

SELECTIVE LASER TRABECULOPLASTY – SHORT TERM EFFICACY AND SAFETY PROFILE IN OPEN ANGLE GLAUCOMA OR OCULAR HYPERTENSION TREATMENT

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Accepted: July 19, 2015

Abstract

Selective laser trabeculoplasty – medium term efficacy and safety profile in open angle glaucoma or ocular hypertension treatment: SLT effect in reducing the intraocular pressure (IOP) in patients with open angle glaucoma or ocular hypertension.

Material and method: 70 eyes from 70 patients were included in the study in 2014 (12 months); the established design for this research was prospective and interventional. Patients received indication for SLT treatment as initial procedure or as adjuvant method in reducing the intraocular pressure when insufficient control with topical medication was noted. A single laser procedure was performed on 360 degrees. The result was verified and compared with baseline values of IOP at 1 month, 3 months respectively. **Results:** IOP decreased at 1 month with 22.47% vs. baseline IOP and with 26.58% at 3 months. The IOP dynamics showed an additional 5.30% decrease between the intermediate and final values, with statistical significance for all the measured parameters ($p=0.001$).

Conclusion:SLT applied on 360 degrees in a single session represents a safe and efficient procedure. The IOP decrease is marked at 1 month, but the effect continues until later, at 3 months interval after treatment. The higher the initial IOP was, the greater effect SLT has in decreasing the IOP level. Most frequently LST helps control the IOP, but rarely allows reducing or eliminating the glaucoma medication.

Key words: glaucoma, slt, efficacy, safety

Glaucoma represents a progressive optical neuropathy that left untreated, leads to blindness. The IOP reduction seems to be the only solution to stop progression in glaucoma and to achieve this goal there are many therapeutic resources: eye drops, laser procedures or surgery [1].

For the glaucoma patient, the clinician will recommend either one of the above-mentioned treatment lines, or a combination between them. The therapeutic options may vary according to the glaucoma type, optic nerve status, symptoms, patient education or compliance [2]. Laser procedures, especially Argon based ones, have

been utilized in trabeculoplasties for over 30 years. After the introduction of a selective method of laser trabeculoplasty a new possibility in IOP decreasing aroused for the patients with glaucoma or ocular hypertension [3]. Selective laser trabeculoplasty (SLT) proved to be equally efficient in IOP reduction when compared to topical medicine or classic Argon laser trabeculoplasty-ALT [4, 5]. The major advantage is the re-treatment possibility because it doesn't produce any trabecular meshwork damage as in any ALT procedure, thus allowing a second laser intervention in cases with previously failed ALT. SLT has indications both for primary open angle glaucoma SLT, pseudoexfoliative/pigmentary or normal tension glaucoma and ocular hypertension or secondary afakic glaucoma. Moreover SLT has a special indication in non-compliant or topical therapy intolerant patients and also it doesn't influence any surgical procedure regarding its potential success. The safety profile includes a transitory inflammatory reaction, ocular pain or certain IOP spikes after treatment. SLT represents a safe and efficient method to lower the IOP in glaucoma patients or subjects with ocular hypertension having a clear indication for treatment due to high risk of glaucoma conversion [6].

Material and method

This interventional and prospective study lasted 12 months in 2014 (January-December). For each patient there were noted demographical data (age, sex) and a complete ophthalmological evaluation that included visual acuity (Snellen chart), IOP (Goldmannaplanotonometer), fundus examination with C/D ratio documentation (Volk lens - 78D) optic nerve status through an OCT exam (Cirrus 6.0 - Carl Zeiss Meditech), gonioscopy (dark room examination, undilated pupil). The anterior chamber angle was classified as open according to the Shaffer system (I-IV) and pigmentation was graded from 0 to 3. Additionally, the investigators performed ultrasonic pachymetry, computerized perimetry (Humphrey perimeter HFA II, SITA-Standard strategy, c24-2); number and type of topical medicine were mentioned for each patient. Pseudo exfoliation syndrome was documented (present/ absent) after mydriasis when anterior segment examination was performed.

IOP measurement and biomicroscopic examination were performed before procedure, after one month and after 3 months. Perimetric evaluation included at least 2 visual field examinations where the defects were constant and compatible with glaucoma damage.

