REVIEW PAPER

SELECTIVE LASER TRABECULOPLASTY- WHAT DO WE KNOW SO FAR? REVIEW

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ABSTRACT

Selective laser trabeculoplasty (SLT) has been used for lowering intraocular pressure (IOP) in patients with different types of glaucoma. It is a safe and effective procedure as initial or additional therapy when target IOP could not be achieved with medical therapy. SLT could specifically target pigmented cells in trabecular meshwork (TM) leaving nonpigmented cells unaffected, which may allow repeat treatments and thus has lower complication rate. It can be successfully used for IOP reduction in primary open angle glaucoma (POAG), normotensive glaucoma (NTG), pigmentary glaucoma (PG), pseudoexfoliation glaucoma (PXFG), primary angle closure glaucoma (PACG), silicone-oil-induced glaucoma, and high IOP after failed trabeculectomy. SLT could also be used in all stages of open agle glaucoma but failure of SLT in advanced glaucoma patients should go to immediate filtering surgery to avoid postoperative fibrosis. SLT reduces IOP fluctuation. IOP-lowering effect of SLT diminishes over time, but it can be repeated in order to achieve additional or recurrent IOP reduction. Higher baseline IOP up to a certain level is the strongest predictor of success after SLT.

Keywords: *Glaucoma, intraocular pressure, selective laser trabeculoplasty, treatment.*

INTRODUCTION

Glaucoma is leading cause of irreverseble blinding in the world. It is an optic neuropathy, with multifactorial risk factors that include increased intraocular pressure, increasing age, and genetic predisposition, characterized by recognizable patterns of optic disc and retinal nerve fiber structural and visual field functional damage (1). Unfortunately, in many cases, glaucoma is discovered late when disease is in its advanced stage and visualconsequences are severe. The goal of glaucoma treatment is to maintain the patients‘ visual function and related qualityof life, at a sustainable cost (2). Individualized glaucoma treatment aims at providing glaucoma menagment tailored to the individual needs of the patient (2). Lowering intraocular pressure can slow progression of the disease and is theonly proven treatment available so far (3). IOP decrease could be achieved with medical, laser and surgical treatment.



Figure 1. Q-swiched frequency-doubled Nd:YAG laser

ARGON LASER TRABECULOPLASTY

Over the years different laser procedures have been used for lowering IOP. Argon laser trabeculoplasty (ALT) was developed by Wise and Witter in 1979 (4). In a prospective study conducted by Srećković et al., 84 eyes with uncontrolled OAG were treated with ALT. The target pressure of ≤ 21 mmHg was achieved after 1 month in 77.8%of the patients, after 6 months in 93.8%, after 1 year in 80.2%, and after 4 years in 66.7% (5). IOP lowering results were good when used as initial or as an adjunct treatment, but it has several side effects and may cause coagulation of trabecular meshwork (TM) (6).

SELECTIVE LASER TRABECULPLASTY

Selective laser trabeculoplasty (SLT) was developed in 1995 by Latina and Park (7) as an alternative to ALT. A532-nm Q-switched, frequency-doubled Nd:YAG laser is used, delivers a short pulse duration of 3 ns, which is shorter than thermal relaxation time of melanin, causing selective photothermolysis, so SLT could specifically target those pigmented cells in trabecular meshwork leaving nonpigmented cells unaffected (8), which may allow repeattreatments and thus has lower complication rate. Even though SLT was initially used for open-angle glaucoma (OAG), later it was applied to a wide range of glaucoma subtypes (9).

Today selective laser trabeculoplasty is widely used in clinical practice as a first line and additional therapy indifferent types of glaucoma.

MECHANISM OF ACTION

Although SLT is well established treatment for glaucoma, it is still not yet fully understood which mechanism leadsto decrease in IOP following this procedure. Cellular theory proposes macrophages migration at the site of laser treatment and their activity of clearing TM of debris and thus allowing better outflow of aqueous humour (10).

Mechanical theory advocates that thermal damage of TM leads to collagen shrinkage and scarf formation (11). Third possible mechanism of action is extra enzyme release known as matrix metalloproteinases (MMPs) and expression and secretion of cytokines, such as IL-1 beta and TNF-alpha which are remodeling juxtacanalicular extracellular matrix allowing better outflow and decrease of IOP (12).

