Influence of Tamsulosin on the Iris and Its Implications for Cataract Surgery

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BACKGROUND. For years, cataract surgery has been considered one of the most frequently performed surgical procedures. Despite a lifetime of research, cataract-related complications have remained a concern for patients and surgeons alike. Recently, intraoperative floppy iris syndrome (IFIS), a symptom complicating cataract surgery, has shown to be dominant in the iris.5 Intraoperative floppy iris syndrome (IFIS) is a condition that occurs during cataract surgery and is characterized by the sudden and unexpected inability of the iris to accommodate during surgery. This condition is often associated with the use of certain medications, such as alpha blockers, which are prescribed to treat conditions such as benign prostatic hyperplasia.6

METHODS. Twenty-one consecutive cataract patients administered tamsulosin and 21 control patients were studied. Characteristic of the iris during surgery were recorded. Pupillary diameters of 16 patients were measured before and after iris surgery. Tamsulosin concentrations in the aqueous humor and serum were analyzed. In five patients, surgery on the second eye was carried out after a 7- to 28-day pause in tamsulosin medication.

RESULTS. Each patient administered tamsulosin had a sluggish hypotonic iris, along with a tendency toward miosis and a tendency for prolapse of the iris into the phaco tunnel or into the side port during cataract surgery. Sluggish irises also often adhered to the phaco tip or to the irrigation-aspiration tip. Despite a pause of 7 to 28 days in the use of tamsulosin, the adverse consequences persisted. Tamsulosin concentrations varied between 0.1 and 1.0 ng/mL in the anterior chamber fluid. In three of five cases, tamsulosin remained in detectable amounts in the aqueous humor after the 7- to 28-day pause. Preoperative pupillary diameter was smaller in the patients using tamsulosin than in the controls.

CONCLUSIONS. Tamsulosin has selective α1A-adrenoceptor antagonistic properties and obviously binds for a long period to the postsynaptic nerve endings of the iris dilator muscle, thus affecting iris dilatation and leading to complications in cataract surgery. The iris remained floppy after 7- to 28-day interruption of the tamsulosin regimen. (Invest Ophthalmol Vis Sci. 2006;47:3766–3771) DOI:10.1167/iovs.06-0153

Tamsulosin, an α1A/α1D subtype selective α1-adrenoceptor antagonist (α1-blocker), is the most frequently prescribed medication for the treatment of lower urinary tract symptoms suggestive of benign prostatic hyperplasia.1,2 Konno and Takayanagi3 and Nakamura et al.4 found in rabbit eyes that tamsulosin concentrations varied between 0.1 and 1.0 ng/mL in the anterior chamber fluid. In three of five cases, tamsulosin remained in detectable amounts in the aqueous humor after a 7- to 28-day pause. Preoperative pupillary diameter was smaller in the patients using tamsulosin than in the controls.

MATERIALS AND METHODS

Study Population

Twenty-one male patients with cataract who were administered tamsulosin (Omnic; Yamanouchi, Astellas, Staines, UK, and Expros; Orion Pharma, Newbury, UK) were recruited for cataract surgery between January 2004 and April 2005 at the Central Hospital of Central Finland. Inclusion criteria were current use of tamsulosin by patients and that OP was on duty at the time of operation. Exclusion criteria were glaucoma, previous ocular trauma, or use of eyedrops other than artificial tears. Four of the tamsulosin patients underwent surgery with other surgeons, and only their preoperative pupillary measures were analyzed in this study.

In five patients, surgery on the second eye was performed after a pause in tamsulosin medication for 7 to 28 days. One of the patients with bilateral cataract had erroneously suspended the use of tamsulosin 7 days before the first operation.

This study adhered to the tenets of the Declaration of Helsinki and was approved by the ethics committee of the Central Hospital of Central Finland. Measurements were taken only after the patients had given their informed consent.

