Selective laser trabeculoplasty as a first-line therapy: a review

Michael Waisbourd, MD, L. Jay Katz, MD

ABSTRACT • RÉSUMÉ

Poor adherence with glaucoma medications has been well documented. There remains a significant unmet need for a relatively safe intraocular pressure (IOP)–lowering procedure that minimizes or eliminates patient participation, and thus reduce the incidence of treatment failures attributable to nonadherence. Selective laser trabeculoplasty (SLT) offers several advantages: It effectively reduces IOP in most patients with open-angle glaucoma, it is cost-effective compared with eye drops, it can be repeated if needed, and it eliminates the issue of adherence to medications when used as an initial treatment. This article reviews the evidence supporting the use of SLT as a first-line therapy in glaucoma.

La piètre adhésion aux traitements du glaucome a été bien documentée. Il reste cependant un important besoin non satisfait de procédure relativement sure d’apaisement de pression intraoculaire (PIO) pour minimiser ou éliminer la participation du patient et réduire ainsi l’incidence des échecs thérapeutiques attribuables à la non observation. La trabéculoplastie au laser sélective (TLS) offre plusieurs avantages : elle réduit effectivement la PIO chez la plupart des patients ayant un glaucome à angle ouvert, elle est plus rentable comparativement aux gouttes ophtalmiques, elle peut être répétée au besoin et élimine le problème d’adhérence aux médicaments lorsqu’elle est utilisée comme premier traitement. Ce manuscrit revoit l’évidence supportant l’utilisation de la TLS comme premier traitement du glaucome.

The introduction of selective laser trabeculoplasty (SLT) in the 1990s provoked interest in several areas: the mechanism of intraocular pressure (IOP) reduction, the placement of laser therapy in the treatment scheme, the recognition of nonadherence with eye drops, and the increasing importance of economics in health care delivery.

Numerous clinical trials, review articles, and meta-analyses were published on the efficacy of SLT as an adjunctive therapy to IOP-lowering medications; however, the purpose of this review is to shed light on the accumulating evidence on the benefits of using SLT as a first-line therapy.

In preparing this article, we performed a review of literature published from 1995 (when SLT was first introduced by Latina and Park) to September 2014. We searched the PubMed database for all manuscripts that included the keywords “selective laser trabeculoplasty” and “primary” or “initial treatment.” We included articles published in English that report the outcomes of SLT as primary treatment for glaucoma.

POOR ADHERENCE WITH GLAUCOMA MEDICATIONS

Although glaucoma drops are usually effective in lowering IOP, patients are often nonadherent. Unfortunately, the rates of persistence with chronic medical therapy are less than 50% at 1 year. This figure may provide a partial explanation why more than a fourth of patients with open-angle glaucoma (OAG) progress to blindness in at least 1 eye after 20 years, even under treatment.

Based on pharmaceutical claims data, only 10% of subjects receiving initial single-bottle glaucoma therapy use it continually for 12 months. Of the patients who do use drops, many use them improperly. A study videotaping patients instilling eye drops found that approximately one third of patients were not able to place the drop into their eye. Another study found that about half of patients who were given electronic dosing-aid devices, used travoprost as instructed less than 75% of the expected dose.

A SHIFT FROM ARGON LASER TRABECULOPLASTY TO SELECTIVE LASER TRABECULOPLASTY

In recent years, efforts have been made to search for a treatment that minimizes the impact of compliance and reduces the need for glaucoma medications. Argon laser trabeculoplasty (ALT) was the first glaucoma laser treatment to address this issue. In the late 1980s, the Glaucoma Laser Trial (GLT), a National Eye Institute-sponsored multicentre program, assessed the efficacy and safety of ALT as primary therapy. This study randomized patients with OAG to initial treatment with ALT in 1 eye versus timolol in the contralateral eye. The eyes treated initially with ALT had lower IOP and better visual field and optic disc stability than their fellow eyes treated initially with topical medication. The authors concluded...
that initial treatment with ALT was at least as efficacious as initial treatment with topical medication.14

However, this study was conducted before prostaglandin analogues became available; consequently, it may not apply to current practices. Moreover, a concern has been raised regarding possible thermal trabecular meshwork damage adjacent to each ALT application, which may have implications on disease progression and response to further medical therapy. This has led to the development of SLT, which selectively targets energy at melanin within the pigmented cells in the trabecular meshwork.7 SLT allows for less energy expended and less destruction of the outflow apparatus in the angle.