RESULTS

Pimary open angle glaucoma and Ocular hypertension

As it is above mentioned, SLT is effective both as primary and additional treatment of patients with POAG and OHT. In the study conducted by Wong et al., SLT resulted in a 6.9-35.9% IOP reduction between patients, rangedfrom newly diagnosed POAG to those on maximally medical therapy (13). In SLT treated patients, IOP lowering effect diminishes over time. Success rates (IOP reduction >20% from baseline IOP)

vary from 66.7% to 75% at 6 months, 58% to 94% at 12 months, 38% to 74% at 3 years, and 11.1% to 31% at 5 years (14).

Mcllraith in his prospective study came to conclusion that SLT is equally efficious as latanoprost in reducing IOPin newly diagnosed patients with OAG or OHT over 12 months regardless of angle pigmentation (15). Another study that compared SLT efficacy with medical therapy, was conducted by Lai. After 5 years of follow-up mean IOP reduction was 32,1% in SLT group and 33,2% in medically treated eyes, so results were similar in terms of IOPreduction between SLT and monotherapy (16). Results suggested that SLT could be used as primary treatment whenconsidering systemic and local side effects and compliance problems associated with long-term medication use.

Melamed in his study followed patients with OHT or OAG who underwent SLT as a first line treatment. Mean IOP drop after SLT was 30% from baseline values. 89% of them had a decrease of 5mmHg or more. That sugested that SLT may be offered as first line treatment in POAG and OHT (17). Another study that has shown and proved safety and efficacy of SLT used as initial therapy in treatment of naive patients with OHT or OAG is study conducted by Garg and coworkers. After 36 months, 74,6% patients in SLT group achieved drop free disease controland 58,2% of them after single SLT. Mean IOP reduction after SLT in naive treatment patients was 29,7% in OHT eyes and 26,1% in OAG eyes. In a group of patients treated with medical therapy as first line, mean IOP reduction was 27,9% in OHT eyes and 27,9% in OAG eyes. Overall, at 2 months, IOP reduction was no different between primary SLT and topical medication (18).

Additional SLT has been shown to be effective in POAG patients with uncontrolled IOP despite maximal medicaltolerated therapy (19). IOP reduction more than 20% was established in 64.58% of eyes with medically uncontrolledPOAG 1 year after SLT. IOP reduction was more significant if the initial IOP was higher and initial reliable results of IOP reduction were confirmed at 1 month after SLT (19).

Zhang investigated efficacy of SLT in patients after trabeculectomy. Patients with POAG whose target IOP could not be achieved with maximal medical tolerated therapy underwent 360 degrees SLT. 77% of patients had reductionof IOP more than 20% (20).

Schlote et al. investigated use of SLT in different stages of glaucoma, early and advanced OAG. SLT was shown to be safe and effective (for early OAG patients, reduction of IOP 20% from the baseline values or a reduction of medication; and for advanced OAG patients reduction of IOP more than 30%) in almost 2/3 of early and 50% of advanced glaucoma patients. Failure of SLT should be followed by filtering surgery which may be associated with lower risk of fibrosis in advanced glaucoma (21). SLT may be used effectively in all stages of OAG. Prasad at el. suggested that extent of SLT treatment may influence IOP fluctuation and demonstrated that 360° SLT reduced IOPfluctuations more than 180° SLT treatment (22).

NORMAL TENSION GLAUCOMA

In two prospective studies, Lee and coworkers evaluated clinical outcomes of SLT in Chinese patients with normal tension glaucoma (NTG) at one and two year follow-up. After one month of medication free 360° SLT was applied. IOP reduction of >20% from the baseline values without additional medication were considered absolute success. After SLT, mean IOP measured at all visits except 1 week post SLT was significantly reduced. At 1 and 2 years, theaverage IOP reduction was 14.7% and 11.5%, average mean number of medication reduction was 26.7% and 41.1%, and absolute success rate was 22% and 11.1% (23) (24). In these studies, predictors of SLT success in NTG were also investigated. It was reported that treatment success was correlated with higher preoperative IOP and lower postoperative IOP 7 days after SLT (25). Although a successful IOP-lowering response to SLT occurs in NTG patients, the efficacy of SLT remains lower than it is achieved in other types of OAG. This happens probably due to the fact that the most dependable predictor of SLT success is a higher preoperative IOP which is in NTG patients in normal range (26).

