

Effect of alpha-2-agonist premedication on intraocular pressure after selective laser trabeculoplasty

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Aim: To determine the effect of alpha-2-agonist (AA) premedication (PM) on intraocular pressure (IOP) following selective laser trabeculoplasty (SLT). **Methods:** Retrospective cohort study of all patients undergoing 360° SLT at an institution with two prevalent practice patterns consisting of SLT performed with PM and without premedication (NPM) with AA. The association between pre- and post-operative IOP was evaluated using a linear regression model in 49 (59%) PM and 34 (41%) NPM eyes. **Results:** The prevalence of IOP elevations up to 5 mmHg 1 h postoperatively was similar in both groups, occurring in 18% of PM and in 15% of NPM. Elevations above 5 mmHg were seen in 4% of PM and 8% of NPM ($P = 0.732$). After correcting for age, gender, diagnosis, number of medications, and preoperative IOP, the presence or absence of AA PM had no significant association with any postoperative IOP ($P > 0.5$). **Conclusion:** The practice of using AAs before SLT and measuring IOP at 1 h has not been validated yet adds to expenses and workflow burden. Our retrospective study showed no significant correlation between PM and postoperative or longer-term IOP. IOP at 1 h should be measured in patients who cannot tolerate transient pressure elevations. Further studies are needed to elucidate this relationship.

Key words: Adrenergic alpha-agonists, glaucoma, premedication, trabeculoplasty

Selective laser trabeculoplasty (SLT) emerged in 1995 as a less energy-intensive alternative to argon laser trabeculoplasty (ALT)^[1] and is now increasingly used as a first-line therapy in the treatment of open-angle glaucoma, while recent studies investigate broadening the indications such as with chronic angle-closure glaucoma.^[2] SLT preferentially disrupts pigmented cells of the trabecular meshwork minimizing damage to adjacent nonpigmented structures,^[1] which may contribute to lower levels of transient postoperative intraocular pressure (IOP) elevation as compared to ALT.

In a multicenter clinical trial, 34% of patients treated with ALT had a 5 mmHg increase in IOP above baseline, and 12% had an increase of 10 mmHg or more from baseline.^[3] Conversely, only 25% of eyes receiving SLT experienced a 5 mmHg or greater transient increase in IOP, while an increase of more than 8 mmHg occurred in 9%.^[4] Another study reported postoperative IOP elevations >5 mmHg in only 11% of those receiving SLT.^[5]

The recommended practice pattern for trabeculoplasty is to premedicate with an aqueous suppressant typically in the form of an alpha-2-adrenoreceptor agonist to prevent IOP elevations and to measure pressure 1 h postoperatively.^[6-8] However, no study has shown compelling benefits of premedication (PM) on 1 h pressures or a correlation between early pressures and longer-term results.

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We hypothesized that the significant costs that incur where local rules dictate single use of preoperative medications and the additional burden of checking postoperative IOP in every trabeculoplasty patient may be avoidable. The aim of this study was to retrospectively determine the effect of alpha-2-agonist (AA) PM on IOP following SLT in the immediate postoperative period at 1 h as well as through 6 months.

Methods

Study population and design

This study was originally designed to be a randomized controlled trial of AA PM (group PM) versus no PM (group NPM) but eventually deemed as too risky by the Institutional Review Board (IRB) and some participating physicians. The redesign resulted in a retrospective cohort study of the two prevalent practice patterns consisting of SLT performed with and without preoperative AA. We reviewed medical charts of 130 patients from the glaucoma service at a large tertiary care referral center. From July 1, 2010, to August 1, 2011, patients were selected based on the current procedural terminology code for laser trabeculoplasty. These patients were screened for this study's inclusion criteria including 360° SLT and a diagnosis of primary open-angle glaucoma (POAG), low-pressure glaucoma, pseudoexfoliation glaucoma, or traumatic glaucoma. Patients with prior trabeculectomy or glaucoma drainage

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device surgery were excluded. IOP data measured by a Goldmann applanation tonometer were collected from patients' medical records. Preoperative IOP was recorded from patient preoperative evaluations, which occurred on the same day as the procedure.

