European Journal of Ophthalmology / Vol. 17 no. 6, 2007 / pp. 909-913

Clinical features, complications, and incidence of intraoperative floppy iris syndrome in patients taking tamsulosin

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PURPOSE. *To evaluate the intraoperative findings, complication rates, effect of intracameral adrenaline, and incidence of intraoperative floppy iris syndrome (IFIS) in patients using tamsulosin.*
METHODS. *In this prospective nonrandomized observational study, 858 eyes of 774 patients who had phacoemulsification between August 2005 and November 2006 were evaluated. Duration and preoperatively discontinuing time of tamsulosin intake were questioned. Preoperative pupil size, intraoperative iris behavior, progressive miosis, adrenalin usage, and complications were recorded.*
RESULTS. *The incidence of IFIS was 1.6% and IFIS was seen in 14 of the 18 eyes of patients using tamsulosin (77.8%). One eye had floppy iris only, 2 eyes had floppy iris and intraoperative miosis, 3 eyes had floppy iris and iris prolapse, and 8 eyes had all three signs of IFIS. IFIS was seen in 7 of the 10 eyes where intracameral adrenaline was used, and in 7 of the 8 eyes without adrenaline (p=0.588). Intraoperative miosis was seen only in 3 of the 10 eyes with adrenaline and in 7 of the 8 eyes without adrenaline (p=0.025). Posterior capsule rupture occurred in 1 of the eyes with IFIS and in 5 eyes focal iris stromal atrophy caused by prolapse was seen.*
CONCLUSIONS. *IFIS occurred in 1.6% of cases having phacoemulsification. Intracameral adrenaline usage did not change the IFIS occurrence rate, but it seemed to be effective in preventing intraoperative miosis. There are still many questions about IFIS, and there is need for future studies strengthening the understanding of IFIS. (Eur J Ophthalmol 2007; 17: 909-13)*

KEY WORDS. *Intracameral adrenaline, Intraoperative floppy iris syndrome, Phacoemulsification, Tamsulosin*

Accepted: June 12, 2007

INTRODUCTION

Intraoperative floppy iris syndrome (IFIS) is a new condition described by Chang and Campbell (1) and characterized by three signs that occur during cataract surgery. The triad observed by Chang and Campbell (1) that distinguishes IFIS includes a flaccid iris stroma that undulates and billows in response to ordinary intraocular fluid currents, a propensity for the floppy iris stroma to prolapse toward the phaco and side-port incisions, and progressive intraoperative pupil constriction.

This new small pupil syndrome is thought to be caused by a lack of dilator smooth muscle tone of the iris and associated with tamsulosin (Flomax), a systemic sympathetic α_{1A} adrenergic receptor blocker, prescribed for treating the symptoms of benign prostatic hyperplasia.

Intraoperative miosis and the other findings make cataract surgery more difficult in these cases, and some complications may occur during surgery. It is important to know if the patient uses any α_1 adrenergic receptor blockers.

In this prospective study, we attempted to evaluate the intraoperative findings, complication rates, effect of intracameral adrenaline, and incidence of IFIS in patients using tamsulosin.

 1120-6721/909-05$15.00/0

PATIENTS AND METHODS

In this prospective nonrandomized observational study patients who had cataract surgery between August 2005 and November 2006 were evaluated. All patients enrolled in this study agreed to participate and met the inclusion criteria and signed an informed consent agreement before any procedures were performed. The study was performed in accordance with the ethical principles as described in the Declaration of Helsinki. All patients were questioned about use of tamsulosin or other α_1 adrenergic receptor blockers. Duration and preoperatively discontinuing time of tamsulosin intake and ocular and systemic histories were also questioned.

