

Selective laser trabeculoplasty in patients with pseudoexfoliative glaucoma *vs* primary open angle glaucoma: a one-year comparative study

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Abstract

• **AIM:** To compare the efficacy of single-session 360-degree selective laser trabeculoplasty (SLT) for reduction of intraocular pressure (IOP) in patients with pseudoexfoliative glaucoma (PXFG) and primary open angle glaucoma (POAG).

• **METHODS:** This is a single-center, prospective, nonrandomized comparative study. Patients older than 18 years of age with uncontrolled PXFG or POAG eyes requiring additional therapy while on maximally tolerated IOP-lowering medications were included. The primary outcome measure changed in IOP from baseline. Success was defined as IOP reduction $\geq 20\%$ from baseline without any additional IOP-lowering medication. All patients were examined at 1d, 1wk, 1, 3, 6, 9, 12mo after SLT.

• **RESULTS:** Nineteen patients (20 eyes) with PXFG and 27 patients (28 eyes) with POAG were included in the study. In the visual fields mean deviation was $-2.88 (\pm 1.67)$ in the POAG and $-3.1 (\pm 1.69)$ in the PXFG groups ($P=0.3$). The mean (\pm SD) IOP was $22.9 (\pm 3.7)$ mm Hg in the POAG group and $25.7 (\pm 4.4)$ mm Hg in the PXFG group at baseline and decreased to $18.4 (\pm 3.2)$ and $18.0 (\pm 3.9)$ mm Hg in the POAG group ($P<0.001$ and $P=0.02$), and to $17.9 (\pm 4.0)$ and $21.0 (\pm 6.6)$ mm Hg in the PXFG group ($P<0.001$ and $P=0.47$) at 6 and 12mo, respectively. The number of medications was $2.6 (\pm 0.8)$ in the POAG group and $2.5 (\pm 0.8)$ in the PXFG group at baseline, and did not change at all follow-up visits in both groups ($P=0.16$ in POAG and 0.57 in PXFG). Based on Kaplan-Meier survival analysis, the success rate was 75% in the POAG group compared to 94.1% in the PXFG group ($P=0.08$; Log-rank test) at 6mo, and 29.1% and 25.0% at 12mo, respectively ($P=0.9$; Log-rank).

• **CONCLUSION:** The 360-degree SLT is an effective and well-tolerated therapeutic modality in patients with POAG and PXFG by reducing IOP without any change in number of medications. The response was more pronounced early in the postoperative period in patients with PXFG whereas there was no statistically significant difference at 12-month follow-up.

• **KEYWORDS:** primary open angle glaucoma; pseudoexfoliative glaucoma; selective laser trabeculoplasty

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INTRODUCTION

Selective laser trabeculoplasty (SLT) was introduced by Latina and Park in 1995 as an option for the treatment of open angle glaucoma^[1]. In this method, a Q-switched, frequency doubled laser with a wavelength of 532 nm and pulse duration of 3ns affects only the pigmented trabecular meshwork cells while the non-pigmented meshwork cells remain intact^[2-3]. SLT has been widely adopted for treatment of glaucoma and is used by some clinicians early in the course of treatment of the disease^[4-5]. Results of different studies have shown that SLT reduces the intraocular pressure (IOP) between 11% to 40% in various types of glaucoma in short to intermediate-term period^[6]. The exact mechanism remains uncertain by which SLT reduces IOP but in particular, cytokine secretion, matrix metalloproteinase induction, increased cell division, repopulation of burn sites and macrophage recruitment are responsible for IOP reduction^[7].

Although the efficacy of SLT in patients with primary open angle glaucoma (POAG) has been well documented, there are few studies that have investigated its efficacy in other types of glaucoma including pigmentary and pseudoexfoliative glaucoma (PXFG)^[8-9]. In this prospective study, we compared the efficacy of 360-degree SLT treatment in patients with PXFG to those with POAG.

