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# Management of Intraocular Floppy Iris Syndrome (IFIS) in Cataract Surgery

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## 1. Introduction

Intraoperative floppy iris syndrome (IFIS) was first described in 2005 (Chang & Campbell 2005; Parssinen 2005). The fullblown syndrome comprises a triad of: 1) billowing of the iris stroma in response to normal irrigation currents, 2) the floppy iris tends to prolapse through the phaco and the side port incisions, and 3) a progressive pupillary constriction during the surgical procedure. Although IFIS may be multifactorial in etiology, systemic treatment with  $\alpha$ -1<sub>a</sub> adrenergic receptor (AR) antagonists, and tamsulosin in particular, seems to play a pivotal role. The clinical presentation varies widely, from a mild form with a fluttering iris only, to the more severe case with the complete triad (Chang et al. 2007). The condition potentially increases the risk of intraoperative complications, such as iris trauma, zonular dehiscence, posterior capsule rupture, vitreous loss, as well as postoperative complications, including increased intraocular pressure and cystoid macular oedema. The prevalence of IFIS in cataract surgery varies among different countries, from 0.5 % to 2.0 % (Chang & Campbell 2005; Cheung et al. 2006; Chadha et al. 2008). The incidence of IFIS during cataract surgery in patients on tamsulosin medication varies from 43 - 100%. In contrast, the incidence of IFIS in patients taking one of the other  $\alpha$ -1<sub>a</sub> AR antagonists, e.g. alfuzosin, is 10-15% (Blouin et al. 2007).

## 2. Etiology

Adrenergic  $\alpha$ -1 receptors are frequently found in smooth muscles of the human prostate / bladder neck, and in the iris dilator muscle of the eye, predominantly the subtypes  $\alpha$ -1<sub>a</sub> and the  $\alpha$ -1<sub>d</sub>. Stimulation of the iris dilator muscle and the smooth muscles in the prostate and the bladder neck is mediated by the adrenergic  $\alpha$ -1<sub>a</sub> and  $\alpha$ -1<sub>d</sub> receptors.

Lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH) is a common condition among elderly male patients and the prevalence of BPH and cataract is similar, increasing with age. Benign prostatic hyperplasia implies both a static and a dynamic component. The static component is characterized by an increased prostatic mass, and the dynamic component by an increased  $\alpha$ -1 AR mediated tone in the smooth muscles of the bladder neck and in the prostate. Inhibition of the  $\alpha$ -1<sub>a</sub> ARs relaxes the muscular tone, which decreases the pressure within the lower urinary tract improving urinary outflow, and at the same time produces relaxation of the iris dilator muscle causing a floppy iris and miosis. Thus, systemic treatment with  $\alpha$ -1 AR inhibitors (alfuzosin, doxazosin, tamsulosin

and terazosin) has been a successful therapy of LUTS including benign prostatic hyperplasia, but the same treatment may cause some degree of IFIS during cataract surgery. Due to a better cardio-vascular profile tamsulosin and alfuzosin seems to be better tolerated than doxazosin and terazosin (Djavan et al. 2004). However, tamsulosin also has a very high affinity for the  $\alpha$ -1a and  $\alpha$ -1d ARs in the smooth muscular tissue of the iris. On the other hand, alfuzosin acts clinically in a more uro-selective manner, which may explain, why alfuzosin causes IFIS less frequent than tamsulosin, decreasing the odd ratio for IFIS to 1:32 compared to patients exposed to tamsulosin (Blouin et al. 2007).

### 3. Management of IFIS

#### 3.1 Preoperative precautions

##### 3.1.1 Medical history

The risk of unexpectedly encountering IFIS during surgery in cataract patients should be minimized through a thorough questioning of the previous and the current medical history. Of particular interest is a history of symptoms from the lower urinary tract and the prostate. This also applies to women, as  $\alpha$ -1a AR inhibitors may be prescribed for LUTS and arterial hypertension in females. IFIS may develop in patients treated with tamsulosin for only a few months. It might seem rational to stop the treatment with  $\alpha$ -1 AR antagonists preoperatively, but there is little or no clinical effects on the severity of IFIS by stopping the treatment with tamsulosin, although the preoperative pupil diameter may be larger (Chang et al. 2007; Nguyen et al. 2007). The authors' institution does not recommend the patients stop treatment with  $\alpha$ -1 AR inhibitors prior to surgery.

