

Selective laser trabeculoplasty as an initial treatment option for open-angle glaucoma

Trabeculoplastia seletiva como opção terapêutica inicial para o tratamento do glaucoma de ângulo aberto

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ABSTRACT

Although eye drops are frequently used as an initial treatment option for open angle glaucoma (OAG), side effects, and poor adherence, among others, may compromise treatment efficacy. In this scenario, laser trabeculoplasty is an interesting therapeutic option for open angle glaucoma cases. Commonly used for many years as a last alternative prior to glaucoma incisional surgery, laser trabeculoplasty has been changing its indication after the advent of selective laser trabeculoplasty (SLT). In the current review, we critically evaluated the published data regarding the use of laser trabeculoplasty as a first treatment option for open angle glaucoma patients. Studies using SLT as a first-line treatment have encouraging findings. One-year efficacy results are comparable to those obtained with prostaglandin analogues, with a good safety profile. Although the laser's effect is known to be transitory, recent data suggest it can be successfully repeated in cases with good response to the first SLT treatment.

Keywords: Glaucoma, open-angle/surgery; Trabeculectomy/methods; Lasers; Intraocular pressure

RESUMO

Embora a terapia tópica seja frequentemente usada como primeira opção para o tratamento inicial do glaucoma de ângulo aberto (GAA), efeitos colaterais, baixa adesão, entre outros fatores podem comprometer a eficácia do tratamento. Nesse cenário, a trabeculoplastia a laser surge como uma opção terapêutica interessante. Comumente usada como última alternativa antes da cirurgia antiglaucomatosa incisional por muitos anos, a trabeculoplastia a laser tem sido indicada cada vez mais cedo com o advento da trabeculoplastia seletiva a laser (SLT). Nessa revisão, nós avaliamos criticamente as publicações sobre trabeculoplastia a laser como primeira opção para glaucoma de ângulo aberto. Os estudos de SLT como primeira opção terapêutica têm apresentado dados animadores. Os resultados de um ano de acompanhamento mostram eficácia semelhante àquela obtida com análogos de prostaglandinas. Embora o efeito do laser seja transitório, estudos recentes sugerem que o procedimento pode ser repetido com sucesso nos casos que tiveram boa resposta ao primeiro tratamento com SLT.

Descritores: Glaucoma de ângulo aberto/cirurgia; Trabeculectomia/métodos; Lasers; Pressão intraocular

INTRODUCTION

Glaucoma is an optic neuropathy characterized by progressive structural and functional damage. Intraocular pressure (IOP) is the most important known risk factor for disease development and progression and until now the only modifiable one^(1,2). That said, effective IOP reduction is the primary goal when it comes to glaucoma treatment⁽³⁾.

When it comes to treatment options for IOP reduction, we have three main categories: topical medication, laser surgery, and incisional surgery. Topical hypotensive medications are often used as a first-line treatment option, while incisional surgery is generally used when topical and laser treatments were not effective in achieving the target IOP. Although usually safe and effective, side effects from eye drops may occur, which can be local (e.g., conjunctival injection of prostaglandin analogues)⁽⁴⁾ or systemic (e.g., cardiorespiratory effects of beta-blockers)⁽⁵⁾. Furthermore, persistence and adherence studies on glaucoma show multiple barriers to an adequate treatment regimen with topical medication⁽⁶⁾. Forgetfulness, medication cost, difficulty to instill eye drops, and patient's misbelief that glaucoma is a blinding disease are frequently reported⁽⁶⁾. As a result, self-reported treatment adherence rates are poor (ranging from 30 to 80%)^(7,8), and many patients interrupt their newly prescribed medications in the

first year of treatment^(9,10). Therefore, an initial therapeutic alternative that minimizes ocular side effects and compliance issues could be very useful in clinical practice.

In this context, laser trabeculoplasty rises as an interesting therapeutic option for open-angle glaucoma (OAG) cases, not relying on patient compliance. Argon laser trabeculoplasty (ALT) was first described in 1979 (Table 1)⁽¹¹⁾. The laser uses a blue-green (488 and 514 nm) continuous wave argon laser with a 50 µm spot diameter and makes a disruption of the trabecular meshwork^(12,13). In 1995, selective laser trabeculoplasty (SLT) was described. This melanin-target tissue sparing procedure uses a green (532 nm), Q-switched, frequency-doubled Nd:YAG laser⁽¹³⁾. It is important to emphasize that ordinary YAG laser devices, commonly used for iridotomy or capsulotomy, cannot be used to perform SLT.