SUBJECTS AND METHODS

Study Subjects This single-center, prospective, nonrandomized comparative study was performed between March 2010 and March 2013 at the Hazrat Rasoul Akram Hospital, Tehran, Iran. The Ethics Committee at Iran University of Medical Sciences, Tehran, Iran, approved the study protocol. Written informed consents were obtained from all patients and the study was carried out in accordance with the principles of Declaration of Helsinki.

Patients aged 18 years or older with uncontrolled PXFG or POAG requiring additional therapy while on maximally tolerated IOP-lowering medications were enrolled. Exclusion criteria were eyes with prior history of laser or incisional surgery such as phacoemulsification, glaucoma procedures or argon laser trabeculoplasty; ocular trauma or any other preexisting corneal disease precluding the angle evaluation; or if the trabecular meshwork could not be viewed for 360 degrees. Preoperative exams included slit-lamp biomicroscopy, IOP measurement using Goldmann applanation tonometry, gonioscopy, dilated fundoscopic examination with a 90 D lens, and standard automated perimetry with 24-2 Swedish interactive threshold Algorithm (SITA; Carl Zeiss Meditec Inc. Dublin, CA, USA).

Outcome Measures The primary outcome measure was IOP (mm Hg) before and after 360-degree SLT in both groups at 1d, 1wk and then every 3mo after surgery. All of IOP measurements performed at morning in sitting position. Other outcome measures included success rate, changes in the number of IOP-lowering medications, and complications. Success was defined as IOP reduction $\geq 20\%$ from the baseline without additional IOP-lowering medications. Failure was defined as IOP reduction $< 20\%$ from the baseline at two consecutive visits and/or addition of IOP-lowering medications.

Laser Procedure All the study eyes underwent 360-degree SLT for the first time. All the procedures were performed by two surgeons (Miraftabi A or Nilforushan N) with the same protocol, which included Q-switched frequency-doubled 532 nm Nd:YAG laser (Ellex Tango SLT/Photodisruptor Combination Laser, Ellex Medical Lasers Ltd., Adelaide, Australia) with pulse duration of 3ns and a spot size of 400 μm for 360 degrees. No pretreatment with IOP-lowering medications was used. After topical anesthesia with 0.5% tetracaine hydrochloride, a laser gonioscope (Ocular Latina SLT Gonio Laser Lens, Ocular Instruments, USA) was placed on the eye and a series of 70-90 non-overlapping shots was evenly carried out for 360 degrees in mid-trabecular meshwork. The laser energy was initially selected based on the intensity of angle pigmentation: 0.4 mJ for eyes with densely pigmented trabecular meshwork, 0.6 mJ for eyes with moderate pigmentation, and 0.8 mJ for lower grades of trabecular meshwork pigmentation, and increased by 0.1-

0.2 mJ until small "champagne bubbles" were observed and then decreased by 0.1 mJ. All patients were given 0.5% bethametasone drops 4 times daily for 7d after the procedure, and instructed to continue routine IOP-lowering medications. The medications were modified at follow-up visits according to IOP measurements as needed.

Statistical Analysis The sample size was calculated based on a difference of at least 1.3 mm Hg in IOP between two groups, standard deviation of 3 mm Hg and a confidence interval of 95%. Kolmogorov-Smirnov test and Q-Q plots were used to evaluate the normality of IOP measurements. To compare the two study groups, we used *t*-test, Mann-Whitney test, Chi-square and Fisher exact test, whenever appropriate. Log-rank test was used to compare survival curves. Univariate and multivariate Cox's regression analyses were used to assess factors associated with time to failure. All statistical analyses were performed with SPSS (version 21.0, Chicago, IL, USA). *P*-values less than 0.05 were considered statistically significant.

RESULTS

Forty-eight eyes of 46 patients (27 females and 19 males) who met the eligibility criteria were consecutively enrolled in the study. There were 27 patients with POAG and 19 patients with PXFG. In each group, one patient had both eyes included in the study. The baseline characteristics of the study subjects are described in Table 1. There were no significant differences between the two study groups in baseline characteristics except for gender (with a higher ratio of female in the POAG group), and IOP, which was higher in the PXFG group ($P=0.025$). In the visual fields the average mean deviation (MD) was -2.88 (± 1.67) in the POAG and -3.1 (± 1.69) in the PXFG groups ($P=0.3$). The number of patients at each follow-up visit, and changes in IOP and number of medications from baseline in each study group are described in Tables 2 and 3.

