

# Rikadosin

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## Educational brochure on "Intraoperative floppy iris syndrome (IFIS)", pre-operative assessment, and management

### A. Clinically relevant literature data about the association of Silodosin with IFIS:

- Silodosin is " **$\alpha_1$  adrenergic receptor antagonist**" indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH).
- In 2005, the investigators detected a **problem (called: Intraoperative Floppy Iris Syndrome "IFIS") occurring during cataract surgery in patients using alpha-blockers.**
  - **IFIS is characterized by a triad of factors:** *a flaccid or floppy iris that billows in response to normal irrigation current in the anterior chamber during the standard phacoemulsification cataract surgery; a marked propensity for the iris to prolapse in the main phacoemulsification and side-port surgical incisions in the eye; and progressive pupil constriction during surgery that makes it significantly more difficult to proceed with the cataract extraction*
  - Several studies suggest that IFIS is **more likely** to occur **with the selective alpha-blocker** (e.g.: Silodosin & tamsulosin) compared to the other nonselective alpha-blockers (e.g.: alfuzocin & terazocin...etc.).
- Following the publication of such findings, and after receiving corroborative reports from ophthalmologists, the U.S. Food and Drug Administration (FDA) instituted a **new label warning** in 2005 for Tamsulosin and other alpha-blocker drugs reading:  
*"The patient's ophthalmologist should be prepared for possible modifications to their surgical technique."*

Besides, **FDA label of Silodosin, dated 01/2013 and the updated label dated 12/2020,** included the following warning:

*"Inform patients planning cataract surgery to notify their ophthalmologist that they are taking Silodosin because of the possibility of Intraoperative Floppy Iris Syndrome (IFIS)".*

- Therefore, **ophthalmologists, primary care physicians, urologists, and patients should be aware of the potential difficulties that these drugs pose for cataract surgery.** The overall risk of serious cataract surgical complications is low, and **when the ophthalmologist is informed of the patient's history of alpha-blocker use, the success rate of cataract surgery remains very high.** However, patients may wish to consider cataract surgery prior to initiating a non-emergency alpha-blocker prescription.

## **B. Pre-operative assessment:**

The pre-operative evaluation is particularly difficult as there is currently no reliable way to predict which patients will demonstrate IFIS. Furthermore, as IFIS can present unilaterally the absence in one eye does not preclude the other eye from demonstrating features of IFIS in a subsequent surgery.

**During the preoperative visit, there are a number of questions and observations which may highlight for the surgeon any patients at potential risk for IFIS.**

➤ Most importantly is to ask all patients about **current or former use of  $\alpha_{1A}$  receptor antagonists.**

➤ Simply reviewing the current medication list is **not sufficient**. Many patients are unable to recall specific medication names or classes they are currently taking, much less a medication they took previously and since discontinued. Because of this, often times **asking a patient or an accompanying family member if they have ever been treated for an enlarged prostate or for difficulty emptying their bladder** will help elicit a more accurate history. If a patient does have a history of  $\alpha_{1A}$  receptor antagonists it is also important to **counsel them on the associated increased risk of IFIS and subsequent risk of complications postoperatively.**

The most reliable **preoperative predictive feature of IFIS** in a patient with a history of  $\alpha_{1A}$  receptor antagonists is **poor pupillary dilation**. This can and should be noted during the office pre-operative cataract surgery evaluation, and not just on the day of surgery.

When the pupil does not dilate well, the surgeon should be wary of IFIS during surgery. Although poor dilation can also be a harbinger of other intra ocular conditions such as pseudo-exfoliation and trauma, recognition will help the surgeon prepare for and adapt intra operative management strategies for all possible complications.

## **C. Management of IFIS:**

### **1) Pre-operative planning:**

- Preoperative planning and anticipation of IFIS can impart significant protective effect in preventing major complications during surgery.
- **Nursing staff involved** in preoperative assessment of cataract surgery should be **educated** regarding the implications of  $\alpha$ -adrenergic receptor blockers (including silodosin) on cataract surgery.
- A full drug history should be included in the physician referral letter and must be carefully reviewed before cataract surgery.
- Patients should also be directly questioned regarding the use of silodosin. In addition, silodosin patients should be educated regarding their increased likelihood of a technically difficult operation and the potential intraoperative risks related to IFIS.

