistence of IFIS long after discontinuing the associated drug reflects permanent anatomic changes within the iris.[16,17] This suggestion begs the question, Is there any evidence within the literature that anatomic changes can occur within the eye following the use of autonomic drugs?

EVIDENCE FOR ANATOMIC STRUCTURAL CHANGES ASSOCIATED WITH DRUGS ACTIVE UPON THE AUTONOMIC NERVOUS SYSTEM

There is clinical and laboratory evidence that anatomic changes can be associated with the topical and systemic administration of drugs used to manipulate the autonomic nervous system. Topically applied parasympathomimetic drugs have long been recognized to break down the blood-aqueous barrier and even result in a fibrinous iritis.[18] This tendency to break down the blood-aqueous barrier has clinical significance for surgery for glaucoma patients and the success of trabeculectomy.[19] Furthermore, permanently miotic pupils and anatomically changed sphincter muscles have accompanied the long-term use of the parasympathomimetics during therapy for glaucoma. These miotic changes make cataract surgery more challenging.

In addition to parasympathomimetics, topically administered sympathomimetic drugs have been associated with an increase in floating cells within the anterior chamber of the human eye that can be mistaken for a persistent iritis.[20] Furthermore, patients treated with sympathomimetics achieving a satisfactory mydriasis on one day will often demonstrate a rebound miosis resulting in a clinically significant decrease in dilatation of 30% to 40% on the following day.[21] For this reason, many retinal and cataract surgeons discourage the use of sympathomimetics for dilation of patients on the day prior to surgery. Therefore, there are reports of clinical examples of autonomic drugs inducing grossly visible anatomic changes within human eyes following their topical administration.

In addition to these clinical observations, laboratory studies provide evidence that anatomic structural change can accompany both topical and systemic sympathomimetic drug treatments in experimental animals and humans. Topically applied 6-hydroxydopamine (6-OHDA), owing to its structural similarity to norepinephrine, can be taken up by postganglionic sympathetic nerve terminals, resulting in nerve terminal destruction.[22] This chemical sympathectomy results in decreased nerve terminal uptake of not only endogenous norepinephrine but also exogenously applied epinephrine, and an enhancement of the therapeutic activity from topically applied epinephrine is achieved. This supersensitive pharmacologic state has been used, clinically, during the treatment of glaucoma to enhance the clinical effects of topically applied epinephrine.[23]

Subsequently, in an effort to prove that the biphasic onset of action of epinephrine on intraocular pressure is a reflection of supersensitivity, epinephrine was studied for an ability to damage adrenergic postganglionic nerve terminals. It was reasoned, insofar as norepinephrine is the endogenous postganglionic sympathetic neurotransmitter within the iris, that exogenous epinephrine, recognized as foreign to these nerve terminals, might induce destructive changes within them, similar to those degenerative changes observed following use of 6-OHDA. Evidence supporting this hypothesis has been provided using electron microscopy, catecholamine radioenzyme assays, and histofluorometric techniques.[24-30] These laboratory investigations culminated in the demonstration of degenerative anatomic structural changes induced by the administration of epinephrine 1% during the treatment of glaucoma.[30] The clinical significance of these pharmacologic observations for the treatment of glaucoma and their relationship to the pharmacodynamics or therapeutic effects of epinephrine remain obscure.

Nevertheless, this demonstration of anatomic changes following use of sympathomimetics in several species, including humans, provides a precedent for the possibility of structural changes following the systemic administration of exogenous sympathomimetic and sympatholytic agents, and this, in turn, could explain the long-lasting effects following termination of treatment. Phenoxybenzamine (1 mg/kg), a nonspecific α_1- and α_2-blocker, was used in one of these studies to enable cats to tolerate supralethal doses of epinephrine.[24] This nonspecific α-blocker treatment was not associated with evidence of anatomic structural changes compared to untreated controls. Although this observation does not provide evidence for structural changes associated with α-blockers, it does not rule out the possibility that anatomic changes may occur in patients treated for longer durations with more specific α_1-antagonists. Clearly, all of these observations simply suggest a potential pathogenesis related to structural damage as a possible explanation for the prolonged effects of α-blockers that have been described, by providing a precedent, but not proof, which would require a more definitive study.