PIGMENTARY GLAUCOMA

Koucheki et al. followed patients with pigmentary glaucoma (PG), pseudoexfoliation glaucoma (PXFG) and POAG after 360° SLT. At 16,6 months mean IOP reduction was 14.5% in PG, 16.6% in the PXFG and 16.7% in POAG group. Percentage of IOP reduction and success rate (reduction of IOP 20% or discontinuing one medication) were not significantly different between the groups. Post SLT IOP spike and inflammation (PG 65.2%, PXFG 40.9%, 37.4% POAG) and mild pain (PG 43.5%, PXFG 19.8%, POAG 18.2%), were higher in patients with pigmentary glaucoma than other types of glaucoma. Other interventions like repeat SLT and trabeculectomy were also noticedin a higher rate in PG patients (27). TM pigmentation is higher in PG which causes more energy absorption. In pigmented angles, like PG, lower power settings should be used and thus decrease number of complications (28).

PSEUDOEXFOLIATION GLAUCOMA

In pseudoexfoliation glaucoma (PXFG) and POAG similar IOP decrease was achieved after SLT whether it is used as an additional (29) or primary (30) treatment. Miraftabi et al. compared efficacy of 360° SLT between PXFG and POAG. Six months following SLT, percentage of IOP reduction was significantly higher in patients with PXFG compared to POAG (29% vs. 19%), but efficacy of SLT decreased over time faster in PXFG group. The IOP reduction was 29.1% in POAG and 25% in PXFG 12 months after SLT. There was no significant difference in IOP reduction or number of glaucoma medications used in PXFG and POAG during the first year after SLT (31). Similarresults were observed

by Kara and his coworkers, in eyes with PXFG there was significantly more IOP decrease than eyes with POAG during one year of follow-up (32). Short-term IOP-lowering efficacy of SLT in PXFG patients seems to be at least equal or more than in POAG patients, but it does not last as long as in POAG patients.

PRIMARY ANGLE-CLOSURE GLAUCOMA

Earlier, ophthalmologist have not considered SLT as a treatment of PACG since for this procedure visualization of TM is necessary. However, recent studies have shown positive results with the use of SLT in eyes with PACG or primary angle closure (PAC) where a portion of the anterior chamber angle still remains open and is manageable totreatment.

Ali Aljasim in his retrospective study evaluated results of SLT in patients with PAC or PACG following YAG laser peripheral iridotomy (PI) and compared results with POAG (33). Fifty-nine eyes after successful PI but with persistent IOP elevation undergone SLT treatment in areas where the angle was open enough for at least 180 degrees. In the PAC/PACG group, SLT resulted in a mean IOP reduction of 38% in patients with uncontrolled preoperative IOP and reduction of 1.6 medications in patients of PAC/PACG who had controlled IOP under medications. The success rate (IOP reduction of ≥20% or reduction of one or more glaucoma medications) was 87.4% in the PAC/PACG group and the safety and efficacy of SLT in PAC/PACG group were similar to POAG group. Narayanaswamy et al. evaluated the efficacy of SLT in comparison to topical prostaglandin analogue (PGA) therapy in 100 patients with PAC or PACG who were treated with PI and afterwards had at least 180° of open angle. Fifty patients (96 eyes) were randomized to SLT and 50 patients (99 eyes) to PGA medical therapy. At 6 months mean IOP reduction was not statistically significantly different between SLT and PGA groups. The overall success rate of SLT group was significantly less than PGA group. More additional medications were needed in SLT group compared to PGA group (34). SLT could be successful in the treatment of PAC or PACG patients in short term if more than 180 degrees of the anterior chamber angle is open after PI.

