

# Intraoperative Floppy Iris Syndrome: Update 2012

BY MITCHELL C. SHULTZ, MD



*Intraoperative floppy iris syndrome (IFIS) was first described in 2005 by Chang and Campbell as a syndrome specific to the use of tamsulosin (Flomax; Boehringer Ingelheim Pharmaceuticals, Inc.).<sup>1</sup> Commonly used for the treatment of benign prostatic hypertrophy, this  $\alpha$ 1A-adrenergic receptor blocker relaxes the bladder neck and smooth muscle of the prostate gland. Although tamsulosin is the most popular medication associated with IFIS, investigators have characterized IFIS as a syndrome that can occur to a lesser degree with other  $\alpha$ -blocking medications used for the treatment of hypertension, renal colic, and voiding dysfunction in women.<sup>2</sup>*

*This month's installment of "Peer Review" focuses on the most current articles available on this problem. Cataract surgeons' aim is to reduce intraoperative complications associated with IFIS and iris prolapse in general. Having extensive personal experience with the management of IFIS over the past 15 years, I have used all of the techniques described herein to manage a floppy iris during cataract surgery. For several years, I used preoperative atropine, iris hooks, and intraoperative epinephrine. Although these modalities help, they do not eliminate IFIS. For pupils smaller than 5 mm after preoperative dilation, I routinely instill preservative-free epinephrine to aid the dilatatory process and improve iris muscle tone. If the iris does not respond, I will place a Malyugin Ring (MicroSurgical Technology) to improve visibility and prevent the iris from presenting to the phaco needle.*

*In my experience, the most prevalent factor resulting in iris prolapse due to IFIS is an increase in vitreous pressure. At the Freedom Vision Surgery Center in Encino, California, my colleagues and I use multiposition operative beds, and I routinely elevate the head of the bed 20° to 30° above the 180° meridian (Figure). For generously proportioned patients, I will elevate the head of the bed up to 45°, while maintaining hyperflexion of the neck to keep the pupillary plane perpendicular to the operative microscope as best as possible. Although elevating the head of the bed can compromise my comfort during a case, in the past 3 years, this strategy has virtually eliminated complications of iris prolapse and the resulting segmental iris atrophy associated with IFIS in my OR.*

*I hope you enjoy this installment of "Peer Review," and I encourage you to seek out and review the articles in their entirety at your convenience.*

## $\alpha$ -BLOCKERS AND IFIS

Tamsulosin was reportedly introduced in Japan in 1993, in the United Kingdom in 1997, and in the United States in 1997. Gupta et al related the popularity of the drug to its high affinity for the  $\alpha$ 1A receptor, which explains the lower incidence of adverse cardiovascular events in patients taking tamsulosin compared with less selective  $\alpha$ -adrenergic blockers.<sup>3</sup> Additionally, they identified three intraoperative findings associated with IFIS: (1) fluttering and billowing of the iris by ordinary intraocular currents, (2) the tendency of the iris to prolapse toward the site of the incision in the eye, and (3) progressive constriction of the pupil during surgery.

Gani et al reviewed the ophthalmologic side effects of urologic medications. The investigators evaluated tam-



Figure. The head of the operative bed is elevated 20° to 30° above the 180° meridian for cataract surgery.

sulosin and IFIS, phosphodiesterase type 5 inhibitors and nonarteritic ischemic optic neuropathy, and anticholinergic medications and glaucoma.<sup>2</sup> Less selective  $\alpha$ -blockers included in the study were alfuzosin, terazosin, and doxazosin. Lower urinary tract symptoms and benign prostatic hypertrophy have been found in 46% of men 70 to 79 years of age, and many of these individuals are currently taking  $\alpha$ -blocker medications, especially tamsulosin.<sup>4</sup>

In the review by Gani et al, the authors referenced Srinivasan et al, who found that, although most patients developing IFIS were using tamsulosin, the condition also occurred in a small number of patients on terazosin, doxazosin, and alfuzosin.<sup>5</sup> Furthermore, Srinivasan and colleagues reported that the incidence of IFIS was not correlated to the dosage of an  $\alpha$ -blocker medication. Because detectable amounts of tamsulosin have been found in the aqueous humor as late as 28 days after discontinuation, Gani et al claimed that there is little evidence to support that the incidence of IFIS can be prevented after the medication is stopped. Finally, it should be noted that an increasing number of women are taking  $\alpha$ -blockers for hypertension, renal colic, and voiding dysfunction. Surgeons should therefore consider the potential for IFIS in women.<sup>2</sup>