STUDIES WITH TAMSULOSIN IN HUMANS

Light microscopy was performed on 14 eyes removed from patients treated with tamsulosin prior to death and compared to specimens taken from untreated controls. Mean iris dilator muscle thickness was significantly less in tamsulosin-treated patients (P = .004) compared to controls, without differences noted within the stroma.[31] There was no correlation with dose of the α-blocker. The presence of diabetes or lens changes did not influence the results. In addition, transmission electron microscopy showed decreased myofibrils and increased vacuoles in the tamsulosin-treated eyes. The investigators concluded that this provides evidence for dilator muscle atrophy related to treatment with this α-blocker.

In different experiments, the eyes of 29 patients treated with tamsulosin were compared to untreated controls with special attention to their irises using ocular coherence tomography (OCT). A significantly decreased dilator muscle thickness was noted in irises of tamsulosin-treated patients (P = .001) compared to controls. This appeared to be dose-related.[32,33] These observations have been considered further evidence for muscle atrophy related to α-blockers.

Although both studies report decreased iris dilator muscle thickness in tamsulosin-treated patients, which may coexist with muscle atrophy, these observed findings could simply reflect the pharmacologic effect of the α-blocker. More specifically, α-blockers produce miosis, which is accompanied by a measurable thinning of the dilator muscle as the pupil becomes smaller and the dilator muscle stretches from its insertion. In contrast, sympathomimetics are associated with a measurable thickening of the dilator muscle as this radial muscle contracts, enlarging the pupil. In addition, decreased myofibrils and increased vacuoles do not necessarily indicate muscular atrophy.

In conclusion, there are clinical observations that reflect anatomic changes that can accompany the use of autonomic drugs,

including evidence for breakdown of the blood-ocular barriers and permanent changes in the iris sphincter muscle. Furthermore, there is evidence using several experimental and laboratory techniques, including electron microscopy, catecholamine radioenzyme assays, and histofluorescence, that drugs used to manipulate the autonomic nervous system can induce anatomic changes within tissues of the eye, including the iris, that persist long after the drug is discontinued. Finally, two clinical studies report observations from humans demonstrating decreased iris dilator muscle thickness in tamsulosin-treated patients, which can coexist with atrophy. In spite of these different lines of evidence, we await a definitive study. For example, a potentially more conclusive study might compare tamsulosin-treated eyes having demonstrated IFIS to tamsulosin-treated eyes that have not manifested the syndrome, looking for a greater effect on iris dilator muscle thickness in treated eyes compared to controls. This comparison would be more relevant to the question of drug-induced atrophy within the dilator muscle that might explain the long duration of IFIS following cessation of the α-blocker. Therefore, the pathogenesis underlying the long duration of IFIS, even present years after cessation of α-blocker treatment, remains a conundrum.

AN ALTERNATIVE TREATMENT FOR BPH: ALPHA-REDUCTASE INHIBITORS

Finasteride is a 5α-reductase inhibitor that blocks the production of endogenous dihydrotestosterone, which helps reduce the size of enlarged prostates, thereby providing relief from symptoms of BPH. It is commercially available as Proscar (Merck & Co Inc, Whitehouse Station, New Jersey) and is approved by the US Food and Drug Administration for relief of the symptoms that accompany BPH. The Prostate Cancer Prevention Trial,[34] sponsored by the National Cancer Institute and Merck & Co Inc, was a prospective, placebo-controlled, randomized trial that followed 19,000 men 55 years of age or older for 7 years looking for the pharmacologic effects, beneficial and detrimental, of finasteride. Recent analysis of the data reports that this treatment not only benefits symptoms of BPH, but it reduces the risk of prostate cancer by 30% and is not associated with prostate cancers that are more aggressive, as originally suggested.[35-38] This medication is available in an inexpensive generic form. These findings provide an incentive to consider finasteride as a first-line treatment for BPH. Side effects include reduced hair loss (the FDA approved a lower-strength finasteride marketed as Propecia, Merck & Co Inc, for this indication) and a low incidence of decreased libido, which diminishes with time.[38] A recent editorial[39] provides a good rationale for trying finasteride as a first-line treatment for BPH symptoms, whether or not cataracts are present, and strongly advocates educating both patients and our internal medicine colleagues about BPH treatment and its relationship to cataract surgery.