Pupillary Measurements

Before surgery, pupillary diameters were measured twice using a pupillometer (P2000; Procyon, Montréal, Canada) at three different levels of illumination: scotopic (0.04 lux), mesopic low (0.4 lux), and mesopic high (4.0 lux). Background illumination of the examination room was 10 to 11 lux. The first set of three measurements was performed for all patients before pupillary dilatation, and the second set of measurements was performed for 16 patients 20 minutes after the...
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In 8 of 17 (47%) patients, intraoperative miosis was high enough to make the surgery considerably more demanding. The average postoperative pupillary diameter in the eye operated on was 4.5 mm compared with preoperative values of 6.39 mm in the right eye and 5.99 mm in the left eye. In 15 of 17 (88%) patients, the iris prolapsed into the phaco tunnel. The iris prolapsed into the side port in 7 of 17 (41%) patients. In all patients with iris prolapse (88%), a lesion was found in the iris pigment epithelium, and in 3 (18%) patients the lesion was noteworthy. Adherence of the iris to the phaco tip occurred in one patient and to the IA-tip in 8 of 17 (47%) patients. Hemorrhage of the iris was seen in one patient. In patients 4 and 9, the iris did not prolapse into the tunnel or side port. Patient 4 had been taking tamsulosin for only 6 months, and patient 9 had been taking it for 2 years. Patients 11 and 15 had also been taking tamsulosin for approximately the same length of time as patients 4 and 9, respectively, but had iris prolapse into both the tunnel and the side port. Postoperative pupillary diameters varied between 2 and 8 mm. Figure 1 shows a poorly dilated pupil and typical iris prolapse into the phaco tunnel.

Only preoperative pupillary measurements were taken in control patients, who underwent surgery unsselectively by doctors in our clinic. Between January 9, 2004 and April 10, 2005, OP personally performed 342 of 1754 cataract operations performed in the department. Iris-related complications encountered during these operations were not systematically recorded. Although some patients—especially those with glaucoma or pseudoexfoliation syndrome—experienced poorly dilated pupils or iris prolapse, the hypotonically flustered iris was typical only of patients taking tamsulosin.

Tamsulosin Measurements

Patients had significant variation in tamsulosin concentrations, both in the aqueous humor and in the serum (Table 1). Tamsulosin concentrations in the aqueous humor did not significantly correlate with those in the serum. Three patients (patients 5, 7, 8) did not have enough aqueous humor to enable reliable quantitative measurement. Their concentrations measured approximately 0.3 to 0.5 ng/mL. No correlation was observed between adverse effects and concentrations of tamsulosin in either the aqueous humor or the serum. Similarly, we found no relationship between the patients’ other medications and the severity of the iris-related complications. Whether included or excluded, the data on patient 7, who had erroneously discontinued the use of tamsulosin 7 days before the first operation, did not influence the results of the analyses.

In five patients with bilateral cataract, the use of tamsulosin was suspended for 7 to 28 days before surgery on the second eye (Table 2). Patient 7, however, had erroneously suspended the use of tamsulosin for 7 days before the first operation. In all patients, the iris continued to be sluggish. With so few cases it is impossible to say whether the pause in the use of tamsulosin caused any significant reduction in the adverse effects. Pupillary diameters remained similar after the pause. Tamsulosin concentrations in serum fell below the limits of quantification in all patients. In the aqueous humor, tamsulosin remained quantifiable after a pause of up to 28 days, except in patient 10. All patients who had suspended the use of tamsulosin experienced intensified urinary problems. Patient 11 underwent unsuccessful catheterization; consequently, a suprapubic cystostomy application had to be performed.

Pupillary Measures

Pupillary diameters of patients and controls were measured in both eyes before and after phenylephrine and tropicamide dilatation (Table 3). Before pupillary dilatation, light intensity had a natural effect on iris size in both groups (P < 0.0001): the
higher the intensity, the smaller the size of the iris. A significant group effect also resulted (P < 0.021). Scheffé post hoc analysis revealed that the size of the iris in patients under tamsulosin treatment was significantly smaller than it was in controls at the mesopic low and high levels of illumination (P < 0.01 and P < 0.002, respectively). The difference was almost significant at the scotopic level (P = 0.005). The difference in iris size between patients taking tamsulosin medication and controls was approximately 1 mm at the same level of illumination. No light intensity group interactions were detected. After dilatation, pupillary diameters in both groups were not significantly influenced by illumination level, and the difference in pupillary size between patients and controls no longer reached significance.