All patients using tamsulosin or other α_1 adrenergic receptor blockers received standard dilation regimen of cyclopentolate HCl 1% (Sikloplejin), phenylephrine HCl (Mydfrin 2.5%), and ketorolac tromethamine 0.5% (Acular), 30 minutes before the operations. All had standard phacoemulsification with intraocular lens (IOL) implantation performed by the authors using Infiniti phacoemulsification unit (Alcon Laboratories). The surgeons were not masked preoperatively to whether the patients were receiving α_1 receptor blockers. Following side-port and clear corneal 3.0 mm incisions, capsulorhexis was performed under sodium hyaluronate 2% (Cohaerens). After hydrodissection, phacoemulsification was performed using the stop-and-chop phacoemulsification technique. In all eyes, a 0.9 mm flared, 30-degree, ABS Kelman microtip was used. The cortex was removed with bimanual infusion/aspiration cannulas. After removing the cortex, sodium hyaluronate 2% (Cohaerens) was injected into the anterior chamber, the incision was enlarged to 4.1 mm, and a foldable, one-piece hydrophilic acrylic IOL (Ocuflex) or hydrophobic acrylic IOL (Acrysof) was inserted in the capsular bag with forceps. The ophthalmic viscosurgical device was removed from the anterior chamber carefully until no viscoelastic material was visible and the procedure was completed after closure of the incisions by stromal hydration.

Adrenaline was injected into the anterior chamber after corneal incisions, before viscoelastic instillation in eyes with small pupils (preoperative pupil smaller than 4.0 mm) to dilate the pupils more and to prevent further constriction during the operations. Intracameral adrenaline was prepared using 0.1 mL of unpreserved adrenaline bitartrate (Adrenalin 0.5 mg) diluted with 2 mL of BSS and 1.0 mL of this solution was injected into the anterior chamber. Before washing out the agent, 30 seconds were waited to ensure maximum effect.

Preoperative pupil size, intraoperative iris behavior (undulation, billowing), iris prolapse, progressive pupil constriction, adrenalin or any other device usage other than standard surgery method, and complications occurring during phacoemulsification were recorded and effective phaco times were calculated. IFIS was defined based on the intraoperative behavior. Preoperative pupil (in the surgery room) greater than 4.0 mm was accepted as well dilated and the others as small.

Statistical analysis was performed using SPSS 13.0 for Windows (SPSS Inc.). Mann-Whitney and Fisher exact tests were used to compare the parameters. Two-way analysis was used for all tests and p values less than 0.05 were considered to be statistically significant in all analyses.

RESULTS

A total of 858 eyes of 774 patients had cataract surgery between August 2005 and November 2006. Seventeen patients (2.2 %) were taking tamsulosin and phacoemulsification was performed in 18 eyes (2.1% of eyes having cataract surgery) of these patients. Three of these eyes (16.7%) had exfoliation syndrome and none of the patients with tamsulosin intake had diabetes mellitus. Mean age of the patients using tamsulosin was 70.2±6.8 years (50–79). The mean duration of tamsulosin intake was 18.4±13.2 months (4–60) and discontinuing time of the drug before operations was 5.5±5.9 months (0.5–12) in 5 eyes. Effective phaco time was 9.4±6.7 seconds (1.5–20.7).

Of the eyes with tamsulosin intake, 4 eyes (22.2%) had no signs of IFIS during phacoemulsification. One eye (5.6%) had floppy iris only, 2 eyes (11.1%) had floppy iris and intraoperative miosis, 3 eyes (16.7%) had floppy iris and iris prolapse, and 8 eyes (44.4%) had all three signs of IFIS. The incidence of IFIS in this study was 1.6% and IFIS was seen in 14 of the 18 eyes of the patients using tamsulosin (77.8%).

The mean duration of tamsulosin intake was 12.8±8.8 months (4–24) in eyes without IFIS and 20.0±14.1 months (4–60) in eyes with IFIS (p=0.307).

IFIS was seen in 7 of the 10 eyes where intracameral adrenaline was used, and in 7 of the 8 eyes without adrenaline (p=0.588). When intraoperative miosis is taken into consideration there was difference between the

groups according to intracameral adrenaline usage and progressive miosis was seen only in 3 of the 10 eyes with adrenaline and in 7 of the 8 eyes without adrenaline (p=0.025).

It was seen that preoperative pupil dilation did not always correlate with IFIS occurrence rate and severity. IFIS was seen in 7 of the 10 eyes with small pupil and 7 of the 8 eyes with well dilated pupil (p=0.588).

