



## CLINICAL EXPERIENCE WITH INTRAOPERATIVE FLOPPY IRIS SYNDROME

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**ABSTRACT** **Purpose:** This study was conducted to recognise the incidence, risk factors, complications and the management of intraoperative floppy iris syndrome (IFIS). **Materials and Methods:** Retrospective analysis of the preoperative data, systemic comorbidities, medication history and intraoperative observations was conducted in 1116 eyes (of 482 males and 634 females), who underwent cataract surgery from January 2021 to June 2022. **Results:** The mean age of patients was 67.08±8.18 years. The incidence of IFIS observed is (44) 3.9%. 28 (84%) men with Tamsulosin dosage had IFIS features. But 16 (36%) patients who were not exposed to any alpha blockers also showed the features of IFIS. Hypertension was found to be a significant risk factor while diabetes, coronary heart diseases were not. The mean duration of drug intake was 23.11 ± 23.42 months not affecting the severity of IFIS. Surgical difficulties like posterior capsule rupture five (11.4%) and iris prolapse were noted in six (13.6%) cases and additional measures like intracameral adrenaline, iris hooks and viscoelastic device were used to manage them. Despite the increased operative time, the surgical outcome was good in all the patients. **Conclusion:** The incidence of IFIS is higher in patients with intake of Tamsulosin. Its usage and hypertension were the risk factors associated. Thus it is imperative to create awareness to elicit a thorough medical history preoperatively. The critical aspects of IFIS are stratification of performative risk, prompt preoperative prophylaxis and surgical technique with the aid of mechanical and pharmacological agents. Eliciting a reliable history of current or past  $\alpha$ 1AR antagonist consumption in the presence of hypertension is essential.

**KEYWORDS :** Phacoemulsification, floppy iris syndrome, Tamsulosin, Adrenaline, miosis.

### INTRODUCTION

Intraoperative floppy iris syndrome (IFIS) that most cataract surgeons encounter was first described by Chang and Campbell in 2005.<sup>1</sup> A variable prevalence of IFIS ranging from two percent to 12.6 percent has been reported in various studies.<sup>1,2</sup> This syndrome causes poor pupillary dilation and increased risk of intraoperative complications during cataract surgery. The characteristic triad is intraoperative billowing of a flaccid iris stroma in response to ordinary intraocular fluid currents, propensity for iris prolapse towards the phaco and/or the side-port incisions and progressive pupil constriction.<sup>3</sup>

The combined presence of all the three features mentioned above results in the intraoperative complications like iris injury, wound dehiscence, hyphema, iridodialysis, nuclear drop, posterior capsule rupture and vitreous loss. Also the propensity of the iris to prolapse towards the incisions increases the risk of postoperative iridocyclitis and pupil distortion resulting in glare and photophobia.<sup>4</sup> Other long-term consequences include retinal-detachment, cystoid macular edema and endophthalmitis.<sup>5</sup>

Intraoperative miosis is attributed to antagonism of  $\alpha$ 1-receptor ( $\alpha$ 1-ARA), which is the main regulator of smooth muscle tone in the human urinary system and also in the musculus dilator pupillae. This inhibition has been observed with most commonly prescribed drug Tamsulosin for the management of benign prostatic hyperplasia which reduces the muscular tone and thus the pressure within prostatic urethra.<sup>6</sup> Hence, this retrospective study was conducted to analyse the risk factors, surgical difficulties and complications in a floppy iris syndrome scenario.

### MATERIALS AND METHODS

This retrospective study was conducted after obtaining approval from the Institutional Ethics Committee and abided by the tenets of the Declaration of Helsinki. The medical records of cataract patients with intraoperative floppy iris syndrome, who underwent phacoemulsification from January 2021 to June 2022 was reviewed for data collection and analysis.

Demographic data, history of medical comorbidities, medications with its dose and duration (at least one month of intake) and details of ophthalmological workup was analysed.

The standard preoperative regime was noted which included topical Flurbiprofen (0.03% w/v, Sunways Pvt LTD, Mumbai, India ) or nepafenac (0.1% w/v, Sun pharma Lab LTD, Assam, India), two hours before surgery followed by pupillary dilatation using topical tropicamide (0.8%w/v, Sunways Pvt LTD, Mumbai, India) and phenylephrine (five percent w/v). Zeiss visalis phaco machine was used for nucleus emulsification by the standard stop and chop technique. Intraoperative notes were analysed for the behaviour of iris, such as meiosis, billowing, prolapse and it was graded as mild (billowing only), moderate (billowing and iris prolapse/  $\geq$ 2mm pupillary constriction) and severe (billowing, iris prolapse and  $\geq$ 2mm pupillary constriction). The measures taken to manage these complications, such as use of iris hooks, 2.3% sodium hyaluronate (Healon 5, AMO Inc., CA, USA) and intracameral Phenocane (Lidocaine one percent + Phenylephrine 0.31% + Tropicamide 0.02% Entod Pharmaceuticals, Mumbai, India) were noted. Difficulties of the operating surgeon and duration of surgery was also noted for analysis.