**DISCUSSION**

The main finding of this study was that each patient taking tamsulosin had a sluggish iris and a small pupillary diameter, making cataract surgery more demanding. In in vitro studies, tamsulosin has been shown to have 12 to 20 times higher affinity for the α1A-adrenoceptors than for the α1D-receptors and 2 to 3 times higher affinity for the α1A-adrenoceptors than for the α1D-receptors. Sato et al found in dogs that the plasma concentration of tamsulosin was close to the limit of detection at 240 minutes, whereas concentrations in the prostate and urethra remained 13 to 44 times higher. This was thought to show sustained binding of tamsulosin to the target tissues. It can be suggested that in the iris tamsulosin binds for a long period to the postsynaptic α1A-receptors than for the α1D-receptors. This was consistent with our findings. Before surgery, pupils were approximately 1 mm smaller at the dilating muscle. This was obviously the effect of tamsulosin preventing the receptor binding of sympathomimetic phenylephrine, which, combined with the simultaneous paralysis of the sphincter pupillae by tropicamide drops, may be factors leading to a sluggish iris with no tonus.

A poorly dilating pupil, which may have various causes—among them glaucoma, diabetes, and pseudoexfoliation—is not an uncommon finding during cataract surgery. Similarly,
Iris prolapse into the phaco tunnel may occur, possibly because of elevated intraocular pressure. Various medicines have systemic sympatholytic and parasympathomimetic effects that in turn may affect pupillary dilatation during cataract surgery. These effects and co-effects of different medicines should be examined more systematically in future studies. However, in patients using tamsulosin, the clinical characteristics of the iris during cataract surgery are typically different from, for example, the characteristics of the iris in patients with diabetes and glaucoma. In particular, the hypotonically fluttering iris during irrigation–aspiration is typical of all IFIS patients.

It has been suggested that IFIS is connected with all four commercially available α1-AR antagonist medications: alfuzosin, doxazosin, tamsulosin, and terazosin. Of these, only alfuzosin and tamsulosin are marketed in Finland. The use of tamsulosin in Finland is fairly common and has steadily increased, from 5.1 defined daily doses (DDD) per 1000 inhabitants with a daily dose of 0.4 g in 2001 to 7.1 in 2005. During the same period, the use of alfuzosin was significantly less but nevertheless increased from 0.1 to 1.9 DDD per 1000 inhabitants. Thus far, we have not observed similar adverse effects in our clinic with alfuzosin (OP, unpublished observations), perhaps in part because of the significantly lower use of this medication compared with tamsulosin. Nevertheless, prospective clinical studies should be performed to compare the characteristics of the iris in patients using different α1A-sympatho-

![Figure 1. Iris prolapse into the phaco tunnel and iris catching into the irrigation-aspiration tip during irrigation–aspiration and poor dilatation of the iris in a patient using tamsulosin.](image)

