Argon laser trabeculoplasty and reduction of ocular hypotensive medication used by glaucoma patients

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ABSTRACT • RÉSUMÉ

Background: We studied the effect of argon laser trabeculoplasty (ALT) on medically controlled, pressure-stable glaucoma patients to verify whether it is possible to reduce ocular hypotensive medication after ALT while keeping intraocular pressure levels similar to those observed before the procedure.

Methods: Seventy-one consecutive chronic glaucoma patients, all of whom were taking ocular hypotensive medication and had intraocular pressure at adequate levels, underwent ALT. After the laser procedure, each patient discontinued one hypotensive drug. Mean follow-up was 16.39 ± 5.39 months. We performed diurnal pressure curves on each patient before and after trabeculoplasty to determine the effect on intraocular pressure.

Results: In 39 (54.9%) patients, it was possible to reduce ocular hypotensive medication and still maintain intraocular pressure levels similar to those achieved before ALT.

Interpretation: For some medically controlled, chronic glaucoma patients, ALT can reduce the amount of ocular hypotensive medication without significantly altering intraocular pressure.

Contexte : Nous avons étudié les effets de la trabéculoplastie par laser à argon (TLA) chez des patients sous contrôle médical ayant un glaucome dont la pression est stable afin de vérifier la possibilité de réduire les médicaments hypotenseurs oculaires après la TLA tout en maintenant la pression intraoculaire aux niveaux observés avant la procédure.

Méthodes : Soixante-et-onze patients atteints de glaucome chronique, qui prenaient tous un médicament hypotenseur oculaire et avaient un niveau de pression oculaire adéquat, ont subi une TLA. Après l'intervention au laser, chaque patient a cessé un médicament hypotenseur. La moyenne du suivi a été de 16,39 ± 5,39 mois. Nous avons calculé les courbes de pression diurne pour chaque patient avant et après la trabéculoplastie pour établir l'effet sur la pression intraoculaire.

Résultats : Chez 39 patients (54,9 %), il a été possible de réduire les médicaments hypotenseurs tout en maintenant la pression intraoculaire aux niveaux observés avant la TLA.

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Interprétation : Pour certains patients atteints de glaucome chronique sous contrôle médical, la TLA peut permettre de réduire la quantité d'hypotenseur oculaire sans modifier significativement la pression intraoculaire.

Glaucoma is a relatively common disease that becomes more prevalent with age. It affects approximately 1% of those 60 to 70 years of age, 3% of those between 70 and 80, and 9% of the population older than 90.[1] As one of the leading causes of irreversible blindness worldwide, it has been estimated that, in the year 2000, 66.8 million persons had the disease, of whom 6.7 million were bilaterally blind.[2]

Intraocular pressure (IOP) is regarded as one of the main risk factors in the development of glaucomatous optic nerve damage, and therapy attempts basically to reduce IOP levels.[3]

Historically, the initial treatment of glaucoma has been prescription of ocular hypotensive drugs aimed at reaching target IOP levels that the ophthalmologist considers safe for the patient (target pressure). In cases where these levels cannot be achieved, surgery is an option.

The introduction of argon laser trabeculoplasty (ALT) in the 1970s added a new therapeutic modality. The hypotensive effect of this laser procedure was initially proposed either for patients whose IOP was uncontrolled despite maximum-tolerated drug therapy, or for patients at presurgical stages, to eliminate or at least postpone the need for surgery.[4,5]

The appearance of studies reporting positive results of ALT in the management of glaucoma[6,7] led to dissemination of the procedure over the following 2 decades and its incorporation as a useful therapeutic tool.[4,5,8] Although it has now become commonplace, some unanswered questions remain, such as the timing of its indication, or its efficacy in substituting for ocular hypotensive drugs.[6,9]

The purpose of the present work was to study the effects of ALT on chronic glaucoma patients. We opted to study medically controlled patients in whom IOP was within acceptable levels. The goal was to verify in what percentage of patients the laser procedure might permit a reduction in the amount of ocular hypotensive medication without significantly altering IOP values.

Methods

We selected 73 consecutive chronic glaucoma patients for whom trabeculoplasty was indicated. According to their individual characteristics, optic disc aspect, and campimetric examinations, each patient's IOP was considered to be adequately maintained within target range.

All participants in this study were patients of the Glaucoma Service of the Ophthalmological Clinic of the University of São Paulo School of Medicine and were using ocular hypotensive medication to control their glaucoma.

