Complicated Cataract Surgery in Patients Receiving Alpha-Blockers for Benign Prostatic Hyperplasia

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ABSTRACT

BACKGROUND
Of adults 50 to 80 years old, 29% of men in Europe and 34% of men in the United States have moderate to severe lower urinary tract symptoms. Alpha-blocker medications are the first line of therapy for men with these urinary symptoms. Among this population, cataracts are similarly common. The “intra-operative floppy iris syndrome” cataract surgery complication has been reported in men using alpha-blockers.

OBJECTIVE
To assess the frequency of cataract surgery complications arising from alpha-blocker therapy in a large patient population.

DESIGN, SETTING, AND PARTICIPANTS
We retrospectively reviewed the outcomes of 2666 consecutive adults who underwent elective unilateral cataract surgery. The surgeries took place between 2000 and 2005 at both a large university hospital system and a Veteran’s Association medical center. Medical records were assessed for medication use, and operative records were reviewed for evidence of difficult procedures.

RESULTS
The risk of complicated cataract surgery was 14.9% in patients using alpha-blockers, approximately 50% higher than those not receiving this medication (9.5%) (p=0.003). The increased rate of complicated surgeries was restricted primarily to patients over 65 years of age, as 15.6% of surgeries performed on these patients resulted in complicated surgery (p=0.03). There was no statistically significant increase in the rate of complicated surgeries in patients under age 65 who were using alpha-blockers (p>0.05).

CONCLUSIONS
If possible, alpha blocker medications should be discontinued prior to eye surgery in older patients.

KEYWORDS:
Alpha-Blocker Medications, Lower Urinary Tract Symptoms, Intra-Operative Floppy Iris Syndrome, Cataract Surgery

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As alpha-blocker medications are the first line of therapy for men with LUTS, these reports of IFIS led the Food and Drug Administration, American Urological Association, American Academy of Ophthalmology, and American Society of Cataract and Refractive Surgery to issue statements alerting physicians and patients to potential difficulties during cataract surgery in patients using alpha-1 blocker therapy \[7,8,9\]. The prevalence of lower urinary tract symptoms is very common. Approximately 29% of men in Europe between the ages of 50 and 80 have moderate to severe symptoms, while in the United States the prevalence rate is 34% in men within the same age bracket \[10\]. The risk of a confluence of both LUTS and cataracts is significant.

An important aspect of safe cataract surgery is adequate pupil dilation, allowing access to and removal of the cataractous lens and replacement with an artificial lens implant. Alpha-receptor antagonist medications potentially interfere with iris muscle dilation, resulting in difficult lens removal and possibly increasing complications. The purpose of this study was to assess the impact of alpha-blocker therapy on complications during cataract surgery in a large patient population.

**MATERIALS AND METHODS**

Clinical data from all patients who underwent cataract surgery between 2000 and 2005 at University Hospital (UH) and Audie L. Murphy Memorial Veterans Hospital (ALMMVH), San Antonio, Texas, were reviewed. This study was approved by the Institutional Review Board at both institutions. Exclusion criteria were trauma, multiple ophthalmologic procedures, children (<18 years), and incomplete records. For patients who had cataract surgery on both eyes during the study time period, only data pertaining to the first procedure were included. 2666 patients met the inclusion criteria of adults undergoing planned, elective, unilateral cataract surgery and were included in the study (UH n=1258, ALMMVH n=1408).

Data evaluated included age, gender, use of any alpha-blockers in the pre-operative period, and presence or absence of a difficult surgical procedure. Complicated surgery was defined as a case in which the operative note documented floppy iris, anterior vitrectomy, vitreous loss, capsular tear or rupture, placement of lens in the sulcus or anterior chamber, use of iris hooks, or iris prolapse. Postoperative visual outcome to determine if these issues resulted in actual surgical complications was not assessed. Analyses of the rate of complicated surgeries by alpha-blocker use, age and gender were compared both with and without adjustment for an institution effect. Following no statistically significant difference between institutions, data from the two institutions were combined. Comparisons of rates of complicated surgeries by alpha-blocker use, gender and age were performed by the chi-square test. A multivariable analysis of alpha-blocker use adjusting for the effect of age was performed using logistic regression, with age treated as a continuous covariate. All statistical tests were two-sided and performed at the alpha=0.05 level.

**RESULTS**

Characteristics of the patient population are given in Table 1. Patients on alpha-blockers were older (median 74 years, range 47 to 92 years) than patients not on alpha-blockers (median 67 years, range 21 to 97 years) and a higher percentage of persons on alpha-blockers were males (97.0%) compared to patients not on alpha-blockers (67.9% male). Hence differences in rates of complicated surgeries between older (>65) and younger patients and between males and females were assessed and adjusted in the analysis of the alpha-blocker effect when statistically significant.

Out of surgeries performed on 328 patients on alpha-blockers, 49 (14.9%) resulted in complicated surgery compared to 223 (9.5%) of 2338 surgeries performed in patients not on alpha-blockers (p=0.003), as shown in Table 2. The increased rate of complicated surgeries was restricted primarily to patients over the age of 65, as shown in Table 2.
65 years of age; 275 (15.6%) of surgeries performed on these patients resulted in complicated surgery (p=0.03). There was no statistically significant increase in the rate of complicated surgeries for alpha-blocker use compared to non-use in the subset of patients under the age of 65 (p>0.05). There was no difference between males and females in the rate of complicated surgeries (p>0.05). 60 of the 328 patients using alpha-blocker medication were on tamsulosin, but there was no statistically significant difference in rate of complicated surgeries between patients on tamsulosin (11.7%) versus patients on other alpha-blockers (15.7%) (p=0.56). The majority of patients on alpha-blockers other than tamsulosin used terazosin; additional agents included alfuzosin, doxazosin, and prazosin.