SILICONE OIL-INDUCED GLAUCOMA

Zhang et al. investigated efficacy of 360° SLT on 42 eyes with silicone oil-induced secondary glaucoma. The meanIOP was decreased from 23.1 to 18.4 mmHg and the mean number of antiglaucoma medications decreased from 2.17 to 1.25 at 12 month follow-up. 59,5% of eyes achieved more than 20% IOP reduction without addition of anyother treatment modality at 12 months (35). The study showed that SLT may be effective in treating silicone oil- induced secondary glaucoma.

SLT AFTER TRABECULECTOMY

Zhang and coworkers investigated safety and efficacy of SLT in patients after trabeculectomy. 18 eyes of 16 patients were enrolled in this study, with POAG whose target IOP could not be achieved with maximal medical therapy, underwent 360 degrees SLT. 78% of patients had reduction of IOP more than 20% (36). The study demonstrated that SLT may safely and effectively reduce IOP and daytime IOP fluctuations in post-trabeculectomy patients withadvanced POAG who can not reach to target IOP with medication.

PREDICTORS OF SUCCESS

Potential factors leading to SLT success or failure in different types of glaucoma have been investigated in many studies. They have shown that the strongest predictor of success after SLT was a higher baseline IOP (37) (38). Since NTG patients have lower baseline IOP values, both absolute IOP reduction and success rates were lower thanin other subtypes (23).

Higher IOP decrease is more in patients with high preoperative IOP. Higher baseline IOP usually means that a higher target IOP should be met, but in patients with too high IOP surgery could be a better alternative to SLT. There are contradictory results about the effect of the number of topical glaucoma medications used before SLT on success rates. Woo et al. found no significant correlation between the number of medications used before SLT and success rates (39). Conversely to this, Lee et al. reported better success rates in patients using various medications especially topical carbonic anhydrase inhibitors (40). Different results of unrelated studies may be explained with different mean baseline IOP, mean follow-up time, mean average age, and definition of success in different studies.Lee et al. revealed that successful laser treatment in one eye may also suggest effective treatment in the fellow eye and a significant correlation was found between the responses to SLT in both eyes (41). With increased angle pigmentation, SLT efficacy also increases. Wasyluk et al. divided 63 eyes into 3 groups based on angle pigmentation. After 270° SLT application, mean IOP decrease by 2.06, 2.46, and 4.75 mmHg in groups with low, marked, and high angle pigmentation, respectively. In patients with bearly pigmented angles, absolute decrease in IOP may be less, but clinically significant and SLT sill may be beneficial (42). Other factors including age, race, gender, central corneal thickness, history of cataract surgery, history of argon laser trabeculoplasty, standard automated perimetry mean deviation, and lens status (phakic or pseudophakic) were also investigated and were notfound to be associated with success rate of SLT (43).

TECHNIQUE

Presently, SLT parameters are 50-100 shots applied over 180°-360° with energy ranged to 0.6-1.4 mJ with a fixed spot size of 400 μm and an end point of just visible small microbubbles. Different studies investigated how many degrees

of angle of TM should be treated with SLT in order to get the highest IOP decrease. Nagar and his coworkers compared 90°, 180°, 360° SLT and reported no difference between 180° and 360° SLT applications, but 90° SLT was less effective than both groups one year following laser procedure (44). Chen et al. compared 90° SLTversus 180° SLT and found no significant difference in IOP values 7 months after SLT between the groups (45).

Currently, SLT is usually applied to 180° or 360° of TM. Effect of energy levels on reducing IOP was also investigated. Lee et al. studied the optimal energy level used in SLT for maximal IOP reduction and found that higher SLT total energy (range of 214.6-234.9 mJ) was associated with a higher IOP-lowering efficacy (46). Also, laser settings have been studied by Tang et al. Thirty-nine patients receiving 100 shots of 360° SLT using low energy settings (0.3-0.5 mJ) were compared with 35 patients receiving 100 shots of 360° SLT using standard energysettings (0.6-1.0 mJ). IOP reduction was not statistically significantly different between the two groups 1 year following SLT (47).

Optimal energy settings for SLT treatment need to be characterized with more studies. The authors believe that total SLT energy level after a certain time may effect maximal IOP reduction. Although higher total SLT energy level may cause greater IOP reduction, safety and repeatability of higher total SLT energy application are not knownclearly.