Laser trabeculoplasty was initially described as an adjunctive treatment in eyes under topical hypotensive medications, often performed as a last alternative prior to incisional surgery in cases of uncontrolled disease⁽¹⁴⁾. With the advent of SLT, there was a shift in the focus of most clinical studies related to laser trabeculoplasty^(12,15). Looking carefully at the most recent publications, one can note that SLT has been evaluated as a first-line treatment option for IOP-lowering in OAG patients without topical medication and less severe damage, with quite encouraging results^(16,17).

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In the current review, we critically evaluated the published data regarding the use of laser trabeculoplasty as a first treatment option for OAG patients. We conducted a PubMed search on March 19, 2016 using the following keywords: "laser trabeculoplasty", "open-angle glaucoma", and "treatment". All types of studies were considered for a first analysis. Only case-reports were excluded. Meeting abstracts were considered if presenting relevant and new data. Studies were then selected based on clinical relevance and contribution to the main focus of this review article. As most studies comparing ALT with SLT results were conducted in glaucoma patients under clinical treatment, we could not restrict our search criteria to studies using laser as first treatment option only. Therefore, we also included data from studies in patients already being treated by medication.

TOPICS

LASER TRABECULOPLASTY AS INITIAL TREATMENT FOR OPEN ANGLE GLAUCOMA

The idea of using laser trabeculoplasty as the first treatment option for glaucoma is not recent nor restrict to SLT. The Glaucoma Laser Trial (GLT) was a multicenter study that evaluated the efficacy and safety of ALT as the primary therapy for glaucoma. In that study, patients with OAG were randomly assigned for initial treatment with ALT in one eye *versus* topical medication in the fellow eye. The main results showed that initial treatment with ALT was associated with a greater IOP reduction (mean difference of 1.2 mmHg) and better visual field outcomes (mean difference of 0.6 dB) than topical treatment with timolol maleate. Additionally, ALT was at least as effective as timolol regarding stability of optic disc status over seven years⁽¹⁴⁾. It is important to note that when GLT was carried out, neither prostaglandin analogs (PGA) nor SLT were available, thus limiting a straight comparison with more recent studies data⁽¹⁸⁾.

There are scant data in the literature comparing ALT vs SLT as the initial treatment options for OAG cases. In a relatively recent study by Gandolfi et al.⁽¹⁹⁾, the authors reported that low power 360° SLT

(repeated every year) was more effective than conventional ALT in achieving adequate IOP control in cases of ocular hypertension. On the other hand, most studies comparing ALT vs SLT for OAG (but not as a first treatment option) found similar success rates between the two laser modalities⁽²⁰⁻²²⁾. However, when it comes to safety, the development of peripheral anterior synechiae seems to be a more frequent complication following ALT (incidence ranging between 12% and 43% in previous studies) than SLT (rarely reported)^(23,24). This procedure-related complication is influenced by technique and laser burns position (higher risk when laser is applied too posteriorly). Moreover, we believe that the ease of application (outcomes of physicians in training are comparable to those of glaucoma specialists)⁽²⁵⁾ and the possibility of repeating the procedure with relatively good success rates (in cases with good response to the first SLT treatment)^(20,26) are two important advantages of SLT over ALT treatment. These factors have certainly contributed to the shift towards SLT use in the past decade and might explain the reason why ALT has not taken its place as a first line therapy.

SELECTIVE LASER TRABECULOPLASTY AS INITIAL TREATMENT FOR OPEN ANGLE GLAUCOMA

Efficacy (IOP reduction)

In most studies, SLT has been investigated as a second-line treatment option for OAG, being performed only after inappropriate response or intolerance to topical medication as an attempt to delay incisional surgery⁽²⁷⁾. As a result, there are few studies evaluating SLT as first treatment option. It is important to note that because the SLT effect is transitory, most of these studies are short-term (one to three years of follow-up). As PGAs are the first line clinical treatment to OAG, most studies compared SLT with PGA results in terms of IOP reduction. Looking carefully at safety and efficacy outcomes of these studies, we believe there is growing evidence that SLT can be used as a primary treatment for IOP-control in OAG cases^(17,28-33). Table 2 provides a summary of the main results of these studies.