Selective laser trabeculoplasty procedure

Prior to trabeculoplasty, patients either received PM with AA or not, based on the provider practice pattern as documented in the chart. A Latina SLT lens (Ocular Instruments, Bellevue, Washington, USA) was used to visualize the angle, with hydroxypropyl methylcellulose used as a coupling agent. The laser beam was focused on the trabecular meshwork. All cases were performed with the Q-switched frequency doubled 532 nm Nd: YAG laser (Lumenis Selecta 700; Coherent Medical Group, Santa Clara, CA, USA). Settings were started at 0.7 mJ and titrated until the appearance of cavitation bubbles and kept at this level. All patients received between 95 and 105 spots covering 360° of the trabecular meshwork. As was standard practice at our institution, IOP was measured 1 h postoperatively, and patients were subsequently scheduled for IOP checks at 2 and 6 months.

Statistical analysis

The association between PM and 1 h IOP elevation was evaluated using multiple regression, controlling for age, gender, diagnosis, number of medications, and preoperative IOP. For this test, given our sample size of 83 and a significance level of 0.05, a difference between groups of 2 mmHg would be detected with a power of 0.47. If the true difference was larger at 3 mmHg, then power increases to 0.81. The relationship between 1 h elevation and 6 months IOP difference was evaluated using a two-sample *t*-test. All statistical analyses were performed in R version 2.15.1 (R Core Team, Vienna, Austria). Statistical significance was set at $\alpha < 0.05$.

Results

Within the study period, 187 procedures were performed in the eyes of 130 patients. Of these, 13 (10%) patients were excluded for having no 1 h postoperative IOP recorded, 29 (22%) were excluded for the treatment of $<360^\circ$, and 5 (4%) were excluded for having cataract extraction prior to 2 months follow-up. The remaining 83 patients met inclusion criteria and were included in this study. Of these, 49 (59%) received PM and 34 (41%) received NPM. Of the 36 patients who received bilateral treatment, only right eyes were included for the analysis to reduce confounding.

There were no significant differences between groups in gender, preoperative IOP, visual field index, or number of patients on chronic AA therapy; however, the mean age in PM was higher (69.6 compared to NPM 62.2, $P = 0.027$), and PM were on more topical medications (mean 1.47 ± 1.0) compared to NPM (mean 0.58 ± 0.8 , $P < 0.001$) [Table 1]. There were significantly more patients with low-pressure glaucoma in the NPM group. The PM group had multiple patients with traumatic and pseudoexfoliation glaucoma, while the NPM group had none.

Four NPM eyes (15%) had a 1 h IOP elevation below 5 mmHg, and 2 (8%) had an elevation above 5 mmHg (6 mmHg in both cases). Similarly, 10 (18%) PM had a 1 h IOP elevation below 5 mmHg, and 2 (4%) had an elevation above 5 mmHg (7 mmHg and 13 mmHg). One of these patients had low-pressure glaucoma and was not using any glaucoma medications, and

the other had POAG and was on three glaucoma medications preoperatively. There was no significant difference between the prevalence of 1 h IOP elevations between groups ($P = 0.732$).

After correcting for age, gender, diagnosis, number of medications, and preoperative IOP, the presence or absence of AA PM had no significant association with 1 h IOP difference ($P = 0.566$).