It is vital that during the consent process, the patient is appropriately informed, thus allowing them to make better judgments on the 'risk-to-benefit' ratio of their surgery.

- Primary care physicians' awareness of the association between silodosin and IFIS also needs to be increased.

### **2) Modification of Surgical Technique:**

Successful management of IFIS includes modification of routine surgical techniques. Attention to wound design with appropriately sized tunnels and entry anterior to the iris root may decrease the risk of iris prolapse during surgery. Use of gentle hydrodissection, low-flow fluidic parameters, bimanual irrigation-aspiration and microincisional phacoemulsification techniques increase anterior chamber stability and may also help reduce the magnitude of iris fluttering and prolapse to the phacoemulsification tip or to the wounds.

### **3) Pharmacological Measures:**

- **Preoperative use of atropine eye drops** can help avoid progressive miosis seen with IFIS. Atropine blocks the cholinergically mediated action of the iris constrictor muscle, resulting in improved pupillary dilatation. When used to prevent IFIS, atropine drops need to be started at least 2 days before surgery. In the prospective tamsulosin trial by Chang *et al.*, preoperative atropine was infrequently used by surgeons in the management of IFIS, and although eyes that received topical atropine drops had the largest mean pupil diameter preoperatively ( $7.2 \pm 0.9$  mm), 58% of these eyes required an additional intraoperative measure to manage IFIS.

- **Use of intracameral a 1 receptor agonist drugs** as a means to counteract the effect of silodosin on the iris receptors. This modality was not investigated by the prospective tamsulosin trial as the trial was initiated before the introduction of this class of drugs into the management of IFIS. In 2006, Sugar was the first to describe the use of intracameral epinephrine for the prophylaxis of IFIS. His regimen includes **intracameral injection of diluted preservative-free epinephrine at a 1:4000 concentration at the beginning of surgery before the installation of the ophthalmic viscosurgical device (OVD)**. He reported uniform success to prevent IFIS in 71 operated tamsulosin patients. Using the same concentration of intracameral epinephrine in combination with preoperative atropine drops, Masket and Belani also reported a high success rate in the prevention of IFIS in a study of 20 eyes.

Manvikar and Allen used diluted intracameral phenylephrine (1:360) prepared from single-use minims in 22 eyes of tamsulosin patients that had small pupils preoperatively or displayed IFIS features intraoperatively. Additional pupillary dilatation was observed in only 73% of eyes. However, in all eyes that had intracameral phenylephrine owing to significant iris prolapse into the incisions or progressive miosis, it resulted in restoration of iris tone, decreased tendency to flutter and prolapse and caused the pupil to dilate back to its preoperative size. Similar results were also reported by Gurbaxani and Packard in another study of seven tamsulosin subjects using an intracameral phenylephrine concentration of 1:200.

Potential ocular toxicity remains a concern with the use of intracameral drugs, although recent safety studies showed that phenylephrine and diluted epinephrine had no discernible deleterious effect on either the corneal endothelium or the macula. It is worth mentioning that intracameral use of a-1 receptor agonists may be associated with systemic side effects, and blood-pressure spikes have been reported.

#### **4) Mechanical Measures:**

Mechanical measures to dilate the pupil and restrain iris movement have been tried with varying success in IFIS.

- Viscomydriasis using Healon5® (sodium hyaluronate 2.3%) is one of these measures. The highly concentrated long-chained molecules of this higher viscosity OVD are able to move the iris effectively, dilate the pupil more than any other OVD and mechanically decrease iris billowing and prolapse. However, the main shortcoming of this method is that Healon5 in the anterior chamber tends to be consumed during surgery, but this may be minimized by using slow-motion fluidics for phacoemulsification and irrigation aspiration. Caution is also needed when using Healon5, as overfilling the anterior chamber can result in difficult manipulation of the anterior capsule and can also predispose to corneal wound burn. Creating a fluid space around the phacoemulsification tip before starting phacoemulsification should circumvent these problems. This can be performed by partially filling the anterior chamber with the OVD and injecting balanced salt solution underneath, as described by Arshinoff in the ultimate soft-shell technique.