##### 3.1.2 Preoperative dilatation

A preoperative maximum pupillary dilatation is mandatory. The author recommends an anticholinergic agent to relax the sphincter of the pupil (cyclopentolate 1%) combined with an  $\alpha$ -1 AR agonist (phenylephrine 2.5 - 10%) to enhance the dilatation and increase the tone of the iris dilator stroma administered twice at 15-20 minutes interval before surgery. The author adds a non-steroid anti-inflammatory drug (diclofenac 0.1% / ketorolac 0.5%) to provide a more stable dilatation throughout the surgery. A poorly dilated pupil preoperatively may predict eyes likely to manifest IFIS during operation. At the authors' institution, a preoperative pupil diameter  $\leq$  6 mm in IFIS patients indicates the need for iris retractors, pupil expansion rings or intracameral phenylephrine.

Atropine 1% applied topically prior to cataract surgery in patients on tamsulosin has been recommended to obtain a maximum preoperative dilatation (Bendel & Phillips 2006; Masket & Belani 2007). In the case series by Bendel & Philips, atropine 1% was prescribed twice daily for 10 days. Thirteen out of 16 patients (81%) on tamsulosin did not require other modification of their cataract surgery. Masket & Belani used a presurgical administration of topical atropine 1% three times daily for two days in addition to routine preoperative mydriatics. During the operative procedure, 0.3 to 0.5 mL intracameral epinephrine diluted 1:2500 with BSS was placed under the iris. They reported 19 eyes out of 20 to have an excellent pupil dilatation without signs of IFIS.

Atropine, a potent anti-cholinergic agent, relaxes the sphincter of the pupil, but care should be taken due to the risk of intensified LUTS and acute urinary retention, especially if tamsulosin is stopped preoperatively. Treatment with atropine 1% also represent a risk in the elderly group of cataract patients because of atropine's well-know cardiac and cerebral side-effects.

### **3.2 Operative strategies**

#### **3.2.1 Epinephrine in irrigation solution**

Epinephrine, a combined  $\alpha$ - and  $\beta$ - AR agonist, should be added to the irrigation solution. The author recommends 1 mL epinephrine 1 mg/mL (preservative- and sulphite free) in 1000 mL balanced salt solution (1: 1 000 000) with a pH within the range of 6.5 - 8.5. Irrigation and aspiration flow rates should be reduced to prevent iris fluttering.

#### **3.2.2 Intracameral injection of epinephrine**

Myers & Shugar reported good effect of an intracameral mydriatic and anesthetic mixture, the "epi-Shugar" solution, comprised of epinephrine 0.025% and lidocaine 0.75% in BSS Plus. The technique showed excellent results in a paired prospective single masked study (Myers & Shugar 2009). The epi-Shugar solution consists of a 1 : 4000 epinephrine mixture with a pH of 6.9. There was no report of corneal endothelial cell damage (Shugar 2006). Masket & Belani injected 0.3 - 0.5 mL epinephrine diluted with BSS (1 : 2500) intracameral and placed under the iris with excellent results (Masket & Belani 2007). Takmaz & Can suggested a mixture of 0.1 mL non-preserved epinephrine (0.5 mg /mL) diluted with 2 mL BSS (1 : 4000 solution) (Takmaz & Can 2007). They reported no change in the incidence of IFIS, but the mixture seemed effective in order to prevent miosis.

However, intracameral injection in these concentrations may cause local damage, since severe changes has been described in corneal endothelial cell morphology after intracameral use of 0.5 mL epinephrine in a 1:10.000 solution (Edelhauser et al. 1982; Pong et al. 2008).

#### **3.2.3 Intracameral injection of phenylephrine**

Intracameral injection of phenylephrine, an  $\alpha$ -1 AR agonist, has been recommended to reverse intraoperative iris fluttering and pupil constriction (Manvikar & Allen 2006; Gurbaxani & Packard 2007). In both studies diluted phenylephrine 2.5% was used (Minims®, buffered with bisulphite and edetate). Manvikar & Allen used a solution with 0.25 mL unpreserved phenylephrine 2.5% (Minims) diluted with 2 mL BSS. This corresponds to a 1:360 dilution with a pH of 6.4. The authors argued in a study comprising 32 eyes that the solution had a good effect in order to prevent IFIS. Gurbaxani & Packard reported on the use of intracameral phenylephrine 2.5% mixed with 1 mL BSS in a study with seven patients on tamsulosin. All patients had significant reduction in the signs of IFIS, and a sustained pupillary dilation in all cases. No clinical signs of corneal edema were reported, but unfortunately the density of endothelial cell was not evaluated.