Mean (\pm standard error [SE]) IOP at 2 months was 15.5 ± 0.60 mmHg in PM and 14.8 ± 0.81 mmHg in NPM ($P = 0.333$) with a mean IOP decrease from baseline of 3.6 ± 0.64 mmHg in PM and 5.2 ± 0.70 mmHg in NPM ($P = 0.114$). At 6 months, the IOP was 15.5 ± 0.48 mmHg in PM and 14.9 ± 0.69 mmHg in NPM ($P = 0.525$) with a mean IOP decrease from baseline of 3.4 ± 0.65 mmHg in PM and 4.9 ± 0.62 mmHg ($P = 0.141$) in NPM [Fig. 1]. There was no IOP difference between the

Table 1: Patient baseline characteristics

	AA premedication (n=49)	NPM (n=34)	P
Sex, male/female	14/35	12/22	0.631
Age, mean (SD) years	69.6 (13.8)	62.2 (13.6)	0.027
Preoperative IOP, mean (SE) mmHg	18.4 (4.9)	20.3 (5.1)	0.107
VFI, mean (SE)	84 (17.8)	90 (15.2)	0.152
Preoperative number of medications (SE)	1.47 (1.02)	0.58 (0.76)	<0.001
Already taking AA, n (%)	15 (26)	3 (12)	0.160
POAG, n (%)	41 (72)	15 (58)	0.062
LPG, n (%)	10 (18)	11 (42)	0.020
PXG, n (%)	4 (7)	0 (0)	
TG, n (%)	2 (4)	0 (0)	

AA: Alpha-2-agonist, IOP: Intraocular pressure, LPG: Low-pressure glaucoma, POAG: Primary open-angle glaucoma, PXG: Pseudoexfoliation glaucoma, SD: Standard deviation, SE: Standard error, TG: Traumatic glaucoma, VFI: Visual field index

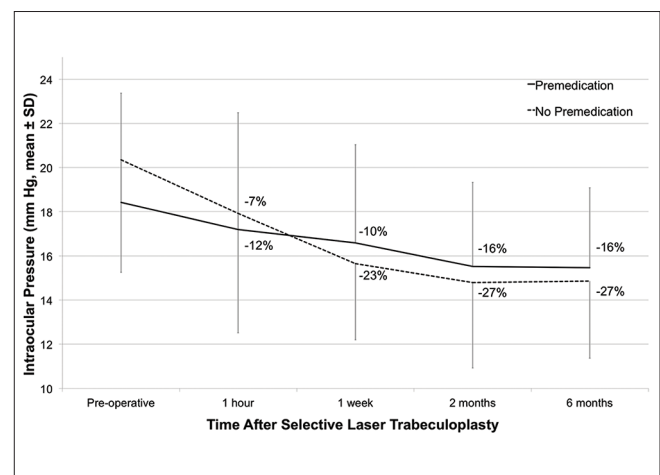


Figure 1: Graph showing mean intraocular pressure before and after selective laser trabeculoplasty in patients who did and did not receive premedication with an alpha-2-agonist. Up error bars (standard deviation) for premedication group, down error bars for no premedication group. Numbers represent percent decrease from preoperative intraocular pressure

two groups at 6 months ($P = 0.141$). Patients with 1 h IOP elevations of 2 mmHg or higher only had an average of 2.2 mmHg IOP decrease at 6 months. In contrast, patients without an immediate postoperative IOP elevation had an average IOP decrease of 4.4 mmHg at 6 months ($P = 0.123$).

Since the most common type of glaucoma in the study was POAG, we analyzed the data looking only at the subset of POAG patients ($n = 41$ PM and 15 NPM). However, when comparing the PM and NPM groups, the results were similar to the original analysis (i.e. including all types of glaucoma). Four NPM eyes (27%) had a 1 h IOP elevation ≤ 5 mmHg versus 10 (24%) in the PM group. One hour IOP elevations >5 mmHg occurred in zero NPM eyes versus 2 (5%) PM eyes. There was no significant difference between the total number of 1 h IOP elevations between groups ($P = 0.809$). The mean (\pm SE) IOP at 2 months was 15.6 ± 0.64 mmHg in PM and 16.4 ± 1.05 mmHg in NPM with a mean IOP decrease from baseline of 3 ± 0.75 mmHg in PM versus 5.6 ± 1.09 mmHg in NPM. There was no statistically significant difference between the two groups ($P = 0.069$). At 6 months, the IOP was 15.7 ± 0.63 mmHg in PM and 16.6 ± 0.96 mmHg in NPM with a mean IOP decrease from baseline of 3.3 ± 0.75 mmHg in PM and 5.4 ± 0.93 mmHg in NPM. Again, there was no statistically significant difference between the two groups ($P = 0.119$).