### PUPILLARY DYNAMICS

In a prospective study, Theodossiadis et al used a handheld, digital pupillometer (ForSite Digital Pupillometer; NeurOptics, Inc.) to assess pupillary dynamics quantitatively in relation to the use of  $\alpha$ 1-adrenoceptor antagonists with regard to the diagnosis of IFIS.<sup>6</sup> The device incorporates a white-light flash emitter and infrared digital video camera to record the changes in the responding pupil. A white-light flash of fixed intensity stimulates the pupil for 0.8 seconds. The video camera captures changes in the pupil's size at 40 frames per second and analyzes 124 images per sequence.

The investigators studied patients taking tamsulosin ( $n = 15$ ) and alfuzosin ( $n = 25$ ) as well as 25 control patients. The researchers recorded the resting pupillary diameter and subsequent contraction, latency, constriction velocity, and dilation velocity using the pupillometer. All pupillary measurements were performed before and after pharmacologic dilation.

Theodossiadis and colleagues reported a decrease in maximum pupillary diameter by  $0.5 \pm 0.19$  mm ( $P = .011$ ) and in the mean percentage of reduction in diameter after stimulation ( $5.23 \pm 2.42\%$ ;  $P = .035$ ) in the tamsulosin group. They also found that alfuzosin induced a significant decrease in maximum pupillary diameter ( $0.49 \pm 0.17$  mm;  $P = .005$ ). With regard to postdilation measurements, however, maximum and minimum pupillary diameters were reduced significantly only in the tamsulo-

sin group ( $1.09 \pm 0.31$  mm [ $P = .001$ ] and  $0.89 \pm 0.36$  mm [ $P = .016$ ], respectively). The investigators concluded that reduced predilation constriction velocity is a dynamic pupillary characteristic that, in combination with a small maximum iris aperture and poor postdilation mydriasis, may signify a triad of features that could represent a strong index for recognizing the tendency of patients treated with  $\alpha$ -blockers for IFIS.

In a prospective cohort study, Casuccio et al evaluated pharmacologic pupillary dilation as a predictive test for the risk of IFIS.<sup>7</sup> They evaluated male subjects taking tamsulosin for at least 1 year ( $n = 50$ ), other  $\alpha$ 1-adrenergic receptor antagonists ( $\alpha$ 1-ARAs) for at least 1 year ( $n = 50$ ), and a control group ( $n = 50$ ) scheduled to undergo phacoemulsification. The study's exclusion criterion included a history of prior eye surgery, diabetes, glaucoma, pseudoexfoliation syndrome, previous ocular trauma, use of any eye drop other than artificial tears, iridocyclitis, iris neovascularization, or zonular dialysis. Pupillary dilation was achieved using two drops of topical tropicamide 0.5% and phenylephrine HCL 10%. No topical atropine or cyclopentolate was used preoperatively. The investigators measured pupils 1 month preoperatively, immediately preoperatively, and postoperatively under mesopic low (0.4 lux) and high (4 lux) illumination after pharmacologic dilation.

Pupillary size was found to be significantly different in all three groups. Preoperative mean pupillary diameter was  $7.1 \pm 0.4$  mm in the tamsulosin group,  $7.7 \pm 0.6$  mm in the other  $\alpha$ 1-ARAs group, and  $8.2 \pm 0.2$  in the control group ( $P = .001$ ). The overall frequency of IFIS incidence was 58% for the tamsulosin group, 34% for the other  $\alpha$ 1-ARAs group, and 12% for the control group ( $P \leq .0005$ ). The relationship between pupil size measurements (mm) after dilation and IFIS grade was most significant at the 1-month preoperative visit. IFIS was not seen in pupil size measurements of  $7.8 \pm 0.9$  mm; mild to moderate IFIS was present in pupil size measurements of  $7.1 \pm 0.7$  mm, and severe IFIS was found in pupil size measurements of  $5.2 \pm 0.2$  mm ( $P \leq .0005$ ). A dilated pupil of 7 mm or smaller had 73% sensitivity and 95% specificity for predicting IFIS ( $P = .0001$ ). The authors hypothesized that the increased incidence in IFIS (12%) among patients not taking any  $\alpha$ 1-ARAs is likely related to other drugs that might induce iris dilation or smooth muscle irregularities, including saw palmetto, finasteride, antipsychotic drugs,  $\beta$ -blockers with particular  $\alpha$ -blocking properties, endothelin-A antagonists, angiotensin antagonists, and nitric oxide donor compounds.