The laser treatment results in an inflammatory reaction, which involves secretion of cytokines and other inflammatory factors, induction of matrix metalloproteinases, and degradation of extracellular matrix components. Recruitment of monocytes also contributes to increased outflow, by clearing away obstructing debris within the trabecular meshwork via phagocytosis.15 SLT was also found to induce intercellular junction disassembly while increasing the permeability of Schlemm canal cells.16 Outflow studies confirmed that there is improvement in trabecular meshwork outflow after laser trabeculoplasty.17,18

Cellular in vitro cultures, cadaver tissue tests, and in vivo studies all confirm different tissue responses in patients who have undergone SLT as compared with patients who have undergone ALT. Even clinical observations suggest a different tissue response to SLT, typically with no peripheral anterior synechiae, unlike the commonly noted peripheral anterior synechiae after ALT.19

Several studies comparing SLT with ALT reported similar short- and long-term IOP-lowering effect for both treatment modalities.20–23 However, a recently published meta-analysis found greater IOP-lowering effect after SLT:6 SLT, unlike ALT, also has the advantage of repeatability,24,25 even after early failure of an initial treatment with SLT.25

SLT also has impact on short- and long-term IOP fluctuations.26–29 A recent study in patients with normal tension glaucoma found significant decrease in nocturnal IOP fluctuations after SLT. This study used the SENSIMED (Sensimed AG, Lausanne, Switzerland) Triggerfish contact lens sensor to assess habitual 24-hour IOP fluctuations.28

**Selective Laser Trabeculoplasty as First-Line Therapy**

SLT has given ophthalmologists an opportunity to re-examine the role of laser trabeculoplasty in the treatment paradigm of OAG. SLT is often used as a second-line treatment, after inadequate response or intolerance to topical medications and before proceeding to glaucoma surgery. However, there is accumulating evidence that SLT may also be useful as a first-line treatment.

A prospective study conducted by Melamed et al.30 followed patients with OAG or ocular hypertension (OHT) initially treated by SLT. They found a mean IOP decrease of 30% from baseline, with only 7% of patients requiring additional topical medications after 18 months.

McIraith et al.31 prospectively assigned patients to either SLT or latanoprost initially, based on the patients’ preferences. The treatments were equally effective, reducing IOP by about 31% after 1 year.31 A randomized, prospective study conducted in the United Kingdom by Nagar et al.32 compared 90-, 180-, and 360-degree SLT with latanoprost for OHT and OAG. This study did not find statistically significant differences between patients treated with 360-degree SLT and those treated with latanoprost: In both groups, more than 80% of patients had an IOP reduction of more than 20% after treatment.32

Lai et al.19 randomized Chinese patients with newly diagnosed primary open-angle glaucoma (POAG) or OHT to receive SLT in 1 eye and medical treatment in the fellow eye. At 5-year follow-up, they concluded that with fewer medications, SLT had similar IOP reduction compared with medical therapy alone.

Shally et al.33 compared long-term results of primary SLT in patients with POAG and pseudoexfoliation glaucoma (PXFG). The cumulative probability of success after 30 months, defined as having no additional medical, laser, or surgical intervention, was 74% for the PXFG group and 77% for the POAG group.33

A study conducted at St. Lucia by Realini34 evaluated the efficacy of bilateral SLT in patients with POAG, after 30-day medication washout. The 12-month survival rate (≥ 10% IOP reduction from post-washout baseline) was 77.7%, and 93% of successful subjects experienced IOP levels less than with-medication values.34