Selective laser trabeculoplasty was indicated as initial treatment in glaucoma patients or in any case with ocular hypertension as adjuvant method in decreasing the intraocular pressure (IOP) when topical therapy was insufficient to control it.

SLT uses Nd-YAG laser with a 532 nm wave length, doubled in frequency. It uses a single pulse (time = 3 nsec) with a spot size around 400 μm . In our study the laser procedure was performed on 360 degrees (100 laser spots). Initially the technique included topical anesthetic (apraclonidine hydrochloride 0.5%) followed by placement of a Latina gonioscope on the anterior ocular surface. Initial laser pulse (Ellex - Ellex Medical, Pty Ltd, Australia) was 0.3 mJ, increasing then the power with 0,1mJ/pulse until a small gas bubble was visible in the anterior chamber; at this point the energy got diminished again in the same manner (0,1 mJ/pulse); the impacts were placed on 360 degrees. By the end of the procedure topical NSAIDs drops were instilled in the eye and same treatment was maintained for the next 4-7 days. Neither apraclonidine nor corticosteroids were used in this study related to the SLT procedure. IOP reduction was evaluated at 1 month and 3 months after SLT, along with the safety profile and efficacy check-up.

Population analysis: volunteer patients were enrolled in 2014, according to our inclusion criteria, after signing the informed consent. The present study respected the Helsinki declaration. We included 70 eyes from 70 patients with primary open angle glaucoma, pseudoexfoliative glaucoma or intraocular hypertension (where a clear indication for treatment was compulsory due to the high risk of glaucoma conversion). There were no retributions given to the subjects or any other compensation. The study was analyzed and proved by the Ethics Committee of "Gr.T. Popa" University of Medicine and Pharmacy - Iasi.

Inclusion criteria:

- POAG (primary open angle glaucoma), pseudoexfoliative glaucoma, high risk OHT (ocular hypertension);

- clear glaucoma diagnosis based on EGS (European Glaucoma Society) guidelines;
- gonioscopy: open anterior chamber angle > grade 2(Schaffer);

Exclusion criteria mentioned any case of non-compliant patient, anterior laser treatment (ALT/ SLT). Lens opacities that interfered with the ophthalmological examination and glaucoma complete evaluation excluded the patient from the study, along with the cases treated with systemic corticosteroids or immunosuppressive drugs, significant eye/general diseases, poor cooperation during laser procedure, any anatomic particularity that prohibited proper SLT treatment (shallow anterior chamber). Subjects priorly treated with pilocarpine prevented patient recruitment for this study due to a high risk of inflammatory reaction after the procedure.

Statistical analysis:

We used for the statistical analysis the SPSS13.0 software (Windows). Descriptive statistics described demographics and baseline parameters (including IOP). IOP dynamics (medium term evaluation) was defined as the mathematical differences between IOP level at baseline and IOP level measured at 3 months after treatment.

The authors evaluated IOP reduction with SLT after 1 month, 3 months respectively (IOP reduction in percentiles, statistical significance defined for $p < 0.05$ in the final model). Pearson correlation coefficient (r) was calculated to assess the relationship between different IOP parameters. Non-parametric data were analyzed using Kolmogorov-Smirnov distribution test. When calculating the difference between sample frequencies, Student Fisher test was used (t, df, p). Equality between variances was evaluated with Levene test.

Results were compared related to the baseline IOP level; also there were noted any side effects, incidents, accidents, complications during SLT procedure for a proper safety profile assessment. Variables that didn't reach the statistical significance level ($p < 0.05$), were excluded from the report.

Results

There were included 70 eyes from 70 patients. If the treatment was bilateral, only one

eye was chosen, randomly. All participants remained in the study throughout its entire duration.

Mean age was 64.16 ± 10.439 years, limits between 40-84 years. Mean baseline IOP level was 22.94 ± 4.19 mmHg, limits between 15-34 mmHg (Fig. 1).