In an early report by Edelhauser et al., a cytotoxic effect on the endothelium of phenylephrine at a concentration of 2.5% was described in cases where the epithelium was removed (Edelhauser et al. 1979). In a recent report on corneal endothelial cell changes in cataract patients on tamsulosin we found no association between the intracameral use of 0.25 mL phenylephrine 2.5% (Minims®) in 2 mL BSS and postoperative endothelial cell loss (Storr-Paulsen et al. 2013).

#### **3.2.4 Capsular staining**

Capsular staining with trypan blue 0.06% (Vision Blue, DORC, The Netherlands) is an excellent technique to visualize an obscured leading edge of the capsulorrhexis at the beginning of the operation due to a small pupil or a mature cataract. Trypan blue is also

very effective to visualize the border of the rhexis, if iris retractors are required later in the procedure due to progressive miosis. Trypan blue is safe and effective as an adjunct for capsule visualization (de Waard et al. 2002; Jacobs et al. 2006)

### **3.2.5 Use of ophthalmic viscosurgical devices (OVDs)**

Injection of Healon5 was one of four different surgical strategies used to manage IFIS in a multicenter study. A total of 98 of 103 cases were completed with Healon5 alone and the remaining five cases required additional use of iris retractors / iris expansion rings (Chang et al. 2007). In a survey of surgeons' experiences with IFIS in the UK, 27% of the responding surgeons answered that they used Healon5, and 85% found it effective (Nguyen et al. 2007). In 1999, Arshinoff described a technique, where a lower viscosity dispersive OVD was used together with a higher viscosity cohesive OVD (Arshinoff 1999). This "soft-shell" technique is performed with the dispersive injected into the anterior chamber until the chamber is 75-80% full. The cohesive is then injected on the surface of the anterior capsule, pushing the dispersive OVD upward and outward until the pupil stops dilating. The technique was later modified to improve surgery, especially in IFIS patients (Arshinoff 2006).

### **3.2.6 Use of iris retractors**

The use of flexible iris retractors to enlarge the pupil was originally described in the early 1990s (de Juan E Jr & Hickingbotham 1991; Nichamin 1993) and later modified to create a diamond shape, which is very suitable in IFIS surgery (Oetting & Omphroy 2002). In the UK survey of surgeons' preferences in cases of IFIS, 61% of the responders chose iris retractors, and 72% of that group found them effective (Nguyen et al. 2007). In the American multicenter study, iris retractors were only used in 31% of the cases. The difference may be explained by the fact that the British survey questioned all UK eye surgeons about their experiences; whereas the American study only asked 15 selected and highly experienced surgeons (Chang et al. 2007). Pupil stretching and sphincterotomies are usually of no effect because of the elasticity of the pupil margin, and may on the contrary worsen the constriction of the pupil (Chang & Campbell 2005).

### **3.2.7 Use of pupil expansion rings**

Pupil expansion rings have been used to enlarge the pupil and to maintain the size throughout the surgery. Expansion rings were only used by 3% of the surgeons in the UK survey (Nguyen et al. 2007), and expansion rings were the least used of four alternatives (4% of cases) in the American multicenter study (Chang et al. 2007). The expansion rings were found to cause less trauma to the iris, but was the most time- and cost consuming method, when compared to the use of iris retractors (Akman et al. 2004).

## **4. Conclusion**

To reduce possible complications in cataract patients taking  $\alpha$ -1 AR antagonists (especially tamsulosin), the surgeon should:

1. highlight the patient's medical history, particularly for symptoms of LUTS and benign prostate hyperplasia. A thorough questioning regarding current and previous therapy is strongly recommended. Remember that  $\alpha$ -1 AR antagonists are also prescribed for LUTS and arterial hypertension in women.

2. use a preoperative dilation including cyclopentolate, phenylephrine, and a NSAID. Atropine may be used, but cautions should be taken in elderly patients because of the risk of cardiac side effects and acute urinary retention.
3. use capsular staining in order to facilitate visualization of the rhexis edge.
4. use a viscoadaptive or the soft-shell technique in all cases of IFIS.
5. keep phenylephrine ready for intracameral injection in case of a progressive pupil constriction during surgery.
6. consider the use of iris retractors or iris expansion rings if preoperative dilation is  $\leq 6$  mm.

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