CLINICAL IMPLICATIONS

What should the surgeon do when a patient is using tamsulosin? Discontinuing any α-blocker for 1 or 2 weeks prior to surgery may help but does not prevent IFIS. In fact, a prospective study[5] reported that discontinuation of tamsulosin before cataract surgery did not decrease the severity of IFIS. Therefore, it is less than prudent to discontinue α-blockers used for BPH abruptly prior to surgery without careful discussion with the patient and urologist. Discontinuing α-blockers in patients with BPH can result in urinary retention, which will be further exacerbated during surgery by the use of concurrent drugs with parasympathomimetic activity, particularly atropine.

IFIS can be prevented and treated by maintaining mydriasis and restraining the iris from prolapsing during cataract surgery. This can be accomplished by mechanical and pharmacologic treatments and the use of intraoperative proper phacoemulsification fluidic parameters. The most reliable method of maintaining an adequate pupil during cataract surgery in severe cases of IFIS is the use of iris hooks, iris retractors, or expansion rings. Iris retractors and hooks are best placed in diamond configuration with incision just posterior to clear corneal incision. Useful pharmacologic agents described in the literature include preoperative atropine at various intervals prior to surgery and intraoperative phenylephrine or epinephrine injected under iris. Modifying phacoemulsification fluidic parameters to include lower aspiration flow (<22 mL/min) and lower vacuum (<200 mm Hg) is helpful. Finally, viscoelastic agents, ideally used with lower phacoaspiration and vacuum settings, can be effective, often requiring repeated injections. Unfortunately, it is difficult to study the relative effectiveness of these techniques, because IFIS is so variable in its relationship to α-blockers and in its severity when manifest even within the same patient. It is not surprising that studies simply conclude that retracting iris or expanding the pupil by some means is the only reliable method to manage severe IFIS.[5]

Recently, members of the American Society of Cataract and Refractive Surgery were surveyed for their opinions. A response from 957 of 6,000 members who were e-mailed the survey revealed that 95% agreed that tamsulosin appears to make cataract surgery more difficult and 77% believed that it increases the risk of surgery.[40] Complications such as iris trauma (52%) and posterior capsule rupture (23%) were reported as more common in eyes with IFIS. Furthermore, 90% believed that IFIS is more likely to accompany tamsulosin use as compared to the nonspecific α_1-antagonists. A significant percentage (64%) polled would avoid tamsulosin themselves if they had early cataracts or would even have the cataract removed before initiating treatment with tamsulosin. Many members (33%) use a combination of techniques and strategies to manage the syndrome, particularly in severe IFIS. Finally, 91% believe physicians prescribing α_1-antagonists should be better educated about the syndrome, and 59% would recommend an ophthalmic evaluation for any patient with known cataracts or decreased vision prior to initiating treatment with the α-blocker.

CONCLUSIONS

IFIS is a relatively rare syndrome, reported in approximately 2% of cataract surgery cases. It is not always bilateral, and while often associated with the use of systemic α-blockers, particularly tamsulosin, it can be observed with other systemic α-blockers and related to other drugs and diseases that influence dilator muscle tone. These conclusions have been confirmed by a recent study.[41]

Laboratory and clinical evidence provides a precedent for the possibility of long-term anatomic structural changes following the use of autonomic drugs, which may help explain the persistence of IFIS months after cessation of treatment with α-blockers. However, we await a definitive study to delineate the pathogenesis of IFIS and its relationship to diseases and drugs. The potential risks of discontinuing α-blockers prior to cataract surgery outweigh potential benefits without thoughtful interaction with the patient and the treating urologist.

Severe IFIS is most effectively managed with iris retractors, hooks, or expanders. Mild to moderate cases can be managed by many different techniques applied alone or, most often, sequentially. Most investigators and clinicians agree that patient and physician education about this syndrome is important. Finally, it seems only prudent to mention finasteride and its potential advantages, including its potential to prevent prostate cancer, to patients with symptoms of BPH.

ACKNOWLEDGMENTS

Funding/Support: None.

Financial Disclosures: None.

APPENDIX

Examples of pharmacologic agents mentioned as "preferred techniques" for cataract surgery in non-refereed publications and in reports from national and international meetings.

