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RESEARCH ARTICLE

THE LONG-TERM EFFICACY OF SELECTIVE LASER TRABECULOPLASTY IN EARLY AND ADVANCED PRIMARY OPEN ANGLE GLAUCOMA

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ABSTRACT

Purpose: To evaluate the long-term efficacy of Selective Laser Trabeculoplasty (SLT) in patients with first diagnosed and advanced primary open angle glaucoma (POAG).
Methods: This study is a retrospective chart review of patients with OHT, first diagnosed early POAG without any medication and uncontrolled POAG with maximum tolerated medical therapy who underwent SLT at the Sifa University, between July 2010 and July 2011.The aforementioned data were gathered from the, 3-month, 6-month, 12-month, 24-month, and 36-month postoperative visits. Both groups were compared regarding decrease in IOP, percentage of IOP decrease, and success rate after SLT treatment. The data were analyzed using independent t-test to compare IOP levels and the decrease of IOP between the both groups at different time points. A P-Value of $P<0.05$ was considered as statistically significant.
Results: The mean IOP in the 3 groups at baseline was similar and did not reach statistical significance. The therapy effect was stronger in the early POAG patients in the first year. The success rate at the last visit at 36th month was 44.4% in the group of first diagnosed POAG, and 23.5% in the group of uncontrolled POAG.
Conclusion: The long-term therapeutic effect in patients with OHT and first diagnosed POAG is moderate. The efficacy is lesser in advanced patients. However, the main advantage of SLT is the protecting of the ocular surface from the toxicity of the preservants of anti-glaucoma drops.

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INTRODUCTION

Glaucoma is a progressive optic neuropathy localized in the optic nerve and it is among the leading causes of blindness worldwide (Sommer *et al*., 1991).Randomized clinical trials, especially EMGT (Early Manifest Glaucoma Trial), have found that intraocular pressure (IOP) reduction to be the only effective treatment preventing the emergence of new glaucomatous visual field defects (Heijl *et al*., 2003). Laser procedures on the iridocorneal angle comprise an approach accepted by the European Glaucoma Society as second line treatment or, alternatively, as first line treatment in selected cases (European Glaucoma Society, 2008). Argon laser trabeculoplasty (ALT), was first described as a laser therapy method in glaucoma by Wise and Witter in 1979 (Wise and Witter, 1979; The Glaucoma Laser Trial (GLT) and glaucoma laser trial follow-up study, 1995). The disadvantage of ALT is the tissue disruption and coagulative damage on the trabecular meshwork (Kramer and Noecker, 2001). Since then, laser trabeculoplasty has undergone considerable development until it earned its current status as the most widely used laser treatment for open-angle glaucoma. SLT is a method of non-invasive IOP reduction, which is first reported by Latina (Latina and Park, 1995).The device is a Q-switched, frequency-doubled Nd:YAG laser that is melanosome-specific and is widely used to lower IOP in patients with open-angle glaucoma or ocular hypertension. In contrast to ALT, SLT works by selective targeting of pigmented trabecular meshwork with minimal structural damage. This makes SLT a repeatable therapy (Barkana and Belkin, 2007). As SLT is a relatively new treatment alternative, it is important for clinicians to assess which patients have a greater probability of achieving acceptable IOP reduction after SLT. To our knowledge, there are not many studies compared various patients groups in regard to the long-term results of SLT. In this study, we evaluated the effectiveness of SLT in patients with early and advanced POAG with maximum tolerated medical therapy in long-term follow-up.

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MATERIALS AND METHODS

This study is a retrospective chart review of patients with early and advanced POAG with maximum tolerated medical therapy who had undergone SLT at the Sifa University Hospital Eye Clinic between July 2010 and July 2011. The study adhered to the tenets of the Declaration of Helsinki. Informed patient consent and approval by the institutional review board were obtained prior to the study commencement. The authors declare no financial or proprietary interests. The aforementioned data were gathered from the, 3-month, 6-month, 12-month, 24-month, and 36-month postoperative visits. As part of routine clinical practice, a full ocular examination was performed for each newly referred patient, including best-corrected visual acuity, slit-lamp evaluation, Goldmannapplanation tonometry (We used in this study two initial IOP measures for each patient to reduce the effect of diurnal variation and improve accuracy), corneal pachymetry, gonioscopy, dilated fundoscopy, visual field testing and imaging as appropriate. Primary open angle glaucoma was defined as an open angle on gonioscopy, presenting an IOP over 21 mmHg, and visual field loss on the Humphrey visual field analyzer as per the Hodap–Parrish–Anderson criteria, or retinal nerve fiber layer thinning on optical coherence tomography (Hodapp *et al*., 1993). Patients with early without any previous anti-glaucoma treatmenand advanced POAG with maximum tolerated medical therapy (MTMT) are enrolled into the study. We determined the patients with early POAG without any therapy as group 1, and patients with advanced POAG with maximum tolerated medical therapy as group 2 who were under treatment of MTMT with 3 antiglaucoma drops (beta blockers, prostaglandin analogues and carbonic anhydrase inhibitor or alpha adrenergic agonists). In group 2, none of the 3 drugs were stopped during the follow-up period. Exclusion criterias were as follows:

- Any pre-existing corneal pathology or scars
- Pseudoexfoliative glaucoma, Juvenil glaucoma, closed-angle or any secondary glaucoma
- Previous ALT or SLT treatment
- Defaulted follow-up
- Any previous intraocular surgery, such as cataract, retinal detachment, glaucoma surgery
- Any previous uveitis or intraocular inflammation

In the present study, the SLT treatment was performed over 360° of the trabecular meshwork (TM) with the SLT LightmedCombi Laser® in two sessions. Approximately 50 non-overlapping shots were applied to the TM at each session. The initial energy of the laser was 0.8 mJ. The energy was increased or decreased until bubble formation appeared. The energy used in the present study was between 0.5 and 1.0 mJ. No more laser energy was necessary to achieve the desired bubble formation. No medication has been given to any patient who were treated with SLT, unless an anterior chamber reaction was detected after the treatment. In this situation, Flourometolon eye drops were used twice in a day for a few days. All patients were initially been treated by SLT over 180° in the lower part of the TM. The second therapy was applied on the upper 180 ^{0} part, one month later. All lasers were performed by the same surgeon (G.B). An IOP reduction of 20% or more from baseline was accepted as effective. The IOPs were measured using a Goldman applanation tonometer by a different ophthalmologist, who was being blind to the patient group. The IOP was measured three times and an average value was calculated.

Statistical Analysis

SPSS, statistical software, version 11.6 (SPSS, Inc, Chicago, IL) was used for statistical analysis. The data were analyzed using independent t-test to compare IOP levels and the decrease of IOP between the both groups at different time points. A P-Value of $P<0.05$ was considered as statistically significant.

RESULTS

The medical records of 85 eyes of 85 patients who underwent SLT treatment for non-treated early and advanced POAG with MTMT were reviewed. The characteristics of the both groups are presented in Table 1.

Table 1. Baseline characteristics of the patients

	First diagnosis POAG (n=48)	Uncontrolled POAG (n=37)	P Value
Age	54.2±5.4	54.5±3.9	0.343
Gender (M/F)	24/24	22/15	0.367
BCVA (log)	0.24±0.17	0.32±0.16	0.060
Average TM pigmentation	2.4±0.9	2.9±0.9	0.093
Average number of spots per eye	57.9±3.1	49.7±3.6	0.112

M/F: Male/Female
BCVA:Best corrected visual acuity, TM:Trabecular meshwork

The mean baseline IOP was 28.7±2.2 mm Hg in the early POAG group and 28.5±1.9 mmHg in the uncontrolled POAG group (p=0.093).The mean IOP in the both groups at baseline as well as at 3, 6, 12, 24, and 36 months after treatment was also similar and did not reach any statistical significance (Table 2), except the third and 12th month.

Table 2. Mean intraocular pressure at baseline and at various time points up to 36 months

	First diagnosed POAG	Uncontrolled POAG	P value
Preoperation	28.7±2.2	28.5±1.9	0.093
3 months	19.8±3.5	23.6±3.3	0.001*
6 months	20.2±3.6	23.3±3.2	0.010
12 months	18.3±1.5	20.6±2.2	0.001*
24 months	20.4±2.7	20.5±3.4	0.117
36 months	20.7±2.9	20.8±3.7	0.195

POAG: Primary Open Angle Glaucoma
* $P<0.05$

The difference of mean decrease of IOP compared to baseline was significantly different between both groups, especially in the first year (Table 3).

Table 3. Decrease in intraocular pressure values from baseline to various time points

	First diagnosis POAG	Uncontrolled POAG	P value
3 months	-8.5±3.8	-4.9±3.7	0.001*
6 months	-8.1±3.7	-5.3±3.9	0.008*
12 months	-10.3±2.5	-5.8±3.1	0.000*
24 months	-8.3±3.6	-6.0±4.3	0.064
36 months	-8.0±3.5	-5.7±4.5	0.086

*$P<0.05$

The patients in whom the effect of SLT failed, underwent medical or surgical glaucoma therapy, regarding to the severity of their disease.