The mean \pm SD IOP at baseline and the last visit was 22.9 \pm 3.7 and 18.0 \pm 3.9 mm Hg in the POAG group ($P=0.02$), and 25.7 \pm 4.4 and 21.0 \pm 6.6 mm Hg in the PXFG group ($P=0.47$), respectively. Mean number of IOP-lowering medications at baseline was 2.6 \pm 0.8 in the POAG group and 2.5 \pm 0.8 in the PXFG group, which decreased to 2.4 \pm 1.1 and increased to 2.7 \pm 0.6 at the last follow-up visit, respectively. The differences were not statistically significant in both groups ($P=0.16$, 0.57). On Kaplan-Meier survival analysis, the success rate was 75.0% in the POAG group compared to 94.1% in the PXFG group ($P=0.08$; Log-rank test) at 6mo, and 29.1% in the POAG group and 25.0% in the PXFG group at 12mo ($P=0.9$; Log-rank test; Figure 1). The median time to failure was 6mo in both groups. The percentage of IOP reduction was statistically significantly ($P=0.02$) in the PXFG group during the first 6mo of follow-up (Table 2) that might be related to higher baseline IOP in PXFG group (Figure 2).

Variables	Total	POAG	PXFG	$\bar{x} \pm s, n (\%)$
No. of eyes	48	28	20	
No. of patients	46	27	19	
Age (a)	64.0±9.0	62.2±8.9	68.6±7.5	0.2
Sex				
Male	19 (41.7)	6	13	0.01
Female	27 (58.3)	21	6	0.01
Laterality				
Right eye	20 (41.7)	13 (46.4)	7 (35.0)	
Left eye	28 (58.3)	15 (53.6)	13 (65.0)	
Diabetes mellitus				
No	35 (72.9)	20 (71.4)	15 (75)	
Yes	13 (27.1)	8 (28.6)	5 (25)	
Central corneal thickness	537±31	531.6±31.84	537.6±29.9	0.5
Cup to disc ratio	0.6±0.2	0.570±0.14	0.591±0.17	0.78
Baseline IOP (mm Hg)	24±4.2	22.9±3.7	25.7±4.4	0.025
Baseline number of medications	3.0±0.8	2.6±0.8	2.5±0.8	0.84
Baseline MD (dB)	-3.0 ±1.67	-2.88±1.67	-3.1±1.69	0.3

POAG: Primary open angle glaucoma; PXFG: Pseudoexfoliative glaucoma.

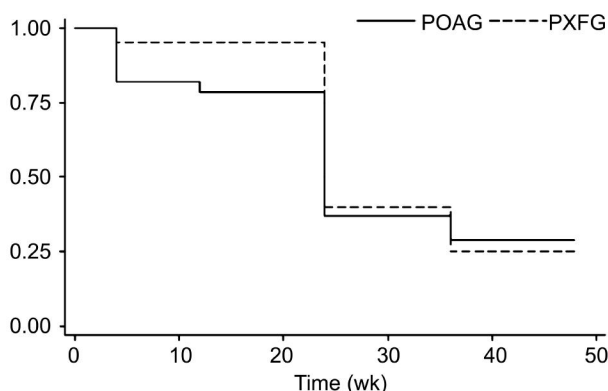


Figure 1 Kaplan–Meier survival curve analysis of event-free rates between the POAG and PXFG groups.

