Incidence, clinical findings and management of intraoperative floppy iris syndrome associated with tamsulosin

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ABSTRACT.

Purpose: To determine the risk ratios and incidence of intraoperative floppy iris syndrome (IFIS) during cataract surgery in patients using tamsulosin, and to assess management strategies for IFIS.

Methods: We performed a non-randomized, observational, prospective study, in which 594 eyes of 579 patients undergoing cataract surgery were enrolled. Surgeons were masked to the patients’ drug history. Usage or non-usage of tamsulosin, duration of tamsulosin use, presence or absence of IFIS, management of IFIS and intraoperative complications were recorded in the patients’ theatre notes.

Results: Twelve of 15 (80%) IFIS patients were taking systemic tamsulosin. Twelve of 23 (52%) patients using tamsulosin showed features of IFIS. The odds ratios (ORs) and relative risk (RR) ratios show strong positive correlations between tamsulosin use and IFIS. The ORs and RR ratios and the 95% confidence intervals (CIs) are as follows: OR 206.5 (95% CI 50.9–836.5); RR 99.3 (95% CI 30.0–327.8). There were no statistically significant differences between patients with or without IFIS, who were using tamsulosin, in terms of age or duration of tamsulosin use (p > 0.05). Seven eyes (46.6%) with IFIS were successfully managed with epinephrine. Eight eyes (53.4%) with IFIS needed iris hooks.

Conclusions: Patients using tamsulosin appear to be at high risk of IFIS during cataract surgery. The occurrence of IFIS may not be affected by duration of tamsulosin use or age. Epinephrine may be effective in approximately 50% of eyes with IFIS. The iris hook procedure represents an effective management strategy in IFIS.

Key words: cataract surgery – epinephrine – floppy iris – iris hook – tamsulosin

Introduction

Tamsulosin is commonly used in the treatment of benign prostatic hyperplasia (BPH). It is a selective alpha-1A receptor antagonist that relaxes the smooth muscle in the bladder neck and prostate, improving urinary flow in patients with BPH (Andersson 2002). However, it not only blocks alpha-1A receptors in the prostate, but is also thought to selectively block alpha-1A receptors common in the iris dilator muscle (Chang & Campbell 2005).

Recent findings have suggested that there is a strong association between use of tamsulosin and intraoperative floppy iris syndrome (IFIS) (Chang & Campbell 2005; Blouin et al. 2007; Chadha et al. 2007). This syndrome is characterized by the clinical triad of initial billowing and flopping of the iris in response to normal irrigation currents in the anterior chamber, repeated iris prolapse to incisions, and progressive miosis. Because of the higher risk for posterior capsule rupture and iris trauma associated with IFIS cases, recognizing and anticipating these cases is important in enabling surgeons to reduce the complication rate (Chang & Campbell 2005).
In this prospective study, we assessed the link between tamsulosin use and the occurrence of IFIS during cataract surgery, and determined strategies for the management of IFIS.

Materials and Methods

We performed a non-randomized, observational, prospective study. Between January 2006 and July 2007, 594 eyes of 579 patients undergoing cataract surgery were enrolled in the study. Patients with pseudoxfoliation syndrome, chronic miotic therapy, previous trauma or surgery, uveitis with synechiae, glaucoma or diabetes mellitus were excluded. All patients underwent pupillary dilation by a standard protocol of 2.5% phenylephrine and 1% cyclopentolate drops. Surgeons were masked to the patients’ drug histories. VisCoat® (Alcon Laboratories, Inc., Fort Worth, TX, USA) was used as a viscoelastic agent in all patients. The appearance of all (floppy + progressive miosis) of three features during surgery was accepted as indicative of IFIS. These patients were treated with a 1 : 2500 dilution of epinephrine, administered intracameral in all eyes. Eight eyes (53.4%) (two floppy + progressive miosis + iris prolapse) and two (floppy + progressive miosis) of three features during surgery was accepted as indicative of IFIS. These patients were treated with a 1 : 2500 dilution of epinephrine, administered intracameral. In cases responding to epinephrine, the surgery was continued by adding 0.5 μg/ml epinephrine to irrigation solution (balanced salt solution [BSS]) in order to maintain pupil dilation. In cases that did not respond to epinephrine, however, iris hooks were applied. Usage or non-usage of tamsulosin, duration of tamsulosin use, presence or absence of IFIS, management of IFIS (intracameral epinephrine, iris hooks) and intraoperative complications were recorded in the patients’ theatre notes.

Statistical analyses

We constructed contingency tables for usage or non-usage of tamsulosin and possible confounding factors (age, duration of tamsulosin use). We used odds ratios (ORs) and relative risk (RR) ratios to estimate the risk of IFIS in patients who used tamsulosin and computed 95% confidence intervals (CIs). Odds and RR ratios are two important indicators with which to measure the strength of association between an exposure and a disease.

Mean, standard deviation (SD) and median values were calculated for descriptive statistics. Mann–Whitney U-test for non-parametric data was used to analyse two independent samples. Data were analysed using spss Version 15.0 (SPSS Inc., Chicago, IL, USA). Two-sided p-values were considered statistically significant at p < 0.05.