- Iris retractors (hooks) are commonly used for tackling IFIS. They can dilate the pupil and resist the tendency of the iris to billow and prolapse.

**Compared with Healon5, Iris retractors have the advantage of maintaining a constant pupil size during the surgery.** While most surgeons usually employ four hooks to stretch the iris in a square or diamond configuration, different techniques for placing the hooks have been described, including the use of a single hook posterior to the main incision, two iris hooks to straddle the main incision and inserting five hooks in a pentagon shape. *Placing four hooks in a diamond configuration offers several advantages in IFIS and has been recommended by the American Society of Cataract and Refractive Surgery (ASCRS) committee for managing IFIS.* The sub-incisional iris is pulled posterior to the phacoemulsification wound through a separate incision, making prolapse far less probable. *In addition, this technique maximizes pupillary dilatation in front of the phacoemulsification tip and provides more space for cataract removal.*

- **Pupil expander rings** have been used successfully for managing IFIS. Similar to hooks, pupil expander rings restrain the iris movement and decrease the severity of billowing and prolapse to the incisions. In general, they are less traumatic than iris hooks, do not overstretch the iris and can be inserted without the need of additional incisions. Several designs are available, including the Morcher Pupil Ring®, the Milvella Perfect Pupil® and the Eagle Vision Graether Ring®. The Malyugin Ring® is the newest form of pupil expansion devices and, compared with the other pupil expansion rings, it has the advantage of being thin and light and hence easier to insert and remove in eyes with shallow anterior chambers using a special injector. Two sizes of this ring are now available; 6.25 and 7 mm. The 6.25 mm is the commonly used size and is easier to insert in eyes with shallow anterior chambers. The 7-mm device has recently been introduced and could be helpful in cases of IFIS with very flaccid iris to increase exposure and keep the iris further way from the surgeon's working plane. In a study of 30 eyes with IFIS, Chang reported excellent results with the Malyugin device in terms of maintaining a constant pupillary expansion of 6 mm and decreasing iris billowing. No major intraoperative adverse events were reported by the author, but iris prolapse still occurred in some cases

### **In conclusion:**

**The best strategy for managing IFIS is still not known.** A surgeon's choice is mainly based on personal experience and case difficulty. Different modalities can also be complementary when combined and having experience with more than one method is an advantage, particularly as clinical circumstances may change during surgery.

Data from the 2008 ASCRS survey that was completed by 957 members showed **intracameral  $\alpha_1$  agonists and iris hooks to be the most preferred methods** in managing IFIS (38 and 23%, respectively), although a third of respondents in this survey also reported that they routinely use more than one strategy for managing IFIS. The practice pattern of ophthalmologist in the **UK** has been reported to be in **favor of using iris hooks and Healon5** in managing floppy iris. In a nationwide survey of consultants' experiences published in 2007, 61% of the participants reported using hooks and 27% used Healon5.

Intracameral phenylephrine was uncommonly used in this survey, with only 2% of surgeons employing this technique; however, 12% of the respondents reported that they would consider using this modality in future

### **D. General recommendations for eye surgeons & ophthalmic teams:**

- a) You should establish whether patients scheduled for cataract surgery are being or have been treated with silodosin in order to ensure that appropriate measures are in place to manage IFIS during surgery.*
- b) Discontinuing treatment with  $\alpha_1$ -adrenoceptor antagonists 2 weeks prior to cataract surgery has been recommended, but the benefit and duration of stopping therapy prior to cataract surgery has not yet been established.*

### **E. Reference links:**

1. [http://www.ascrs.org/sites/default/files/resources/Flomax%20Patient%20Advisory%20revision\\_JH\\_3%20FINAL\\_FL%20DC%20edited.pdf](http://www.ascrs.org/sites/default/files/resources/Flomax%20Patient%20Advisory%20revision_JH_3%20FINAL_FL%20DC%20edited.pdf)
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