### Table 2. Iris-Related Complications and Urinary Symptoms before and after Pause in Tamsulosin Therapy

<table>
<thead>
<tr>
<th>Patient</th>
<th>Duration of Pause (d)</th>
<th>Daily Dose (mg), and Length of Tamsulosin Treatment</th>
<th>Complications during Cataract Surgery</th>
<th>Postoperative Pupillary Diameter (mm)</th>
<th>Tamsulosin Concentration in Serum (ng/mL)</th>
<th>Tamsulosin Concentration in Aqueous Humor (ng/mL)</th>
<th>Urinary Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>7</td>
<td>0.4 × 1, 2 y</td>
<td>M, S, PT, PS, CP, CIA, H</td>
<td>3</td>
<td>&lt;0.1</td>
<td>†</td>
<td>—</td>
</tr>
<tr>
<td>14</td>
<td></td>
<td></td>
<td>M, S, PT, CP, CIA</td>
<td>5</td>
<td>&lt;0.1</td>
<td>†</td>
<td>Increased urination</td>
</tr>
<tr>
<td>8</td>
<td>0</td>
<td>0.4 × 1, 2 y</td>
<td>S, PT, CIA, IL</td>
<td>7.5</td>
<td>14.7</td>
<td>†</td>
<td>—</td>
</tr>
<tr>
<td>28</td>
<td></td>
<td></td>
<td>S</td>
<td>8</td>
<td>&lt;0.1</td>
<td>0.3</td>
<td>Increased urination</td>
</tr>
<tr>
<td>9</td>
<td>0</td>
<td>0.4 × 1, 2–3 y</td>
<td>S</td>
<td>7.5</td>
<td>14.8</td>
<td>0.3</td>
<td>—</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td>0.4 × 1, ? y</td>
<td>S, PT</td>
<td>5</td>
<td>&lt;0.1</td>
<td>0.1</td>
<td>Increased urination</td>
</tr>
<tr>
<td>21</td>
<td></td>
<td></td>
<td>S, PT, PS</td>
<td>4.75</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
<td>Increased urination</td>
</tr>
<tr>
<td>11</td>
<td>0</td>
<td>0.4 × 1, 7 mo</td>
<td>S, PT, PS, CIA</td>
<td>5.25</td>
<td>8.1</td>
<td>0.1</td>
<td>—</td>
</tr>
<tr>
<td>7*</td>
<td></td>
<td></td>
<td>S, PT</td>
<td>7</td>
<td>&lt;0.1</td>
<td>0.2</td>
<td>Urinary retention, complicated catheterization, suprapubic cystostomy</td>
</tr>
</tbody>
</table>

M, miosis; S, sluggish iris; PT, iris prolapse into phaco tunnel; PS, iris prolapse into side port; CIA, iris catches into irrigation-aspiration tip; CP, iris catches on phaco tip; IL, iris lesion; H, iris hemorrhage; SS, slightly sluggish.

* Took 1 tablet tamsulosin 0.4 mg/d before surgery because of urinary retention.
† Positive result (>0.1 ng/mL) but not enough aqueous humor available for reliable quantitative measurement.
‡ Aqueous humor not available.
lytics. However, long experience leads us to suspect that similar cases of a floppy iris existed before the market entry of tamsulosin, some of which might have been linked to the use of chlorpromazine, which has α-sympatholytic and miotic effects.15

Different organic and inorganic substances, amino acids, and medicines are present in the aqueous humor.16 However, to our knowledge, this study is the first to show tamsulosin in the aqueous humor. Given that tamsulosin remained in the aqueous humor after a pause in its use of up to 28 days, it can be suggested that prolonged binding of tamsulosin to the iris, and perhaps to the corpus ciliare, occurred.

The concentration of tamsulosin in serum was below the limit of quantification in all five patients after a pause in its use of 7 to 28 days. Our relatively small sample does not permit conclusions on the possible relationship between the concentration of tamsulosin in the blood or in the aqueous humor and the severity of the reported adverse effects. It is suggested that the severity of IFIS may be related more to the duration of tamsulosin therapy than to its concentration in serum or in the aqueous humor. In the present study, it was not possible to determine the magnitude of the adverse effects in relation to the duration of tamsulosin therapy with the measures used. Nevertheless, the consensus was that the longer the period of tamsulosin use, the more sluggish the iris.