In a multivariable analysis of all patients adjusting for the effect of age, the odds of a complicated surgery was approximately 50% higher for operations performed on patients using alpha-blocker agents compared to operations performed on patients who were not (odds ratio=1.47, 95% confidence interval from 1.05 to 2.07, p=0.026).

DISCUSSION
The discovery of intra-operative floppy iris syndrome has called into question the safety of alpha-blockers in patients who are undergoing or could potentially undergo cataract surgery. When originally reported, IFIS was seen in all patients using tamsulosin regardless of when it was stopped. A single patient was reported to experience IFIS over one year after discontinuing the alpha-blocker and the authors suggested that disuse atrophy of the muscles of the iris might be the etiology for IFIS [2]. The concept of disuse atrophy has been refuted for a variety of reasons including compensatory neuromuscular pathways, non-adrenergic pathway regulation of iris muscle function, and receptor up-regulation [9]. If IFIS is not due to disuse atrophy then a likely explanation is a reversible inhibition of the alpha-adrenergic blockers by certain medicines in susceptible patient populations. The four currently available alpha-1 blockers are competitive antagonists, and thus their binding and clinical effects can be competed off or reversed [9]. The reversible inhibition of iris dilation by the alpha-blockers supports discontinuation of these medications prior to elective surgery.

In an animal model, all available alpha-blocker medications induced miosis (reduced pupil size) in a dose dependent manner. Additionally, the miotic effects of all alpha-1 androgen receptor antagonists completely resolved within 8 hours of drug administration in the test animals [11]. The reversible nature of the alpha-blocker agents is consistent with their action as competitive antagonists.

Some have suggested that the association between IFIS and tamsulosin may be “the tip of the iceberg” and other medications can potentially cause the syndrome. If true, IFIS should be considered prior to cataract surgery in all patients using medications that potentially relax the iris dilator muscle (angiotensin antagonists and nitrates), and patients with diseases that are known to be associated with vascular endothelial dysregulation such as congestive heart failure, diabetes, and hypertension [5,9]. If preoperative evaluation elicits a history of alpha-blocker use, then modified cataract surgical techniques can, if IFIS is encountered, allow for complication rates comparable to patients without the syndrome [7,12,13].

Table 2. Rates of complicated surgery for the 2666 participants by alpha-blocker use
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<table>
<thead>
<tr>
<th></th>
<th>Patients not on alpha-blockers</th>
<th>Number of complicated surgeries (%)</th>
<th>Patients on alpha-blockers</th>
<th>Number of complicated surgeries (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>2338</td>
<td>223 (9.5%)</td>
<td>328</td>
<td>49 (14.9%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤65</td>
<td>1052</td>
<td>83 (7.9%)</td>
<td>53</td>
<td>6 (11.3%)</td>
<td>0.52</td>
</tr>
<tr>
<td>&gt;65</td>
<td>1286</td>
<td>140 (10.9%)</td>
<td>275</td>
<td>43 (15.6%)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

These data demonstrate that patients over age 65 were significantly more likely to have complicated cataract surgery if they were on alpha-blockers at the time of their surgery. Older patients are more likely to use polypharmacy and medications that could affect iris muscle relaxation and are at greater risk to have co-morbidities associated with vascular endothelial dysregulation, which might place them at higher risk for IFIS. In addition, an influence of age and male gender were found in a large study of nuclear fragment dislocation following cataract surgery, and this was attributed...
to age-related lens nucleus density and probable IFIS, though IFIS was not specifically queried in the study [14]. In our study, there was a slight increase in complicated surgeries in patients less than age 65 using alpha-blockers, which did not achieve statistical significance. The increased risk of complicated surgery was found for all available alpha-blockers with no statistically significant difference among the currently available medications. Unlike prior studies that focused on men taking alpha-blockers for lower urinary tract symptoms, since cataract disease is gender neutral, we elected to look at all individuals at risk. Alpha-blockers are prescribed for voiding difficulties and hypertension in women, and IFIS can arise in either gender [15]. These findings provide an easily identifiable patient population that may benefit from withdrawal of alpha-blocker medications prior to cataract surgery.

Discontinuation of this medication prior to surgery should allow for adequate clearance of the agent, as is standard practice for most surgical patients using aspirin and other anti-coagulants. The pharmaco-kinetics of most drugs show no effective dose after 4.5 half-lives has passed once medication use is stopped [16]. Given the half-lives of alpha-blocker agents (alfuzosin=9 hours, terazosin=12 hours, tamsulosin=15 hours, doxazosin=22 hours) [17], it seems prudent to ask patients to discontinue their medication 3 to 5 days prior to planned cataract surgery to limit any potential effect on intra-operative iris dilation. Given the results of this study, the recommendation should be made for patients age 65 and older.

Our data and conclusions are limited by the retrospective nature of the study with potential under-reporting of complicated procedures as well as incomplete ascertainment of alpha-blocker use in some patients. The electronic pharmacy records for the ALMMVH patient population reduce the risk of the latter in this group. It is also possible that other co-morbidities may have affected surgical procedures, unrelated to alpha-blocker use.

CONCLUSIONS

The risk of complicated cataract surgery was 14.9% in patients receiving alpha-blockers, approximately 50% higher than those not taking this medication. This increased rate was seen primarily in patients over the age of 65. If possible, alpha-blocker medications should be discontinued 3 to 5 days prior to eye surgery in older patients.

REFERENCES