Discussion

The main finding of this retrospective study is that there is no compelling difference in IOP between patients undergoing SLT who have received AA as a pretreatment and those who have not. IOP elevations were observed regardless in 23% and 22% of patients, respectively, and elevations above 5 mmHg occurred in $<8\%$ in both groups, similar to prior studies.^[4,5] It is possible that these patients have such an acutely reduced conventional outflow that any incomplete suppression of aqueous humor leads to a moderate pressure rise despite a small increase of pressure independent outflow.^[9] Our study was limited by its retrospective design and moderate sample size, and although both groups were very similar in disease status, preoperative IOP, and pretreatment use of AA, there was a difference in average age and number of topical eye drops. Patients who received AA were older, on more eye drops and possibly perceived as more vulnerable or frail. This practice pattern is reflective of the concern of some participating physicians and the IRB, which led to the dismissal of our initial randomized study design.

The custom to use prophylactic, preoperative IOP lowering, and postoperative anti-inflammatory drops may be explained historically by the coagulative, thermal damage of ALT that releases more energy and causes more anterior chamber inflammation and pain than SLT.^[10] Animal studies of ALT showed fibrin covering trabecular openings during acute IOP elevation.^[11] Different from SLT used here; ALT irreversibly alters structure and function with juxtacanalicular herniations of laser lesions shifting aqueous flow to adjacent regions.^[11] In contrast, SLT primarily causes repairing and remodeling of the extracellular matrix^[12] as well as changes in the trabecular meshwork cells^[13] including increased phagocytosis and cell division.^[1,14] Trabecular meshwork cells play an active role in permitting outflow in the form of giant vacuoles and pores and this function may be temporarily lost after trabeculoplasty and further impaired by additional obstruction.^[15]

The increasing use of SLT as the first-line treatment with an efficiency that is similar to prostaglandin analogs^[16] while reducing costs and problems of medication adherence^[17] make the present study relevant. Clinicians choose to use PM for many reasons including historic clinical practice, perceived risk of IOP spike, and concern regarding a specific patient's ability to tolerate a transient increase in IOP. This was demonstrated by the higher prevalence of patients with pseudoexfoliation, pigmentary, and traumatic glaucoma in the group that received PM. The downside of routine pretreatment with AA is the added economic burden in practices that are required to use a new bottle of eye drops for each patient as mandated by the joint commission.^[18] There is also a risk of interactions with monoamine oxidase inhibitors or tricyclic antidepressants^[7] and the rare potential for brimonidine-induced uveitis.^[19] In addition, given the risk of IOP elevation in patients with heavily pigmented trabecular meshworks,^[20] it would be reasonable to consider routine PM in all patients with pigmentary glaucoma. Our results suggest that PM with AA may be avoidable, but that IOP should be checked postoperatively in patients who would not be able to tolerate temporary, more than moderate elevations. Interestingly, our data show a higher percentage of patients with pigmentary glaucoma in the group receiving PM and a higher percentage of patients with low-pressure glaucoma in the group receiving no PM, which is likely secondary to perceived physician risk. That said, this represents a potential weakness of this study in that patients with higher risk for an IOP spike were more likely to receive PM.

Conclusion

Our findings indicate that there may not be a compelling correlation between PM and postoperative IOP to justify workflow burden, additional costs, and potential risks. A randomized, prospective, double-blinded study with a larger sample size may be able to detect an effect that is smaller than described here. Because transient pressure elevations occurred at an equally low rate in both groups, we recommend minimizing routine use of preoperative AA, but to instead check IOP postoperatively in vulnerable patients to initiate treatment if needed.

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Conflicts of interest

There are no conflicts of interest.

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