Table 1. Comparison of the different features of argon laser trabeculoplasty (ALT) and selective laser trabeculoplasty (SLT)

	ALT	SLT
Described in	1979	1995
Laser type	Argon laser	Q-switched, frequency-doubled Nd:YAG laser
Laser wavelength	488 and 514 nm (blue-green)	532 nm (green)
Spot diameter	50 µm	400 µm
Main action mechanisms	Disruption of the trabecular meshwork	Melanin-target tissue sparing

Table 2. Studies of selective laser trabeculoplasty as the first treatment option for open-angle glaucoma and ocular hypertension

Study	Design	Key findings
Katz et al., (2012) ^{16*}	SLT versus PGA Total of 127 eyes	Mean IOP reduction of 25.7% Equally efficacy FU: 12 months
Shazly et al., (2010) ³¹	SLT-POAG and PXFG Total of 37 eyes	Mean IOP reduction of 23% FU: 49 months
Mahdy (2008) ²⁹	SLT-OAG and OHT Total of 35 eyes	Mean IOP reduction of 27.8% FU: 12 months
McIlraith et al., (2006) ¹⁷	SLT versus PGA Total of 100 eyes	Mean IOP reduction of 31% Equally efficacy FU: 12 months
Nagar et al., (2005) ^{18*}	SLT versus PGA Total of 167 eyes	In 360° SLT, 82% of eyes achieved a >20% IOP reduction Equally efficacy (360° SLT vs PGA) FU: 12 months
Melamed et al., (2003) ³³	SLT-OAG and OHT Total of 45 eyes	Mean IOP reduction of 30% FU: 18 months

*= randomized studies.

OAG= open-angle glaucoma; OHT= ocular hypertension; PGA= prostaglandin analogs; POAG= primary open-angle glaucoma; PXFG= pseudoexfoliative glaucoma; SLT= selective laser trabeculoplasty; FU= follow up.

At this point, we believe it is important to briefly discuss the main aspects of each study. When evaluating patients with OAG or ocular hypertension (OHT) treated with SLT, Melamed et al.⁽³³⁾ observed a $\geq 19.6\%$ IOP reduction in 89% of the patients, while Mahdy⁽²⁹⁾ found an IOP-reduction $\geq 25\%$ in 77.1% of the cases. Overall, in an attempt to summarize IOP data from the available studies, we found that average absolute IOP-reduction following SLT as first treatment ranges from 3 to 8 mmHg (percentage IOP reduction: 20% to 38%)^(17,18,29,31,33,34).

Other studies compared SLT *versus* PGA as a primary therapy, with similar efficacy between the two treatment modalities⁽¹⁶⁻¹⁸⁾. When the extension of the laser was considered, PGA showed better results than 90° and 180° SLT, but not 360°⁽¹⁸⁾. The efficacy of SLT was also evaluated in OAG eyes previously treated with glaucoma medication (monotherapy)⁽³⁴⁾. After a 30-day medication washout, SLT reduced IOP significantly, and IOP remained stable without medical therapy for 12 months⁽³⁴⁾. In addition, another study also evaluated SLT results after topical medication washout, and SLT 360° was effective [mean IOP reduction of 2.9 mmHg (40%) at 3 months and 2.1 mmHg (29.2%) at 6 months after the laser]⁽³⁵⁾. Besides that, another study that included eyes with pseudoexfoliative glaucoma (XFG) and primary open-angle glaucoma (POAG) revealed that SLT was effective as a primary treatment in both groups⁽³¹⁾.

Safety, duration, and repeatability

In general, SLT is considered a safe procedure⁽³⁶⁾. Serious complications are rare, but conjunctival redness and injection^(33,37), transient IOP-increase^(33,38,39), and mild anterior chamber reaction^(37,38,40) are issues that the ophthalmologist and the patient should be aware of. Special attention must be given to sustained IOP increase⁽⁴¹⁾, particularly in higher risk patients, such as individuals with highly pigmented trabecular meshwork, multiple topical medications, and previous ALT treatment⁽⁴²⁾. Although loss of corneal endothelial cells has been reported, it does not seem to be permanent, as recovery was observed after one month of the procedure⁽⁴³⁾. Additionally, anterior chamber volume and central corneal thickness decrease after SLT, retuning back to pre-SLT values after three months of the laser procedure⁽⁴⁴⁾.