### Statistical Methods

Data was entered into Microsoft excel data sheet and analysed using SPSS 22 version software (IBM SPSS Statistics, Somers NY, USA). Both intraoperative and postoperative complications are expressed in percentage.

### RESULTS

The study included 1116 eyes (482 males, 634 females) with mean age of 67.08±8.18 years (range 37-77 years). IFIS was observed in 33(75%) males and 11(25%) females. The incidence of IFIS encountered in 44 eyes is 3.9%.

**Table 1: Risk factors**

Risk factors	N	%	
Gender	Male	33	75
	Female	11	25
Diabetes mellitus	15	34	
Hypertension	18	41	
Coronary heart diseases	5	11.4	
Benign Prostatic Hyperplasia	28	63.6	
Tamsulosin use	28	63.6	

### Grading of IFIS

Distribution of affected eyes according to IFIS grading is 20 (mild), 18 (moderate), and 6 (severe).

### Complications

Details of complications in the study group are provided in Table 2. Of the total 44 eyes with IFIS, intraoperative complications observed were miosis (10), Iris billowing (11), Iris prolapse (6), Posterior capsule rupture (5) and vitreous loss (3). Fifteen eyes showed various complications such as Iritis (11.4%), striate keratopathy (9%), Secondary glaucoma (6.8%), iris chafing (4.5%) and iris incarceration (2.3%).

**Table 2: Intraoperative And Postoperative Complications**

COMPLICATIONS		N	%
Intraoperative	Miosis	10	22.7
	Iris billowing	11	25
	Iris prolapse	6	13.6
	Posterior capsule rupture	5	11.4
	Vitreous Loss	3	6.8
Postoperative	Iritis	6	13.6
	Striate keratopathy	8	18.1
	Secondary glaucoma	4	9
	Iris chafing	2	4.5
	Iris incarceration	2	4.5

### DISCUSSION

Most cataract surgeons have encountered Intraoperative floppy iris syndrome a condition where the atonic iris dilates poorly and billows and prolapses during surgery. It has been associated with the use of systemic sympathetic  $\alpha$ -1A antagonists in general (Finasteride, Angiotensin II receptor inhibitors, Benzodiazepines, anti-psychotics, hypertension drugs) and Tamsulosin in particular which is prescribed to treat benign prostatic hyperplasia (BPH). It has been observed that several patients had IFIS even after discontinuation of the drug intake for more than a year because of muscular atrophy and loss of tone, while few patients demonstrated a better preoperative pupillary dilatation.

### Incidence

The incidence of IFIS encountered in 44 eyes is 3.9%. (28 male of 41 cases who were on Tamsulosin treatment, five males and 11 females who were not on any medications). The reported incidence of IFIS in literature varies across different countries ranging from 1.1-12.6%.<sup>7-9</sup>

**Table 3: The rate of IFIS in studies**

Data source	IFIS cases/All cases	Rate
Our study (2022)	43/1116	3.9%
Kaczmarek (2019) <sup>10</sup>	29/319	9 %
Wen (2018) <sup>9</sup>	53/482	11%
Wahl (2017) <sup>2</sup>	119/947	12.6%
Chatziralli (2016) <sup>17</sup>	63/1,274	4.9%

### Risk factors

#### Age

In our study IFIS was observed in patients with a mean age of 67.08±8.18 years. It has been positively correlated to advanced age group owing to increased prevalence of cataract and other age related degenerative diseases.<sup>10</sup> Some of the earlier studies have shown that, the potency of norepinephrine is proportional to the receptor reserve in the iris dilator muscle which is altered with aging.<sup>11</sup> And the incidence of fluorescein leakage as an indicator for iris vasculature dysfunction, suggested a positive correlation between ageing and vascular dysfunction.<sup>12</sup> The localization of  $\alpha$ -1AR to the human iris arteriolar muscularis was confirmed in addition to the iris dilator muscle, which suggests that IFIS may develop as a consequence of iris vascular dysfunction.<sup>13</sup>

#### Gender

The male gender was found to be a risk factor for IFIS. It was noted that 75% of IFIS patients were males among whom 63.6% had a history of Benign Prostatic Hyperplasia. Many studies reveal that incidence of IFIS is significantly higher in male than in female.<sup>10,14</sup> Because the use of  $\alpha$ 1 adrenoceptor antagonist for men with BPH definitely increases the rate of IFIS. However, women also take this drug to treat lower urinary tract symptoms. M. Wahl et al., revealed a gender distribution of 57.1% males and 42.9% females.<sup>2</sup>

#### Tamsulosin

Since the strongest cause of IFIS is attributed to the current or past use of tamsulosin is well-proven in the literature, majority of our subjects