One eye was treated with trabeculoplasty per patient. In those cases where the same medication was used on both eyes, one eye was randomly chosen. In cases where more drugs were used on one eye than on the other, the laser procedure was applied on the eye that received more medication. The study was approved by the ethics committee and each patient gave informed consent.

Only chronic, open-angle, exfoliative, pigmentary, and normal-tension glaucoma patients were included. An age limit of 40 years was set as the minimum, without limit to the maximal age. It was necessary for each patient to be achieving adequate IOP control (i.e., target pressure) with the use of at least 1 ocular hypotensive medication and to have an optic disc cup-to-disc ratio no more than 0.8 × 0.8. There could be no visual field defect that threatened the central area, defined as the central 3°. We excluded patients with active ocular infectious conditions, narrow anterior chamber angles, or a history of previous trabeculoplasty, or those who were unable to cooperate with study protocol.

Patient preparation and laser procedure

An IOP diurnal pressure curve (DPC) was obtained for each patient by recording IOP daily at 08:00, 10:30, 13:00, and 15:30 by applanation tonometry (Goldmann tonometer, Haag-Streit, Bern, Switzerland) and calculating the mean intraocular pressure for each eye as the arithmetic average of the 4 measurements.

On the day of the trabeculoplasty, a single drop of an alpha-agonistic drug (0.2% brimonidine) was instilled on the eye to be treated, 30 min before the laser session.

The same Ritch trabeculoplasty laser lens (Ocular

Instruments, Bellevue, Wash.) was used for all patients, and the instrument to deliver the laser energy was the blue–green bichromatic argon laser, 532 nm wavelength (Alcon, Irvine, Calif.). The settings were 50 µm target size and 0.1 s exposure duration. Initial power was set at 700 mW, which could be increased or decreased to achieve the desired tissue reaction in the trabecular meshwork of either local blanching or minimal bubble formation. We placed 50 burns equally spaced over the anterior half of the trabecular meshwork on the 2 inferior quadrants in 1 session.

Immediately after the procedure, a cortisone drop was instilled and the bottle given to the patient, who was instructed to use it 3 times a day for 5 days and return on the following week.

Follow-up

At the first follow-up appointment after the laser procedure, if the IOP remained at a similar level as before the ALT, the patient was instructed to return in 6 weeks. They were also told to discontinue 1 hypotensive eye drop medication on the laser-treated eye 2 weeks before the next follow-up appointment. If the patient chose oral acetazolamide, then in the case of daily intake up to 375 mg, the drug was entirely discontinued. When larger dosages were used, they were reduced to half. Each patient was allowed to choose which drug to discontinue.

On the next follow-up appointment, another DPC was obtained, with the mean IOP being calculated again. It is to be noted that a smaller amount of ocular hypotensive medication would already be in use by the patient on that occasion.

It is known that IOP values, and hence IOP mean levels obtained at a DPC, can be different when measured in the same patient on different days.[10,11] Therefore, a tolerance of < 5 mm Hg to the total 4 IOP measurements was allowed. That meant a tolerance of < 1.25 mm Hg was allowed for the mean daily IOP (5 mm Hg/4 measures).

If the mean IOP value at the next follow-up appointment was higher, therefore, by 1.25 mm Hg or more when compared with that observed at the preoperative DPC, the case was considered a failure and the patient was told to restart the discontinued medication.

The same DPC and mean IOP calculations with the 1.25 mm Hg tolerance criteria were followed on each new visit, until the end of the follow-up period.

Success and failure criteria

At the end of the study, patients were classified as belonging to 1 of 2 groups. The success group comprised patients whose mean IOP values, on the ALT-treated eye, were not higher by ≥ 1.25 mm Hg after trabeculoplasty and discontinuation of 1 ocular hypotensive drug, when compared with the mean IOP values obtained at the DPC before the laser procedure. The failure group comprised patients whose mean IOP values, on the ALT-treated eye, were higher by ≥ 1.25 mm Hg after trabeculoplasty and discontinuation of 1 ocular hypotensive drug, when compared with the mean IOP values obtained at the DPC before the laser procedure.

Statistical analysis

The χ^2 test was used to compare the success and failure groups concerning sex, race, and the drug that was discontinued. The Student *t* test was used to compare the success and failure groups regarding patient age and the number of pre-ALT in-use medications.