It is well established that the IOP-lowering effect of SLT decreases over time⁽³⁸⁾. Although it is usually attributed to the transitory effectiveness of the procedure^(21,38), the progressive trabecular meshwork dysfunction presented by glaucomatous patients along the years should also be considered⁽⁴⁵⁾. In this context, the possibility of repeating the laser procedure in eyes that lost IOP control over time became an important point to be investigated. Looking close at the more recent literature, one can note several studies showing that SLT can be repeated with similar efficacy when compared to the first SLT treatment. In these studies, POAG patients presented a significant IOP reduction at 1⁽⁴⁶⁾, 4⁽⁴⁷⁾, 6⁽⁴⁶⁾, 12^(19,48), 15⁽⁴⁶⁾, and 24 months after repeating SLT^(26,49). Corroborating these findings, Gandolfi and Ungaro demonstrated that repeated low power SLT as initial treatment postponed the initiation of medical therapy by a mean time of 6.2 years in patients with OHT⁽¹⁹⁾.

Success predictors of selective laser trabeculoplasty

As mentioned above, SLT does not work for everyone, as approximately one quarter of the patients do not achieve a significant IOP reduction⁽⁵⁰⁾. Therefore, the knowledge of success predictors is important for a proper indication and to estimate treatment outcomes. Some success predictors are well established. For instance, better results are usually observed in patients with POAG^(33,37,51-56), pseudoexfoliative glaucoma^(31,40,57,58), and higher baseline IOP^(40,41,46,47). A few isolated studies observed better results in eyes with thinner corneas⁽⁵⁹⁾, with earlier disease stage⁽⁶⁰⁾, and with higher refractive errors⁽⁵²⁾. Conversely, the use of PGA before laser was associated with a decreased IOP-lowering response⁽⁶¹⁾, and SLT treatment had limited results in eyes with OAG receiving maximal-tolerable medical therapy^(50,62). Other factors remain controversial, such as iridocorneal angle

pigmentation^(63,64) and advanced age^(57,61). While some studies found a positive correlation between these factors and success rates, others did not. Regarding laser parameters itself, although good results have been recently reported with low power SLT (0.4 mJ per shot; repeated annually)⁽¹⁹⁾, most studies have suggested better outcomes with higher power settings (energy per shot), more extensive laser treatment (360 degree), and greater number of shots^(18,25,65,66).

There is also a strong correlation between SLT outcomes when we consider both eyes from the same patient⁽⁶⁷⁾. Shazly and Latina, evaluating eyes with OAG and OHT, found that in patients with SLT failure in the first treated eye, success odds in the fellow eye were less than 35%⁽⁶⁷⁾. Considering those with good response in the first treated eye, success rates of the fellow eye varied between 80% and 100% in two different studies⁽⁶⁸⁾. In this context, it seems reasonable to perform SLT in one eye at a time. Not only because success odds of the second eye are remote in cases of failure of the first treated eye (and therefore the second eye should not be indicated in such cases), but also because the IOP values of the fellow untreated eye can be used to adjust SLT outcomes of the first treated eye (mitigating the influence of inter-visits IOP fluctuation and reducing the influence of regression to the mean).

COMMENT

During the course of OAG, patients will often need one or more medications to maintain IOP control and prevent progression of the disease. Ocular and systemic side effects of topical medications, forgetfulness, difficulties in handling the bottle and instill eye drops properly, and consequently poor compliance with the proposed medical regimen are important issues for clinicians when starting a therapy that will last a lifetime⁽⁶⁸⁾. Moreover, growing concern exists with drug-related chronic ocular surface inflammation, which may have a negative impact on success of a future filtration surgery⁽⁶⁹⁾. With this in mind, we believe it is reasonable to consider alternative treatments, such as laser therapy, as first-line treatment options^(17,28,29). SLT has a good safety profile, does not rely on patient compliance, and has shown to be at least as effective as topical medications in lowering IOP as an initial treatment (for at least one year)⁽⁷⁰⁻⁷²⁾ and can be repeated when IOP control is lost over time^(19,46-48), possibly allowing patients to remain free of topical medication for years^(73,74). In a chronic disease such as OAG, time is always a key parameter. We believe that SLT can be a way to buy it. Additionally, if this strategy does not work, topical medications can be promptly started. Nevertheless, it should be emphasized that studies are needed to evaluate whether SLT treatment would affect the efficacy of topical hypotensive medications. All these things considered, SLT seems to be a reasonable, but still underused, form of initial treatment for patients with OAG and OHT.

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