(41) also had history of Tamsulosin usage. Whereas, M. Wahl et al reported IFIS in 119 of 947 cases (12.6%), among which 31 patients (26.1%) had an associated medical history of taking various drugs such as Tamsulosin (11), combination of drugs (seven), Doxazosin (four), Quetiapine (four), Finasteride (two), Prothipendyl (two), and Mianserin (one).<sup>2</sup> Prata et al stated that "patients using systemic  $\alpha$ -1 adrenoceptor antagonists have significantly lower values of iris dilator muscle thickness and of dilator/sphincter ratio and smaller pupil diameter when compared with age- matched controls."<sup>15</sup>

### Systemic diseases

Hypertension (41%), Diabetes mellitus (34%) and Coronary heart disease (11.4%) were the associated comorbidities. Although Diabetes mellitus has not been reported to the occurrence of IFIS, there are inconsistent results regarding the association of hypertension and IFIS. A study including 319 cases have revealed no statistical connection between hypertension and IFIS.<sup>10,16</sup> While another prospective study consisting of 1,274 cataract patients revealed hypertension as an independent risk factor for IFIS.<sup>17,18</sup> The proposed pathogenetic mechanism suggests that systemic diseases cause endothelial dysregulation that lead to increased resistance of the iris dilator muscle to adrenergic agonists.<sup>19</sup> Therefore, it is unclear whether the increased risk in the development of IFIS should be attributed to hypertension as an independent risk factor or whether it is associated with specific antihypertensive drugs.

### Severity

A wide range of severity of IFIS has been reported in literature. Mild cases have minimal billowing of the iris and dilates well was noted in 20 cases which was managed successfully by intracameral Phenocaine and boluses of 2.3% sodium hyaluronate (Healon 5). Bolus injection of intracameral mydriatics is said to decrease the surgical time and 65% less use of mechanical pupil expanders. 18 cases of moderate IFIS demonstrating billowing and iris prolapse /  $\geq$  2mm pupillary constriction and 6 severe IFIS cases with marked iris billowing, repeated iris prolapse and intraoperative miosis required additional iris retractors (Product code MIPL/D1, Madhu Instruments Pvt LTD, New Delhi, India) to complete the surgery comfortably. Studies have reported similar measures along with iris rings, being adopted to manage the intraoperative complications.<sup>1,20,21</sup>

### Complications

Discontinuing  $\alpha$ -blocker prior to surgery may help, but does not prevent IFIS. The complications vary from mild and transient to severe including posterior capsule rupture, vitreous prolapse, retained lens fragments, iris trauma, wound dehiscence, nuclear drop, postoperative inflammation and intraocular hypertension among others. The long-term consequences of IFIS include permanent pupil deformity and vision loss secondary to endophthalmitis, macular edema or retinal detachment.<sup>1,22,23</sup>

Out of 44 eyes difficulty in the performance was noticed in 21 eyes thus increasing the surgical time. The mean duration of surgery in the IFIS group was 20.07± 8.31 mins whereas in the Non -IFIS group it was 16.13± 5.44 mins which was statistically significant. 29 cases required additional measures like intracameral epinephrine, Healon-5 in 5 cases and iris hooks with diamond configuration in 6 cases. Despite this the surgical outcome was good in all cases. The commonest complication encountered in our study was intraoperative miosis (22.7%), iris billowing (25%), striate keratopathy (18.1%), iris prolapse and iritis (13.6%), posterior capsule rupture (11.4%), Iris chafing and incarceration (4.5%).

The complications of IFIS can be prevented and managed by maintaining mydriasis and restraining the iris from prolapsing during cataract surgery which can be achieved by use of mechanical dilators and pharmacologic agents, and the low fluidic parameters during phacoemulsification. Adequate pupil dilation can be maintained by using iris hooks, iris retractors, or expansion rings. Malyugin ring is said to inhibit iris movement by increasing the required critical pressures that can mechanically stiffens and dilate the pupil.<sup>24</sup>

They are easier to use, require less operating time, do not require extra incisions, provide a stable pupil during surgery and minimise the postoperative pupil deformity.

Pharmacologic agents include preoperative atropine at various intervals prior to surgery and intraoperative phenylephrine or

epinephrine injected under iris. Phacoemulsification fluidic parameters include lower aspiration flow (<22 mL/min) and lower vacuum (<200 mm Hg).<sup>25</sup>

## CONCLUSION

The critical aspects of IFIS are stratification of performative risk, prompt preoperative prophylaxis and surgical technique with the aid of mechanical and pharmacological agents.

Practising urologists, ophthalmologists and primary care physicians are aware of this possible association. However, still there exists a knowledge gap about IFIS among urologists and General physicians, indicating that continuing medical education is required to create awareness about IFIS. Surgeons should elicit a reliable history of  $\alpha$ 1AR antagonist consumption in the presence of hypertension.

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## Conflict of interest

The authors confirm that this article content has no conflict of interest

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