For each participant of this study, we calculated the difference (ΔIOP) between the final mean IOP (obtained at the last DPC) and the initial mean IOP (at the DPC made before the laser procedure). The Kolmogorov–Smirnov test was used to study the distribution pattern of the ΔIOP of the 71 patients

Analysis of variance (ANOVA) was used to analyze all participating patients' ΔIOP in relation to the discontinued drug. The Mann–Whitney test was used to compare the patients' mean ages in the success and failure groups. Differences were considered significant at $p < 0.05$.

RESULTS

The investigation originally included 73 patients. Of these, 2 were excluded because they passed away before the study was finished. Of the remaining 71, 64 (90.2%) had primary open-angle glaucoma, 6 (8.4%) had normotensive glaucoma, and 1 (1.4%) had pigmentary glaucoma. They were followed for 16.39 ± 5.39 months.

The mean age was 65.23 ± 9.67 years (range 40–85 years). Of the total, 50 (70.4%) were women and 21 (29.6%) were men. The patient population was 59.1% (42) white, 21.1% (15) colored, 17.0% (12) black, and 2.8% (2) asian.

No statistically significant differences between the success and failure groups were observed regarding

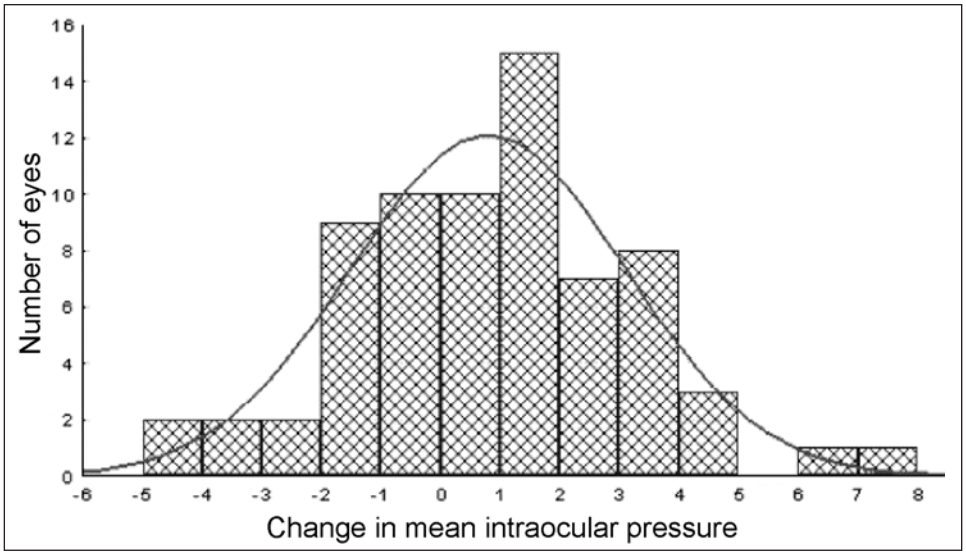

Fig. 1—Change in mean intraocular pressure (ΔIOP, mm Hg) in trabeculoplasty-treated eyes (n = 71). D_{max} = 0.068671, p > 0.20. ΔIOP = difference between mean IOPs obtained at the last and the initial diurnal pressure curves.

patient age (t = 1.67, p = 0.10), sex (χ^2 = 0.003, p = 0.99), or race (χ^2 = 1.78, p = 0.62), confirmed by the Mann–Whitney test (U = 486.0, p = 0.11).

For the 71 patients, ΔIOP varied between –5.41 mm Hg and +7.00 mm Hg, with 39 patients belonging to the success group (ΔIOP < 1.25 mm Hg). The remaining 32 patients were in the failure group (ΔIOP ≥ 1.25 mm Hg).

When graphed, the ΔIOP values showed a normal distribution pattern, as demonstrated by the Kolmogorov–Smirnov test statistic, D_{max} (Fig. 1).

Mean IOP levels for the patients belonging to the success group were 17.30 ± 3.03 mm Hg before ALT and 16.33 ± 2.98 mm Hg after ALT, a mean decrease of 0.97 ± 1.59 mm Hg. Mean IOP levels for the patients belonging to the failure group were 16.15 ± 2.76 mm Hg before ALT and 18.91 ± 2.52 mm Hg after ALT, a mean increase of 2.75 ± 1.48 mm Hg. Also, of the 32 patients in the failure group, 30 had an increase in mean IOP up to 4 mm Hg, 1 had an increase of 6.75 mm Hg, and 1 had an increase of 7.00 mm Hg. All decreases and increases in IOP levels were recorded after 1 hypotensive medication was withdrawn after ALT. Patients who belonged to the failure group were told to restart the discontinued medication and all managed to regain adequate IOP control. Mean IOP levels, before and after ALT, for all the participating patients can be viewed on the scattergram (Fig. 2).