Results

The mean patient age was 63.6 ± 11.3 years (range 38–91 years). The 579 patients included 328 (57%) men and 251 (43%) women. Intraoperative floppy iris syndrome occurred in 15 (2.5%) of the 594 eyes of 579 patients. All the patients with IFIS were men. Twelve of the 15 (80%) IFIS patients were taking systemic tamsulosin. A total of 23 patients (3.9%) used tamsulosin, and 12 of the 23 (52%) patients receiving tamsulosin showed features of IFIS compared with three of the 571 (0.5%) patients who did not use tamsulosin. Nine eyes (60%) displayed all three features of IFIS. However, six eyes (40%) displayed two features of IFIS. Epinephrine was administered intracameral in all eyes with IFIS. Seven eyes (46.6%) (four eyes with two features and three eyes with three features of IFIS) were successfully managed with intracameral epinephrine. Eight eyes (53.4%) (two eyes with two features and six eyes with three features of IFIS) were managed with iris hooks. The odds and RR ratios show a strong positive correlation between tamsulosin and IFIS (Table 1). There were no statistically significant differences between patients with or without IFIS, who were using tamsulosin, in terms of age and duration of tamsulosin use (p > 0.05) (Table 2). In terms of complications, iris trauma with the phaco tip occurred in one eye of one patient (6.6%), and corneal oedema occurred in one patient (6.6%) with IFIS. Best corrected visual acuity at 3 months postoperatively was 10/10 in the patient with iris trauma, and 8/10 in the patient with corneal oedema.

Discussion

The overall incidence of IFIS among patients undergoing cataract surgery is 1.1–2.3%, but 37.9–73.0% in patients receiving tamsulosin (Chang & Campbell 2005; Blouin et al. 2007; Chadha et al. 2007; Oshika et al. 2007). Similarly, in this study, IFIS occurred in 2.5% of patients undergoing cataract surgery and in 52% of patients receiving tamsulosin. The syndrome was first described by Chang & Campbell (2005), who suggested that IFIS occurrence in cataract surgery was strongly related to tamsulosin use. Chadha et al. (2007) assessed the

| Table 1. The results of odds and relative risk ratios. |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Patients        | IFIS (+) (%)    | IFIS (-) (%)    | Odds ratio      | RR (95% CI)     | Total           |
| Tamsulosin (+)  | 12 (52.1)       | 11 (47.9)       | 206.5 (50.9–836.5) | 99.3 (30.0–327.8) | 23              |
| Tamsulosin (-)  | 3 (0.5)         | 568 (99.5)      |                 |                 | 571             |
| Total           | 15 (2.5)        | 579 (97.5)      |                 |                 | 594             |
| IFIS = intraoperative floppy iris syndrome; RR = relative risk; 95% CI = 95% confidence interval. The odds and relative risk ratios show a strong positive correlation between tamsulosin and IFIS.

| Table 2. Differences in age and duration of tamsulosin use in patients with and without intraoperative floppy iris syndrome. |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| Patients using tamsulosin | Age, years | p | Duration of tamsulosin use, years | p |
| IFIS (+)        | Median = 64.5   | 0.975           | Mean ± SD = 25.08 ± 15.92 | 0.902          |
| IFIS (-)        | Median = 60.0   |               | Mean ± SD = 25.6 ± 16.65   |               |
| IFIS = intraoperative floppy iris syndrome; SD = standard deviation.
association of floppy iris behaviour during cataract surgery with use of alpha-1 antagonists and with diabetes mellitus in large prospective series and reported that tamsulosin was significantly associated with floppy iris behaviour during cataract surgery. However, they found that diabetes mellitus and other alpha-1 receptor antagonists were not associated with IFIS. In this study, odds and RR ratios for IFIS were found to be very high in patients receiving tamsulosin. Our findings support the view that a strong positive correlation exists between the occurrence of IFIS and use of tamsulosin.

Cheung et al. (2006) reported that IFIS is not linked to duration of tamsulosin use. Our study investigated the association between IFIS and duration of tamsulosin use, as well as that between age and IFIS. However, we did not find any association between IFIS and duration of tamsulosin use or age. We believe that duration of tamsulosin use or age may not affect the occurrence of IFIS during cataract surgery.

The subjectivity of IFIS features has been highlighted previously. The criteria offered for the diagnosis of IFIS are subjective and initial reports do not state whether all features are required for the diagnosis, and do not provide a system for grading features for inclusion (Chang & Campbell 2005; Lawrentschuk & Bylsma 2006). Therefore, in this study, eyes displaying all three features of IFIS and eyes displaying two features only were accepted as demonstrating IFIS. However, in a recent study by Chang et al. (2007) IFIS was categorized as mild (floppy iris without prolapse or miosis), moderate (floppy iris, significant miosis and a small tendency towards iris prolapse), or severe (floppy iris, significant miosis and a strong tendency towards iris prolapse). We believe that categorization of IFIS may be important to the determination of management strategies.