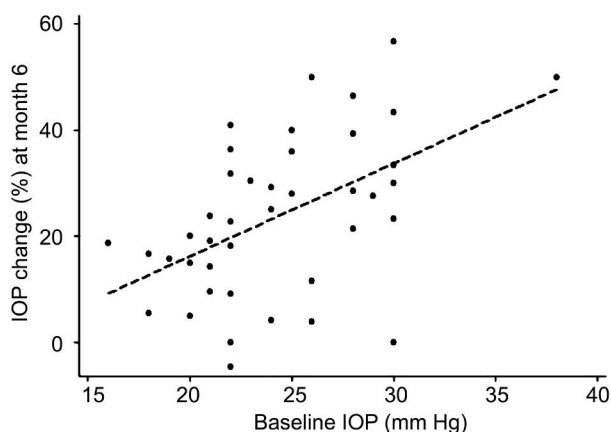


Figure 2 Graph showing the relationship between baseline IOP and changes of IOP at month 6 from baseline.

On univariate analyses, there was no statistically significant association between time to failure and the following factors: age, gender, glaucoma type, laterality, diabetes, central corneal thickness, cup to disc ratio, preoperative IOP and

number of medications, and the percentage of IOP reduction at postoperative week 1. The only observed complication was redness without intraocular inflammation in one eye in each group one day after SLT, which resolved spontaneously after 3d.

DISCUSSION

In this prospective comparative study, we investigated intermediate-term outcomes of 360-degree SLT in patients with mild to moderate POAG and PXFG with uncontrolled IOP despite maximally tolerated IOP-lowering medications. Although the absolute post-laser IOP measurements were similar in both study groups at all follow-up visits (except 1d), the percent IOP reduction was statistically significantly more pronounced in the PXFG group during the first 6mo of follow-up; this might be attributed to higher baseline IOP in the PXFG group. The mean number of IOP-lowering medications was statistically similar in both groups at baseline and SLT did not significantly reduce the number of medications at any of the follow-up visits in both groups. In a retrospective study, Kara *et al*^[10] similarly reported that the PXFG patients had significantly higher percentage of IOP reduction compared to POAG patients over one year of follow-up^[10]. They also found that SLT did not reduce the number of medications at any follow-up visits in both POAG and PXFG groups^[10]. In another prospective study, Ayala and Chen^[11] found that SLT reduced IOP by about 6-7 mm Hg in both POAG and PXFG patients one month after the procedure. Although the reduction was slightly better in their PXFG patients, the difference was not statistically significant^[11]. In our study, the efficacy of SLT decreased over time in both groups, and this was more pronounced in the PXFG group.

Table 2 IOP measurements in the study groups at different follow-up visits

Time	POAG	PXFG	$\bar{x} \pm s$ ¹ P
Baseline			
No. of eyes	28	20	
Value	22.9±3.7	25.7±4.4	0.02
1d			
No. of eyes	28	20	
Value	17.8±5.1	14.7±4.3	0.03
Change	-5.2±5.0	-11±5.3	<0.001
Change %	-22±20	-42±18	<0.001
1wk			
No. of eyes	23	20	
Value	19.8±3.6	18.7±4.2	0.33
Change	-3.2±3.2	-7.1±6.2	0.01
Change %	-13±13	-26±21	0.02
1mo			
No. of eyes	27	20	
Value	18.4±4.9	17.7±4.3	0.61
Change	-4.5±4.0	-7.9±5.6	0.02
Change %	-20±18	-30±19	0.04
3mo			
No. of eyes	28	20	
Value	18.1±2.7	17.0±3.4	0.22
Change	-4.8±3.0	-8.7±5.8	0.005
Change %	-20±11	-32±19	0.009
6mo			
No. of eyes	28	20	
Value	18.4±3.2	17.9±4.0	0.62
Change	-4.6±3.0	-7.8±5.5	0.01
Change %	-19±11	-29±17	0.02
9mo			
No. of eyes	23	17	
Value	17.9±3.3	16.3±1.0	0.96
Change	-4.9±3.5	-6.7±2.9	0.30
Change %	-21±13	-28±11	0.22
12mo			
No. of eyes	18	15	
Value	18.0±3.9	21.0±6.6	0.32
Change	-3.5±4.2	-4.7±9.3	0.75
Change %	-16±17	-16±32	0.9

POAG: Primary open angle glaucoma; PXFG: Pseudoexfoliative glaucoma. ¹t-test.