Before ALT, the participants used at least 1 of the following 6 medications: pilocarpine, beta-adrenergic blockers, carbonic anhydrase inhibitors, alpha-adrenergic agonists, latanoprost (all in eye drop form) and oral acetazolamide. The mean number of in-use drugs was 2.44 ± 0.84 (range 1–4, median 2) and did not differ significantly in both success and failure groups (t = 0.27, p = 0.78).

Table 1 tabulates ΔIOP of the treated eye according to the discontinued medication. It displays the difference in mean IOP values when the last DPC is compared with the preoperative DPC. ANOVA showed a statistically significant difference of drug removal on ΔIOP levels when the 6 medications were compared (F = 4.01, p = 0.003). Discontinuation of the 6 drugs, when considered together, caused the mean IOP values to increase by 2.41 mm Hg. It should be noticed that Table 1 concerns all 71 patients considered as a whole. It indicates that the aforementioned drugs, when discontinued, caused statistically significant IOP variations on the ALT-treated eye.

Table 2 displays the success and failure groups according to the drug that was discontinued. The χ^2 test demonstrated no statistically significant differences regarding the presence of the different drugs in

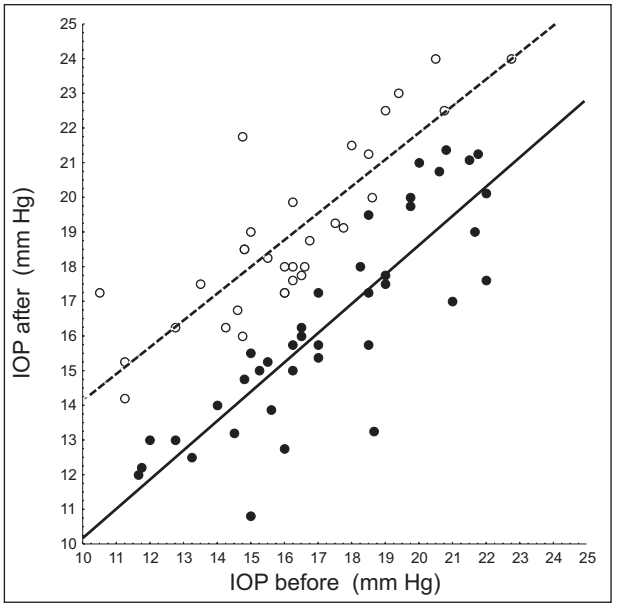

Fig. 2—Scattergram of mean intraocular pressures before and after argon laser trabeculoplasty (n = 71). Full circles = success group; empty circles = failure group.

Table 1—Change in intraocular pressure after argon laser trabeculoplasty and discontinued medication, n = 71

Discontinued medication	ΔIOP (mm Hg)
Pilocarpine	+ 2.27
Timolol	+ 1.97
Dorzolamide	+ 2.15
Brimonidine	+ 2.30
Oral acetazolamide	+ 2.58
Latanoprost	+ 1.82
All discontinued medications	+ 2.41
F = 4.01	p = 0.003*

Note: ΔIOP = difference between mean intraocular pressures obtained at the last and initial diurnal pressure curves (positive values indicate an increase in IOP); *statistically significant.

the success and failure columns (χ^2 = 9.40, p = 0.09). It indicates that there was no statistically significant relationship between the drug that was discontinued after ALT and the achievement of success or failure on the laser procedure.

Interpretation

The role of trabeculoplasty on the intraocular pressure control of glaucoma patients has been changing with time. Its initial purpose was to be applied to patients on maximum medication who were candidates for filtration surgery.[5] The goal, then, was to obtain a reduction in IOP levels that would make it possible to avoid, or at least postpone, surgery.

Of particular relevance was the Glaucoma Laser Trial,[12] which performed trabeculoplasty as initial therapy. According to its results, the laser procedure enabled 44% of the participating glaucoma patients to keep adequate IOP control without the use of ocular hypotensive medication, on a 2-year follow-up.

Less common were studies that proposed trabeculoplasty on clinically stable, medically controlled glaucoma patients. Moreover, few focused on evaluating the possibility of reducing the amount of ocular hypotensive drugs needed to control glaucoma in such patients after ALT.