DISCUSSION

Review of the literature showed that SLT is a viable option as a primary or adjuvant treatment for patients with POAG, OHT, and pseudoexfoliation glaucoma (Melamed *et al*., 2003; Kano *et al*., 1999). The published success rate of SLT ranges from 65% to 100% in short term (Kajiya *et al*., 2000; Gracner 2001). Success has been previously defined as an IOP reduction of 3 mm Hg or more (Lanzetta *et al*., 1999), or more commonly by an IOP reduction more than 20% (Kim *et al*., 2000). In our series, the short term effect (3-12 months) of SLT was similar to the studies which were reported before. 39.5% of the treated eyes had a success (IOP reduction ≥20%) with SLT and the mean IOP reduction for all treated eyes was 21.7%, which achieves the accepted 20% reduction cutoff for SLT success. The overall percentage of success in the present study was slightly lower than that previously reported in the literature because most of the previous publications were based on the POAG subjects, whereas 21.0% of the subjects in our series had POAG which were uncontrolled with maximum tolerated antiglaucoma drugs. The most remarkable finding of our study was the low success rate in patients with uncontrolled glaucoma. The efficacy of SLT on such cases has not been widely published. Schlote *et al* reported a success rate about 50 % in advanced cases (Schlote and Kynigopoulos, 2015). But this was only a one- year report and our one-year results were similar. Sayin *et al* reported a success rate of 64.5% in cases with maximum tolerated medical therapy. The patients of this study had a follow-up period of one year also (Sayin *et al*., 2013). In the current study, the success rate at the last visit was 44.4% in cases of first diagnosed early POAG. In patients with uncontrolled POAG the success rate was 88.2% at 3 months, 70.6% at 6 months but only 23.5% at the last visit. Furthermore, in our study the most decrease in the IOP was achieved in the patients of first diagnosis POAG, in which SLT was performed as a first-step treatment. The decrease in the patients of first diagnosis POAG was found to be significantly higher compared with the other 2 groups until 12 months, whereas the difference was not statistically significant at the visits of 24 and 36 months. Khouri *et al* and Katz *et al* reported similar results in POAG (Khouri *et al*., 2014; Katz *et al*., 2012). According to these results, SLT seems to be more effective in the short term. With the time, the effect of SLT decreases on IOP reducing. This might be due to the minimal destructive and/or reversible tissue effects of SLT.

It has been reported that SLT was more successful in those without prior use of IOP-lowering medication and high pretreatment IOP (Lee *et al*., 2014).On the other hand, others have reported on the lesser effective influence of prostaglandin eye drops on SLT success (Kara *et al*., 2011).The use of topical carbonic anhydrase inhibitors (CAI) was also associated with greater SLT success (Lee *et al*., 2014). It has been reported that prostaglandin eye drops may be associated with SLT failure because SLT works by increasing the metalloproteinase and macrophages in the trabecular meshwork; thus, the use of prostaglandin analogs can theoretically lead to hypoperfusion of the trabecular meshwork by increased uveoscleral outflow or suppression of metalloproteinases (Song *et al*, 2005). Unfortunately in our study all of the patients with advanced glaucoma were using similar groups of drugs and it was impossible to compare different drugs in regard to SLT success. One other remarkable point was, although the baseline IOP values were similar in both groups, a higher decrease was noted in the early glaucoma group without prior anti-glaucoma treatment, which was compatible to the results in the literature (Hodge *et al*., 2005). The aim of our study was to compare patients with early and and advanced POAG, according to the effectiveness of SLT. We believe that further prospective studies will be very valuable to have more information about the role of SLT in different indications. As we observed in our study, the success rate in patients of uncontrolled POAG with maximum tolerated medication was only 23.5% at 36 months. Most of the patients in this group needed further surgical treatments after SLT. This might be due to some morphological or pathological alterations of the eye in advanced glaucoma, which are still unknown, and which are resistant to medical or laser therapy.

The relatively small number of patients and its retrospective design are the main limitations of our study. On the other hand, studies which comparing the efficacy of SLT for long-term in early and advanced POAG are very few in the literature. Our belief is, prospective designed similar studies with larger patient groups will give more information to understand the long-term effects of SLT in various stages of glaucoma. Another important question which has to be answered is that, why the IOP-lowering effect of SLT is lesser in advanced glaucoma. In conclusion, we might say that, SLT is an effective method in patients with first diagnosed early POAG in short term and the success rate was over40% at 36 months after initial treatment. The effect of SLT in advanced glaucoma is weaker. The advantage of SLT is to keep the IOP in a safe level without any medication. Thus, the ocular surface is protected from preservative substances, such as benzalchonium chloride (BAC), or polyquad (PQ), which are used widely in anti-glaucoma drops. Waisbourd *et al* suggested the SLT to consider as a first step treatment in OHT and POAG (Waisbourd *et al*., 2014). In our opinion, although this is a good therapy aspect, but one must be kept in mind that, the effect of SLT decreases with time. Therefore, the patients who underwent SLT should be kept under strict control, because patients who underwent a surgical intervention tend to believe that their health problem is solved. This leads to disruption of their glaucoma controls. Giving detailed information about this procedure is here essential. The second aim of the studies in this field should be focused on the repeatability and investigating the increase of the long-term effect of SLT.

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