The SLT/Med study, a recently published multicentre, prospective, randomized study performed by Katz et al.35 aimed to compare outcomes of SLT with drug therapy as an initial therapy. Sixty-nine patients (127 eyes) with OAG or OHT were randomly assigned to either 360-degree SLT or prostaglandin analogue. If the target IOP range was not attained with SLT, additional SLT was the next step (repeat 180-degree SLT followed by another 180-degree SLT). In the medical group, medications were added. Data collection terminated with 54 patients reaching 9 to 12 months of follow-up. Researchers found a comparable reduction in IOP between the groups with 26.4% mean IOP reduction in the SLT arm and 27.8% mean IOP reduction in the medical arm, at the last follow-up visit. By the last follow-up visit, 11% of eyes received additional SLT, and 27% required additional medication. One of the strengths of this study is that, by randomizing patients rather than eyes (unlike the GLT study), researchers eliminated the concern of the possible crossover effect of glaucoma medications. One of the limitations is the
small sample size, which limited the power to detect differences between the groups.

Primary SLT also has fewer IOP fluctuations when the treatment is applied over 360 degrees as compared with 180 degrees. Prasad et al. showed that the odds of achieving IOP fluctuation ≤2 mm Hg were 5.7 times greater with 360-degree than with 180-degree SLT during the follow-up period of 6 to 24 months. Also, a recent study found lower energy to be adequate for the therapeutic effect of IOP reduction with lower risk profile for adverse effects. In contrast, another study concluded that high-energy application yielded a more favourable effect.

Other studies support the use of SLT as a first-line therapy not only in POAG and OHT, but also in other OAG subtypes, including normal-tension glaucoma and PXFG. It would be prudent to be vigilant in follow-up of patients with PXFG, given the more aggressive course of eyes with pseudoexfoliation. Eyes with PXFG have been observed to fail sooner and more rapidly compared with POAG.

The limited research on long-term results of primary SLT suggests that the majority of patients maintain the IOP-lowering effect of SLT up to 30 months and even 5 years after treatment. Once SLT shows attrition of response over time, repeat SLT may be a valid treatment option.

Complications

A major serious potential complication of SLT is an IOP spike immediately after laser application. In using topical alpha agonists in the perilaser period and titrating the laser power to achieve only slight cavitation bubbling, the risk for a persistent IOP elevation has been markedly reduced.

Other complications include uveitis, corneal edema, hyphema, macular burn, and irreversible IOP spikes, especially in heavily pigmented meshworks. There is also a potential risk in some cases when the patient does not return for follow-up visits because of the faulty assumption that the glaucoma was “cured.”

Cost Considerations

Several studies have concluded that laser trabeculoplasty may be less expensive than medical therapy. Lee and Hutnik compared the cost of primary medical therapy with primary SLT in Ontario. They found modest potential savings for using SLT as an initial treatment at a per-patient level. Seider et al. showed similar findings, with SLT being less expensive than most brand-name medications within 1 year and less expensive than generic latanoprost and generic timolol after 13 and 40 months, respectively.

Cantor et al. compared the 5-year costs of medication, laser trabeculoplasty (SLT/ALT), and filtration surgeries for patients with glaucoma with inadequate IOP control with 2 glaucoma medications. They also found the laser trabeculoplasty arm to have the lowest total costs.

Stein et al. found both generic topical prostaglandin analogues and laser trabeculoplasty cost-effective options for the management of newly diagnosed mild OAG compared with observation. With optimal (100%) medication adherence, prostaglandin analogues conferred greater economic value compared with laser trabeculoplasty. However, when adjusting for more realistic levels of medication adherence (e.g., 25% less effective than the documented effectiveness reported in clinical trials), laser trabeculoplasty was found to be potentially more cost-effective.

Summary

SLT is comparable with using a prostaglandin analogue as a first-line therapy and has the advantages of minimizing adherence concerns and side effect issues that are associated with chronic medical therapy. SLT may also be more cost-effective than glaucoma medications.

When discussing treatment options with patients with OAG, it may be prudent to offer SLT as an alternative to medications. Both physicians and patients should be educated on the possible role of SLT as initial therapy, based on the recent studies reporting SLT as a primary therapy.

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References

SLT as first line therapy—Waisbourd and Katz