### ANATOMICAL EFFECTS

Santaella and colleagues reported on the effects of tamsulosin on iris dilator smooth muscle anatomy.<sup>8</sup>

The retrospective study included 51 cadaveric eyes from 27 patients (14 with a history of tamsulosin use and 13 control patients) who underwent autopsy. The investigators sectioned the specimens through the pupillary axis in the horizontal meridian and performed light microscopy to evaluate the specimens. They performed a morphometric analysis to measure the maximum and minimum iris dilator muscle thickness and the iris stromal thickness at six points in each eye. The authors found a statistically significant difference in both smooth muscle and iris stromal thickness in the tamsulosin group compared with the control group. The average smooth muscle thickness in the control group was  $8.5 \pm 1.61 \mu\text{m}$  compared with  $6.53 \pm 1.99 \mu\text{m}$  ( $P = .006$ ) in the tamsulosin group. Iris stromal thickness was  $302 \pm 46.1 \mu\text{m}$  in the control group compared with  $281.4 \pm 47.5 \mu\text{m}$  ( $P = .268$ ) in the tamsulosin group. Given that the iris stroma is made of dense fibrocollagenous tissue with interspersed vessels, melanocytes, and fibroblasts, the authors concluded that the loss of thickness or atrophy of the dilator muscle associated with tamsulosin likely contributes to the reduction in structural rigidity of the iris due to the hydrostatic forces that occur within the anterior chamber during phacoemulsification.

### IFIS PROPHYLAXIS

In a prospective, multicenter, randomized, comparative, fellow eye study, Lorente et al evaluated the effects of intracameral phenylephrine (IPH) 1.5% for prophylaxis against IFIS in patients taking tamsulosin.<sup>9</sup> The study included 42 patients on tamsulosin who underwent cataract surgery between January and April 2011. One eye of each patient was randomized to receive 0.6 mL of nonpreserved bisulfate-free IPH 1.5% (group 1) or balanced saline solution (group 2). If significant miosis or iris prolapse occurred in group 2, IPH 1.5% was injected during phacoemulsification.

According to the study, signs of IFIS were observed in 88.09% of eyes in group 2, and no signs were noted in group 1 ( $P < .001$ ). Significant miosis, iris prolapse, or both occurred in 54.76% of eyes in group 2, although the condition was successfully reversed with IPH, with a significant increase in pupillary size after IPH administration (from  $4.77 \pm 0.88 \text{ mm}$  to  $6.68 \pm 0.93 \text{ mm}$ ;  $P = .001$ ). The authors concluded that IPH is a highly effective measure for prophylaxis against IFIS. Moreover, the drug can reverse IFIS, restoring the iris' rigidity and causing the pupil to return to its preoperative size.

### MANAGERIAL STRATEGIES FOR IRIS PROLAPSE

Tint et al proposed a stepwise approach for the management of intraoperative iris prolapse.<sup>10</sup> According to the

authors, predisposing factors for intraoperative iris prolapse include iris configuration, anterior chamber depth, and position and architecture of the corneal tunnel. They stated that strategies for the prevention and management of this complication include the use of pharmacological agents, ophthalmic viscosurgical devices (OVDs), and iris retractors. The authors acknowledged that IPH is popular in Europe and that intracameral epinephrine is more common in the United States. The role of these adrenergic agonists is to improve and augment iris smooth muscle tone and therefore reduce the iris' propensity for billowing and subsequent prolapse. These drugs have potentially adverse effects, the authors said, such as local toxicity to the endothelium, systemic hypertension, cystoid macular edema, toxic anterior segment syndrome, and even one reported fatality. Highly cohesive OVDs work best to create a physical barrier. Care must be taken to reduce aspiration and vacuum settings to prolong the presence of the OVD in the desired location. Although various techniques have been described for the use of iris retractors or expanders, according to Tint and colleagues, the two most popular methods found to be successful for the prevention of IFIS are the use of four iris retractors in a diamond pattern and iris expanders such as the Malyugin Ring. Finally, the authors recommended modifications to one's surgical technique, including low-flow surgery, bimanual I/A, and the more anterior placement of surgical wounds to aid in the reduction of iris prolapse. ■

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