Table 3 Number of IOP-lowering medications in the study groups at different follow-up visits

Time	POAG	PXFG	$\bar{x} \pm s$ ¹ P
Baseline	2.6±0.8	2.5±0.8	0.84
1d	2.5±0.8	2.3±0.9	0.49
1wk	3.0±3.0	2.3±0.7	0.41
1mo	3.0±2.3	2.3±0.8	0.10
3mo	2.4±0.8	2.3±0.7	0.72
6mo	2.4±0.7	2.4±0.8	1.00
9mo	2.6±0.9	2.5±1.0	0.75
12mo	2.4±1.1	2.7±0.6	0.74

POAG: Primary open angle glaucoma; PXFG: Pseudoexfoliative glaucoma. ¹Mann-Whitney test.

Our results are similar to Gracner findings in PXFG patients^[12]. This study showed that SLT is an effective procedure for lowering IOP in PXFG and POAG eyes, although the effect seems to last less in PXFG eyes. In another study, Kara *et al*^[10] showed that SLT was more effective in reducing IOP in PXFG compared to POAG, and the effect did not decrease over one year of follow-up^[10]. They found that IOP significantly decreased by 4.4 ±2.1 mm Hg in the POAG group and by 6.1 ±3.6 mm Hg in the PXFG group at the 12-month follow up^[10].

A recent Meta-analysis showed that IOP reduction at 12mo post-SLT in 35 studies ranged from 6.9% to 35.9%^[13]. Although few studies have included other types of glaucoma than POAG, the efficacy of SLT appears to vary according to type of glaucoma^[8,14]. Overall, it seems that the IOP-lowering effect of SLT is less in patients with normal tension glaucoma (range: 14% to 16%), and relatively greater in PXFG patients (range: 11% to 32%)^[13,15-16]. The result of this Meta-analysis also showed that medications reduced IOP more than SLT (0.9 mm Hg more with multi therapy and 0.6 mm Hg more with mono-therapy); however, the difference was not statistically significant^[13]. The effect of SLT on reducing the number of medications varies in different studies. While some studies have shown that the number of medications did not change after SLT, others have reported that SLT reduced the number for medications^[13,15,17-18]. In our study, the mean number of IOP-lowering medications was statistically similar in both groups at baseline and SLT did not significantly reduce the number of medications at any of the follow-up visits in both groups. Lee *et al*^[19] studied different predictors of success/failure of SLT in 111 eyes (65 patients) with normal tension glaucoma and POAG^[19]. They reported that higher baseline IOP, use of carbonic anhydrase inhibitors, thinner retinal nerve fiber layer, and lower day 1 IOP were predictors of success^[19]. Their definition for success was IOP reduction ≥20%. Martow *et al*^[20] also found that the only predictive factor of SLT success was the pretreatment IOP and that glaucoma type including PXF was not a predictor^[20].

Tzimis *et al*^[21] showed that only baseline IOP was the most powerful variable in predicting outcome of SLT^[21]. In contrast, no baseline factors were found to be a predictor for failure after SLT in our study. This may be a factor of the fairly small sample size of our study since the sample size was determined for a different outcome measure.

The most common side effects of SLT are IOP spike, anterior chamber inflammation, eye pain or discomfort, photophobia, and conjunctival hyperemia^[13]. These side effects are generally transient and minor. The reported incidence of IOP spike varied from 0 to 62% in different studies^[13]. In studies where prophylactic IOP-lowering medications were used, the reported incidence was lower (between 0 and 29%)^[13]. In our

study, we did not observe any significant complications during and after the procedure although we did not use any prophylactic medication.

This study has some shortcomings. The fairly small number of patients in our study limited the power of our study for finding predictors of failure after SLT as mentioned above. Furthermore, the degree of angle pigmentation was not recorded in our study and therefore, the potential role of this variable could not be explored.

In conclusion, we found that 360-degree SLT is an effective and well-tolerated therapeutic modality in patients with POAG and PXFG. We found that SLT was more effective early in the postoperative period in patients with PXFG compared with patients with POAG. However, the efficacy of SLT decreased over time and this was more pronounced in PXFG patients.

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