Intraoperative complications occurred in 6 of the 14 eyes (42.9%) with IFIS. Posterior capsule rupture occurred in 1 eye (the IOL was successfully implanted in the capsular bag) and in 5 eyes focal iris stromal atrophy caused by prolapse were seen. Irregular pupil was seen in 2 of these eyes postoperatively. Surgery was uneventful in 4 eyes without IFIS. Complication rates were not different between the eyes with and without IFIS in patients taking tamsulosin (p=0.245).

In one patient, although all of the preoperative and intraoperative methods were same, one eye had IFIS with all three signs and the other had no sign.

When α_1 adrenergic receptor blockers other than tamsulosin were investigated it was seen that IFIS occurred in one of the four eyes of patients taking terazosin (Hytrin) and in one of the two eyes of patients taking alfuzosin (Uroxatral).

DISCUSSION

The IFIS triad, thought to be caused by lack of dilator smooth muscle tone of the iris, is seen in a high proportion of patients using tamsulosin (Flomax) (1-3). The basis of IFIS is thought to be antagonism of α_{1A} receptors located in the iris, which results in miosis. There are three known α_1 receptor blocker subtypes (α_{1A}, α_{1B}, and α_{1D}) (4). The α_{1A} and α_{1D} receptors which are present in prostate and detrusor, respectively, are targeted in treating lower urinary tract symptoms seen in benign prostatic hyperplasia. Tamsulosin is an α_1 adrenergic receptor blocker. Contraction of the iris dilator muscle in rabbits, rats, and probably humans is mediated via α_1 receptors, and this may explain why tamsulosin is associated with IFIS (2, 4).

The prevalence of IFIS is reported to be approximately 2% in the cataract surgery population (1). Besides, 63 % of patients using tamsulosin in the retrospective study and 100% of patients in the prospective study experienced IFIS (1). This discrepancy was explained by the fact that in the retrospective study, the presence of IFIS could be determined only by operation reports and because the surgeons were not investigating IFIS several cases may not have been diagnosed. IFIS was not seen in all eyes of patients using tamsulosin in some other studies (2, 3, 5). Cheung et al (3) reported that of 2390 cataract operations performed, 15 patients (17 eyes) were taking tamsulosin and 6 eyes did not display any IFIS feature. IFIS occurred in 1.1% of cases in another study (6). Manvikar and Allen (2) noted IFIS in 32 (1.2%) of 2678 eyes having cataract surgery. In our study incidence of IFIS was 1.6% in 858 eyes. We have not seen IFIS in all eyes of the patients using tamsulosin and IFIS was seen in 14 of the 18 eyes (77.8 %).

The severity of IFIS is often variable and it presents in varying degrees, even in different eyes of the same patient and surgery becomes more difficult in eyes with all three signs. The syndrome is also seen in some patients who are not taking tamsulosin or other systemic sympathetic α_1 receptor blockers. The floppy iris in IFIS is frequently not recognized until hydrodissection is performed. Iris prolapse also can be caused by poor incision construction or by excessive injection of fluids or viscosurgical devices. Furthermore, surgically induced miosis during phacoemulsification may be seen in patients with diabetes mellitus (7). However, Chadha et al (8) reported that diabetes does not have a contributory role in IFIS occurrence. Therefore, all these parameters should be controlled before considering true IFIS. In our study incision constructions were well performed and excessive injection of fluids or viscosurgical devices was not performed in any eyes with IFIS and none of the patients with tamsulosin intake had diabetes mellitus. Therefore, we believe that they were all true IFIS.

It may be thought that to stop tamsulosin before cataract surgery may avoid the possibility of IFIS. However, the exact time to stop the drug and the efficacy of this action need to be determined, because the effect is unclear. IFIS effects can be seen several months after stopping tamsulosin. IFIS has been observed in patients who discontinued therapy as long as 9 months (9) and even 3 years (1) before cataract surgery (9). Discontinuation of α_1 adrenergic receptor blockers before surgery seems to be important because therapeutic blood level of these drugs would compete with mydriatic agents and make pupil dilation more difficult (10). In Parssinen et al (11) study the iris remained floppy after 7- to 28-day interruption of the tamsulosin regimen. The occurrence of IFIS months after

withdrawal of tamsulosin suggests that it has long-lasting effects on iris function and may produce atrophic changes in the iris (1). In some studies IFIS was seen as early as 3 months after the patient started taking tamsulosin (3). In our study there was no difference between the mean duration of tamsulosin intake in eyes with and without IFIS and there was no significant trend toward IFIS occurrence according to tamsulosin taking or discontinuation time. Future studies will clarify whether discontinuation of these drugs should be considered before cataract surgery. All these findings should be evaluated with caution because the number of patients on tamsulosin and eyes with IFIS are too small.