All the reported adverse effects connected with the use of tamsulosin tend to make cataract surgery more difficult and demand much patience and concentration on the part of the surgeon while increasing the risk for complications. In this sample, no posterior capsular rupture or vitreous complications occurred. Chang and Campell6 reported posterior capsular ruptures and vitreous loss in 12% of their patients, a frequency higher than usually found in patients with cataract. When the surgeon is aware of the possibility of adverse effects, he can try to perform the surgery more meticulously and thereby prevent posterior capsular complications. An iris that prolapses into the side port or into the phaco tunnel is liable to tear or lose its pigment layer, or it may become deformed, leading to impaired postoperative pupillary function.

Chang and Campell6 recommend suspending tamsulosin therapy 1 to 2 weeks before cataract surgery. Interestingly, their data include a patient who had mild IFIS despite the fact that the medication had been discontinued 3 years before the cataract surgery. Lawrentschuk and Bylsma17 recommend that urologists not change the prescribing habits of α-blockers but discontinue the use of tamsulosin 7 days before planned intraoperative surgery. In the present study, the sluggish iris remained in all five patients after a pause in the use of tamsulosin for 1 to 4 weeks. Additionally, as a direct result, all these patients reported increased difficulties in urination, and one patient had to undergo catheterization after a pause of only 1 week. Thus, suspending the use of tamsulosin seems to cause only annoying urinary symptoms while not alleviating the adverse effects on the iris.

This study supports earlier suggestions that tamsulosin causes long-term or permanent changes in iris function, a finding also supported by the recent poster presentation at the American Society of Cataract and Refractive Surgery–American Society of Ophthalmic Administrators (ASCRS-ASOA) Congress that showed, on transmission electron microscopy, a lack of identifiable myofibrils of iris dilator muscle of patients taking tamsulosin.18

Recently, it was shown that intracameral injection of phenylephrine at cataract extraction causes a significant reduction in the mobility of the iris, a reduction in fluttering, and sustained papillary dilatation.19 Helzner12 summarizes some of the suggested ways to minimize complications in patients with IFIS. Various properties of different viscoelastics, such as Healon 5, may have effects on iris undulation during cataract surgery. Fluttering of the iris is usually more pronounced during irrigation–aspiration. A reduction in the flow values may be helpful in some patients. Whether significant miosis is present, iris hooks obviously help make possible better visualization during surgery, but they do not prevent sluggishness of the iris.

Tamsulosin has been prescribed for urinary retention in women.50 Physicians who prescribe medicines for problems of the lower urinary tract—for women or for men—must be aware that in the event of later cataract surgery, tamsulosin significantly increases the risk for complications. In turn, the surgeon should find out before cataract surgery what medicines the patient is using and should be prepared for difficulty if they include tamsulosin.

### References


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**Table 3. Pupillary Diameters of the Right Eyes in Patients Using Tamsulosin and in Their Matched Controls at Three Levels of Illumination before and after Pupillary Dilatation with Phenylephrine 10% and Tropicamide 5% Drops**

<table>
<thead>
<tr>
<th>Pupillary Dilatation</th>
<th>Scotopic</th>
<th>Mesopic Low</th>
<th>Mesopic High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls (n = 21)</td>
<td>−</td>
<td>5.03 ± 0.82</td>
<td>4.55 ± 0.88*†</td>
</tr>
<tr>
<td>Patients (n = 21)</td>
<td>−</td>
<td>4.35 ± 1.33</td>
<td>3.68 ± 0.87+†</td>
</tr>
<tr>
<td>Controls (n = 21)</td>
<td>+</td>
<td>6.75 ± 0.90</td>
<td>6.55 ± 0.73</td>
</tr>
<tr>
<td>Patients (n = 16)</td>
<td>+</td>
<td>6.18 ± 1.00</td>
<td>6.07 ± 0.97</td>
</tr>
</tbody>
</table>

Statistical analysis was performed with ANOVA for repeated measurements and the Scheffe test. Multicomparison significance level was set at 95%.

* Significantly different from the values observed in the same patients at the scotopic level of illumination.
† Significantly different from the values observed in the controls at the same level of illumination.
‡ Significantly different from the values observed in the same patients at the mesopic level of illumination.