POSTOPERATIVE CARE

After SLT procedure topical anti-inflammatory drops are usually prescribed to inhibit early inflammation, but SLTeffect occurs partly by biological pathway and counteraction of antiinflammatory drops on IOP-lowering effect canbe considered. This effect was investigated by De Keyser et al. 66 patients with NTG, POAG or OHT who undergone 360° SLT were followed. One of the eyes treated with indomethacin 0.1% or dexamethasone 0.1% 3 times daily for 7 days; the other eye had no anti-inflammatory treatment. Anti-inflammatory drugs did not make a significant difference in redness, pain, anterior chamber cells, and peak IOP at 1 h following SLT. During 6-monthfollow-up IOP-lowering effect of the SLT was not influenced by the use of indomethacin or dexamethasone (48).

ADVERSE EVENTS

Most of the complications of SLT are usually mild, transient, and self-limiting and usually related to inflammation of anterior chamber. The incidence of complications found in different studies ranges from none to 83% of eyes showing some degree of inflammation. Pain, redness, discomfort and photophobia may occur usually during the firstweek following SLT and vanish without any treatment within a few days (49). A transient IOP spike of ≥5 mmHg after SLT is reported in up to 28% of eyes (50). Ali Aljasim et al. reported an IOP spike of 10 mmHg in 10% of PAC/PACG patients and 5% of POAG patients 1 h after SLT (33). In silicone oil-induced glaucoma, 26.2% of eyes experienced greater than 6 mmHg IOP spike on the same day of SLT (35). In addition to PXFG, eyes with heavily pigmented TMs were also more commonly associated with IOP spikes. IOP spike can be prevented by a drop of brimonidine before or immediately after SLT and IOP elevation can usually be treated with antiglaucoma medications. Transient corneal edema and haze were reported with or without residual corneal scarring and hyperopic shift in a few case reports (51). Peripheral anterior syneshia (PAS) were noticed in 2.86% of cases after SLT (13) and increased PAS occurrence after repeat SLT was reported in two cases by Baser et al. (52). Other rare complications are hyphema (53) and bilateral anterior uveitis (54).

REPEATABILITY

Even though initial IOP-lowering effect of SLT was successful, its effect diminishes over time. Retreatment to the same previously treated area is normally applied if target IOP was achieved with intial SLT but its effect has been decreased over time. It is almost rarely applied when initial SLT is not enough to gain target IOP (55). Safety and efficacy of repeat SLT were investigated after initially successful but diminishing effect of SLT. The magnitude of IOP reduction in repeat 360° SLT was similar to initial 360° SLT and the number of medications did not decrease neither in initial nor in repeat SLT applications in OAG patients (55). Repeat 360° SLT which is applied when the initial SLT could not reach target IOP has similar efficacy as primary 360° SLT even with a longer duration of treatment success (56). The success rate of repeat SLT was significantly higher when there is a shorter interval between initial and repeat SLT. Previous argon laser trabeculoplasty did not affect mean IOP reduction at initial and repeat SLT (55). Repeat SLT is a safe procedure. Polat et al. reported that in 38 eyes with OAG treated with repeat SLT had no IOP spike of more than 10 mmHg or anterior chamber inflammation (57). The authors advice repeating SLT to the same previously treated area in patients whose initial 360° treatment was successful, lasted at least 6 months and than diminished over time. If initial SLT was not successful, repeat treatment is not likely to be effectiveeither. It is advisable and preferable to treat these patients with medications or surgery. Shorter interval between the initial and repeat SLT can result in higher success rates because of still present action of initial SLT application. Thetechnique of initial and repeat SLT procedures are the same.

CONCLUSION

Selective laser trabeculoplasty may be successfully and safely used for the reduction of IOP in POAG, NTG, PG, PXFG, PACG, silicone-oil-induced glaucoma, and high IOP after failed trabeculectomy, also it could be used in allstages of OAG but failure of SLT in advanced glaucoma patients should go to immediate filtering surgery to avoid postoperative fibrosis. SLT reduces IOP fluctuation and is successful as initial and adjunctive treatment of glaucoma. IOP-lowering effect of SLT diminishes over time, but it can be repeated in order to achieve additional or recurrent IOP

reduction. Higher baseline IOP up to a certain level is the strongest predictor of success after SLT.

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