There is no simple solution to reduce IFIS. Management strategies can be mainly divided into three categories: pharmacologic (preoperative atropine, intracameral adrenaline) (2, 5, 12-14), visco mydriasis (Healon 5) (1, 15), and use of devices (iris stretching [which is often ineffective], partial thickness iris sphincterotomies, pupil expansion ring, iris hooks) (1, 2). One of the most important parts of safe cataract surgery is adequate pupil dilation. We know that the injection of adrenaline intracamerally causes additional dilation in small to mid-dilated pupils. In our patients we only used intracameral adrenaline, which is said to be effective for dilating the pupils and preventing further constriction during the operation. Intracameral adrenaline was used at the beginning of the surgery for pupil dilation. Manvikar and Allen (2) suggested that the intracameral injection of phenylephrine acts directly on the α_1 receptors and provides maximum stimulation that causes the pupil to dilate or at least increases the tone of the dilator muscle and prevents iris billowing. Gurbaxani and Packard (5) used intracameral phenylephrine in seven eyes of patients taking tamsulosin and reported no significant problems caused by IFIS. In our study we have seen that preoperative pupil dilation did not always correlate with IFIS occurrence rate and severity. Intracameral adrenaline usage also did not change the IFIS occurrence, but when intraoperative progressive miosis is taken into consideration there was a difference between the eyes with and without adrenaline. Adrenaline usage seemed to be effective only in preventing intraoperative miosis, although the final concentration of intracameral adrenaline was more than Shugar's (13).

Although Chang and Campbell (1) reported that IFIS was seen in both eyes of five patients using tamsulosin, in one of our cases, one of the eyes had IFIS while the other did not. The 76-year-old man had been on tamsulosin for 4 months and then stopped the medication 1 year before the cataract surgery. The left eye had uneventful phacoemulsification. One week after the surgery, the right eye was operated with the same method and had IFIS with all three signs. We have many questions to be answered in this case: Why was IFIS seen only in one eye? Are intake and stopping time of tamsulosin important for IFIS occurrence? Is intracameral adrenaline effective for prevention?

Complications of IFIS include the risk for posterior capsule rupture, vitreous loss, iris stromal atrophy, iris prolapse, capsulorhexis tear, iridodialysis, and anterior chamber hemorrhage.

Although in our study complication rates were not statistically different between the eyes with and without IFIS in patients taking tamsulosin, the risk level was inherently higher. Posterior capsule rupture occurred in one eye but the IOL was successfully implanted in the capsular bag. In five eyes focal iris stromal atrophy caused by prolapse occurred and of these, two eyes had irregular pupil postoperatively.

Other available α_1 adrenergic receptor blockers include alfuzosin, doxazosin, and terazosin. IFIS may also be associated with these α_1 adrenergic receptor blockers (10). We have also seen IFIS in eyes of patients taking terazosin (Hytrin) and alfuzosin (Uroxatral).

In conclusion, surgeons may encounter new and unusual surgical problems, like IFIS, during phacoemulsification. The three characteristics of IFIS make cataract surgery more difficult in patients using α_1 adrenergic receptor blockers and some complications may occur during surgery, but skilled surgeons can safely tackle the surgical challenges faced in IFIS. Careful medical history should be taken from every patient undergoing cataract surgery to elucidate IFIS predisposition and probable related complications. In these patients proper incision constructions should be performed and excessive hydrodissection or use of viscoelastics should be avoided. Many questions about IFIS remain, and future studies strengthening the understanding of IFIS are needed.

None of the authors has a financial or proprietary interest in any material or method mentioned and no author received public or private support.

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