Recent studies report some success with pharmacological approaches to IFIS. The drugs involved are usually administered intracameraly and include phenylephrine (Gurbaxani & Packard 2007), epinephrine (Backstrom & Behndig 2006; Shugar 2006; Lundberg & Behndig 2007), atropine (Bendel & Philips 2006) and atropine plus epinephrine (Masket & Belani 2007). Because tamsulosin blocks the alpha-1 adrenergic receptors of the iris dilator muscle, it seems plausible that this blockade might be overcome by flooding the receptors with an intracameral administration of their natural agonist, epinephrine or phenylephrine. Gurbaxani & Packard (2007) described the use of intracameral phenylephrine in cataract surgery in seven patients with a history of tamsulosin use. The authors mixed 0.25 ml of phenylephrine hydrochloride 2.5% with 1 ml BSS and instilled this mixture prior to injecting the viscoelastic into the anterior chamber. The results showed sustained pupillary dilatation and no iris prolapse in all seven cases. Backstrom & Behndig (2006) described the use of intracameral epinephrine for redilating the pupil during cataract surgery, and 0.6 µg/ml of epinephrine added to the BSS used for irrigation. They showed that, in cases of intraoperative pupil contraction, intracameral epinephrine is effective in redilating the pupil. Shugar (2006) described a new formulation which he termed 'epi-shugarcaine' for IFIS. The formulation for epi-shugarcaine requires the mixing of 9 ml of BSS Plus with 3 ml of 4% preservative-free lidocaine and 4 ml 1 : 1000 bisulphite-free epinephrine. Shugar (2006) suggested epi-shugarcaine as the preferred agent for IFIS prophylaxis in all patients with a history of using tamsulosin. Masket & Belani (2007) also described a technique combining preoperative atropine sulphate 1% and intraoperative intracameral epinephrine in a 1 : 2500 dilution for the management of IFIS induced by tamsulosin. They reported that stimulation of the iris dilator by epinephrine combined with atropine provides powerful synergism.

In this study, epinephrine in a 1 : 2500 dilution was instilled intracameraly when the symptoms of IFIS appeared during surgery. In cases responding to epinephrine, 0.5 µg/ml epinephrine was added to irrigation solution (BSS) to maintain pupil dilatation. Intracameral epinephrine was effective in approximately 50% of eyes with IFIS, but it was ineffective in most of the eyes with all three features of IFIS. Epinephrine is convenient because it can be instilled at any time during a case, so if a surgeon is surprised by the sudden appearance of symptoms, he or she can deal with them and proceed.

Iris retractors or pupil expansion rings are the most reliable means of maintaining a safe pupil diameter during surgery (Oetting & Omphroy 2002; Chang & Campbell 2005). Heavy-chain ophthalmic viscosurgical devices (OVDs) such as sodium hyaluronate 2.3% (Healon 5) are a useful adjunct as long as the substance stays in the eyes, but even with low flow and vacuum, it may be necessary to replenish Healon 5 several times during a procedure (Chang & Campbell 2005). Chang et al. (2007) recommended using iris retractors in tamsulosin patients if the pupil is small, the nucleus dense (requiring high vacuum), the anterior chamber shallow, or if the surgeon is not experienced in using Healon 5. These authors believe that use of iris retractors, a pupil expansion ring or the Healon 5 technique should result in cataract surgical outcomes comparable with those in non-IFIS eyes. The surgeon sometimes hesitates to use iris hooks for fear of damaging the iris sphincter. However, the pupillary margin is very elastic and not fibrotic in eyes with IFIS (Chang & Campbell 2005). In this study, approximately half the eyes with IFIS needed iris hooks (especially the eyes with all three features of IFIS). We also observed that the pupillary margin was very elastic and not fibrotic, and we did not experience any difficulty using this equipment. A hook located under the main phaco incision keeps that part of the iris secure and prevents prolapse. It also ensures ample space to the nucleus for the phaco needle. Similarly, we are of the opinion that the iris hook is a reliable means of maintaining a safe pupil diameter during surgery.

In a recent multicentre study, Chang et al. (2007) reported that when experienced surgeons were able to anticipate IFIS and employ compensatory surgical techniques, the complication (posterior rupture with vitreous loss) rate from cataract surgery was low (0.6%) in eyes of patients with a history of tamsulosin use. In our study, no severe complications occurred in any patient with IFIS. However, iris trauma with the phaco tip occurred in one eye of one patient, and corneal oedema occurred
in one patient with IFIS. We believe that management of IFIS with epinephrine or the iris hook may decrease the rate of severe complications.

We found a strong link between the occurrence of IFIS and use of tamsulosin. Patients using tamsulosin appear to be at high risk for IFIS during cataract surgery. The occurrence of IFIS during cataract surgery may not be affected by the duration of tamsulosin use or by age. Management by intracameral epinephrine may be effective in approximately 50% of eyes with IFIS. The iris hook also provides an effective management tool in IFIS when intracameral epinephrine is not effective.

References


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