Preoperative

- Atropine, 1%, one drop daily for 10 days (Kevin Smith, MD, Canada)
- Atropine, 1%, and brimonidine (Alphagan), one drop each for two doses, 1 hour before surgery (Ernest Howerton, MD, Austin, Texas)
- Atropine, 1%, every 10 minutes for three doses (Eugene Liu, MD, Canada)
- Atropine ointment the day before surgery (Jon-Marc Weston, MD, Oregon)

(Often various combinations of the above regimens are added to a "usual regimen.")

Intraoperative

- Phenylephrine, 2.5%, preservative-free (Minims, Chauvin Pharmaceuticals, UK), given intracamerally, 7 drops in 1 mL saline solution (Richard Packard, MD, London, England)
- Epinephrine, 1:100,000, nonpreserved, in 0.9 mL balanced salt solution, given intracamerally (Jeffrey Nightingale, MD, New York, New York)
- Epinephrine and anesthetic

3 mL BSS Plus and 1 mL nonpreserved lidocaine, 4% (Abbott Labs) ("Shugarcaine") combined with 1:1000 bisulfite-free epinephrine (American Reagent, Shirley, New York). Final mixture is one part epinephrine to three parts "Shugarcaine" (Joel Shugar, MD, Perry Florida)

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PEER DISCUSSION

DR. PRESTON H. BLOMQUIST: Dr. Flach presents an excellent review of our current state of knowledge of intraoperative floppy iris syndrome (IFIS), and his discussion has illuminated several areas requiring further investigation. Why does the uroselective α_1-adrenoreceptor (α_1-ADR) blocker, tamsulosin, preferentially cause IFIS to a far greater degree than the nonselective α_1-ADR blockers? Is it due to higher maximum plasma concentrations obtained by tamsulosin or due to a second unidentified receptor in iris dilator smooth muscle that is preferentially activated by tamsulosin, both possibilities suggested by the work of Stefano Palea and associates.[1]

While the reports of IFIS occurring months to years after discontinuation of tamsulosin suggest a chronic anatomical change from exposure, Dr. Flach correctly states that a definitive study is lacking. If a structural change is confirmed in the iris dilator muscle, should we not also see a similar change in the smooth muscle of the bladder and prostate? In the absence of a structural change, is withholding tamsulosin or switching to an alternate therapy several weeks prior to cataract surgery a viable prophylactic option? In Chang and associates' study,[2] tamsulosin was stopped for 1 to 8 weeks prior to surgery in only 32 of the 167 eyes studied, and, while the severity of IFIS was unchanged, preoperative pupil size was larger in patients who held tamsulosin. Tamsulosin has been detected in aqueous humor 28 days after the last dose, suggesting a very prolonged drug receptor binding time.[3]

As ophthalmologists we may wonder why urologists continue to prescribe tamsulosin. Symptoms of benign prostatic hypertrophy (BPH) develop as a result of static and/or dynamic disease factors.[4] Static factors refer to an obstruction of the bladder neck caused by an enlarged prostate. Finasteride is the drug of choice for patients with enlarged prostate glands ($\geq$40 g), but takes 6 months to reach peak onset. Moreover, some patients' symptoms may be due to dynamic factors resulting from excessive α-adrenergic tone in the prostate, bladder neck, and urethral smooth muscle. The α_{1A} subtype is the predominant α-ADR in these tissues. Nonselective α_1-ADR blockers also effect α_{1B}-ADRs on vascular smooth muscle and are associated with vasodilatory adverse effects. Because tamsulosin has much less affinity for α_{1B}-ADRs, it is less likely to produce hypotension and can be safely be used concurrently with antihypertensive agents without need for dose adjustment. Other benefits of tamsulosin include: (1) dose titration is not necessary when initiating treatment, (2) the once daily dose can be taken any time of the day, and (3) it has a faster onset of action, with the peak effect occurring within one to two weeks. These factors make tamsulosin extremely attractive to both the patient with BPH and the prescribing urologist. It remains to be seen if the newly approved uroselective α_1-ADR blocker, silodosin, is also associated with high rates of IFIS.