Our study targeted medically stable, IOP-controlled patients. It was designed to verify the feasibility of substituting trabeculoplasty for ocular hypotensive drugs that were already in use. As patients often complain about their medical regimens, allowing them to use fewer drugs and still keep their intraocular pressure not significantly altered could prove advantageous. Also, our study participants were allowed to choose which medication to discontinue after ALT. That way each patient could consider the costs of the medicine, its side effects, and the convenience of each medical regimen.

We observed that the ΔIOPs of all the participating patients varied between –5.41 and +7.00 mm Hg (Fig. 2) and conformed to a normal distribution pattern (Fig. 1). The likely explanation for this variation in IOP response to trabeculoplasty probably lies with individual disease dynamics, as well as their multiple associated factors. It might be reasonable to assume that the medication employed in glaucoma treatment is related to the results obtained, although the study of the whole set of drugs used by each patient and their possible interactions was not in the scope of this study.

We found the different races responded similarly to the laser procedure (χ^2 = 1.78, p = 0.62), as other authors have already reported when white and black patients were compared,[13] or asian patients.[14] It should be remembered, though, that the mean

Table 2—Patient distribution in success and failure groups and total, according to discontinued medication after trabeculoplasty

Medication	Success $n = 39$ (%)	Failure $n = 32$ (%)	Total $n = 71$
Pilocarpine	14 (35.9)	7 (21.9)	21
Timolol	9 (23.1)	3 (9.4)	12
Dorzolamide	10 (25.6)	10 (31.2)	20
Brimonidine	4 (10.3)	8 (25.0)	12
Oral acetazolamide	2 (5.1)	1 (3.1)	3
Latanoprost	0 (0.0)	3 (9.4)	3
All medications	39 (100.0)	32 (100.0)	71 (100%)

$\chi^2 = 9.40$; $p = 0.09$.

follow-up period in our study was less than 2 years. Schwartz et al[15] studied long-term results and noticed that 5 years after ALT, black patients showed a success rate significantly lower than that of white patients.

Table 1 shows that the different drugs discontinued after trabeculoplasty produced a statistically significant variation on intraocular pressure levels ($F = 4.01$, $p = 0.003$). Those data relate to all 71 patients, taken as a whole. When, however, the data were separated into the success and failure groups and analyzed according to what drug was discontinued after ALT, the χ^2 test showed no statistically significant differences to exist ($\chi^2 = 9.40$, $p = 0.94$) (Table 2).

The analysis of the data shown in Table 1 indicates that the discontinuation of the different drugs caused a significantly different ocular pressure variation in the treated eyes. This result would be expected because these medications are known to differ remarkably on hypotensive power.

The data on Table 2 show, however, that the discontinued drugs were not statistically different when patients of both the success and failure groups were compared. That means that each patient's possibilities of achieving success or failure on ALT were not influenced by which discontinued drug was chosen. This finding bears a resemblance to other studies,[4,16] which also report that the success rate of trabeculoplasty does not appear to be influenced by the ocular hypotensive medications employed prior to the procedure.

Patients belonging to the success group were able to discontinue 1 ocular hypotensive drug after ALT without significantly altering their mean IOP levels. This finding has clinical relevance, since the need for less drugs could mean fewer interruptions in a patient's daily chores, less potential for drug toxicity (both local and systemic), and financial savings on the costs of the medical regimen.

Complex therapeutic regimens requiring multiple doses during the day are related to lower adherence rates,[17,18] and it is relevant to remember that 25% to 57% of chronic glaucoma patients depend on third parties to instill their eyedrops.[17] Hence, if the glaucoma can be controlled with fewer medications, the result may be a higher compliance to the medical prescription.

Side effects, both local and systemic, of ocular hypotensive medications are frequent patient complaints[19] and an important cause of poor compliance.[17,18] A medical regimen requiring less medication, and thus a lower potential for side effects and systemic toxicity, might in turn favor adherence.

Another consideration regarding glaucoma treatment is financial. Treatment costs constitute a common patient complaint.[19,20]

Overall, if patients could reduce the number of drugs needed to control their glaucoma, the impact on their life should be positive. It might lead to fewer interruptions in daily activities, reduce potential side effects, and bring the economic benefit of lower medical costs, all of which should favor therapeutic fidelity and enhance higher treatment success rates.

In conclusion, our study showed that the success group encompassed 39 (54.9%) of the 71 participants. After the laser procedure, they were able to reduce the number of ocular hypotensive medications and still keep mean IOP levels not significantly altered.

It should be noted that the reduction in the number of drugs needed to control IOP observed in the success group was likely related to the length of follow-up. As ALT efficacy tends to diminish with time, observations over a longer follow-up might show lower success rates than those found in our study.

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