ACKNOWLEDGMENTS

Funding/Support: None

Financial Disclosures: None

REFERENCES

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DR. VERINDER S. NIRANKARI: No conflict. I really enjoyed your paper Dr. Flach. I believe that it is really a good summary of the problem that we all face. One of the tips that the patient might develop IFIS, even though sometimes you do not get a history from patients of being on these medications, is that the pupils do not dilate properly. Even if you do not suspect this, anytime a patient's pupil does not dilate adequately, I consider using an iris retractor as the treatment of choice. If you review all the studies, a small pupil is the main risk of complication in cataract surgery. Secondly, if you do not insert retractors early in the case and you begin phacoemulsification and suddenly notice a very floppy iris, you can still certainly inject viscoelastic between the capsulorrhexis and the iris to permit safely inserting the iris retractors and proceeding uneventfully. Thirdly when we notice the pupil is very small, we are more likely put the implant in the capsular bag before removing the iris retractors. Sometimes the pupil is so mobile that if we remove the iris retractors, the pupil constricts and we completely loose the visualization of the capsular bag. We also have cared for patients who stopped taking tamsulosin HCl (Flomax, Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield CT) 7 or 8 months earlier who still have floppy iris syndrome. I am not sure that this syndrome ever goes away, even if patients have not taken the medication for a long period of time. I believe that it is very critical to ask the patients if they are using it or have you ever used a similar medication.

DR. M. EDWARD WILSON: No conflicts of interest. It was a nice review. The paper that you mentioned at the end, from Christiana Neff and co-authors, was from our institution. Dr. Neff did that work as a resident project and the list of agents that were shown to cause IFIS was very impressive. Another comment that might be interesting is that we published intraocular floppy iris syndrome in a child. We published the case in the *Journal of Cataract and Refractive Surgery* but also showed it as a video at an

ASCRS meeting. The interesting observation is that we have realized that infants and young children can all have floppy irises. We use intraocular epinephrine in every case and then use iris retractors liberally if we need them. In this one particular case an immature iris was very floppy and the epinephrine was inadvertently left out of the bottle on one eye. We did not realize it until we were in the middle of the case. I have this video where I am fighting the floppy iris and then I have video from the other eye of the same patient one week later with epinephrine HCl in the bottle. I showed them side by side to emphasize the difference the epinephrine HCl makes in these infants. When you think about the etiology of IFIS it is interesting to know that kids are predisposed to this floppy iris all the time, especially the babies with microphthalmia and immature irises. We have just gotten used to using epinephrine in every single case to try and reduce the floppiness.

DR. MARIAN S. MACSAI: That was an excellent review of the condition. Thank you. I am curious to learn if anyone has looked at the possible effects based on iris color or patient skin pigmentation or heritage because we seem to see some different effects. I agree with the comment that it is almost as if you have taken it once, then it does not matter.

DR. ALLAN J. FLACH***:*** Thank you for the kind discussion from everyone. First of all, to my discussant, I have finally met someone who speaks faster than I do. He reminds me that I should disclose not only have I been on tamsulosin HCl (Flomax, Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield CT), but that it lost its therapeutic effect. I have had the ultimate procedure, so I believe that it is important for me to say that as a bias. I agree with all of my discussants comments and I thank them for elaborating upon the syndrome in ways I wish I had time to do.

Dr. Nirankari also elaborated upon my paper with some good points. It is definitely possible to use viscous agents to make the insertion of the iris retractors safer and we do that. It is interesting to read the literature from the last three or four years since the syndrome was first noted. These techniques with the use of viscous agents and epinephrine are all mentioned in passing, but no well designed prospective study has demonstrated an improved outcome. There is no question that a small pupil is the biggest danger during cataract surgery. When the nonsteroidals were approved by the FDA, I believe the authors name was Gudek, published a paper that demonstrated that having a small pupil was the major problem leading to operative complications. The FDA used information in that article on the risks of having a small pupil as the primary reason to approve the use of preoperative nonsteroidal medications.

Dr. Wilson brings up a very important point. If somebody does not use the epinephrine in the irrigating solution we recognize the problem; however, I often do not know if the residents have used nonsteroidals preoperatively. If you omit epinephrine and do not use topical nonsteroidal agents, then you are in big trouble. Seven months after discontinuing tamsulosin HCl may be associated with problems of floppy iris syndrome; however, there are reports in the literature of the problem persisting up to three years after discontinuation. With respect to iris color and genetic predisposition, many studies have included these considerations, but thus far no statistical difference has been demonstrated. My clinical experience is a little different.