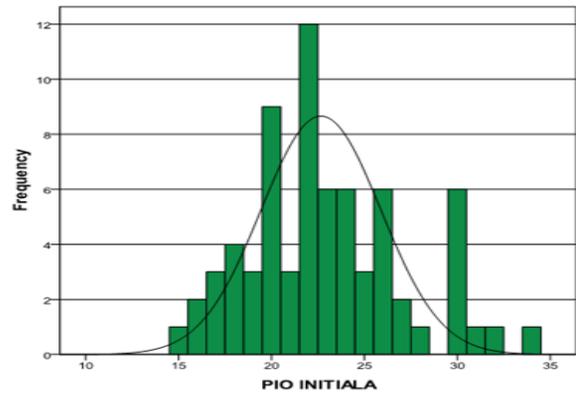


Fig. 1 IOP – baseline distribution values

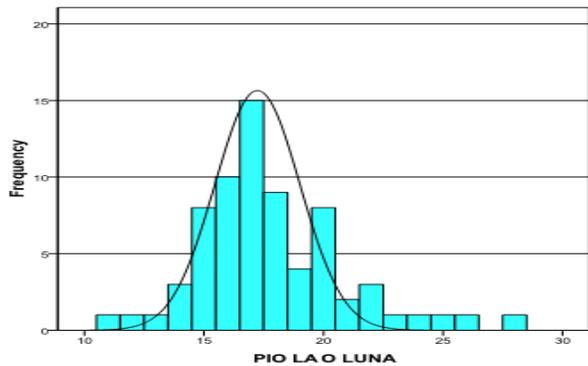


Fig. 2 IOP distribution values at 1 month after SLT

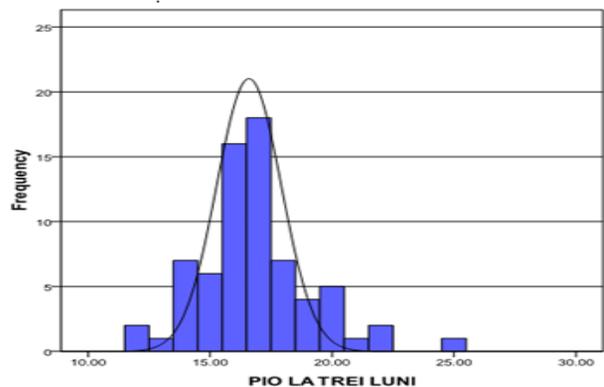
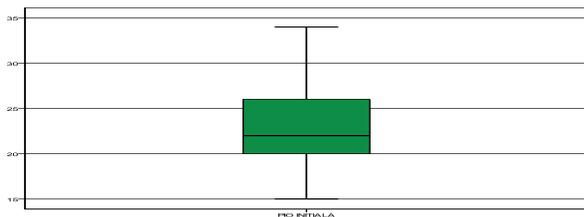


Fig. 3 IOP distribution values at 3 months after SLT

Patients' distribution within the study group showed 40 cases with primary open angle glaucoma (POAG), 20 cases with pseudoexfoliative glaucoma (PXG) and 10 cases with ocular hypertension (OHT). Each patient had a single SLT procedure, applied on 360 degrees. Before the procedure, each patient received at least one type IOP lowering topical medication.

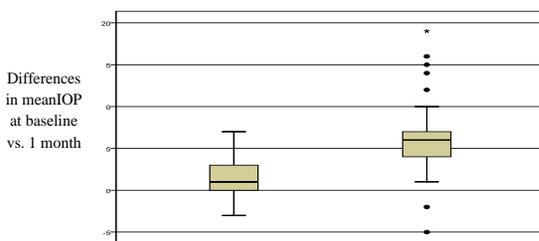
IOP reduction after SLT at 1 month interval after the procedure was statistically significant, with mean values of 17.79 +/- 3.088 mmHg (Fig. 2). 3 months later after SLT the mean IOP was 16.84 +/- 2.301 mmHg (Fig. 3). The IOP lowering effect was 22.47% at 1 month and 26.58% at 3 months when compared to baseline levels.

Procedure safety was noted in both visits (no pain, neither IOP spikes or signs of inflammation), while proven efficacy (IOP reduction) was mostly noted after one month (Fig. 4-5); later the SLT effect continued to be "active" and lower the IOP compared to baseline, but the hypotensive effect was not as much noted as after the first month follow-up (Fig. 6).

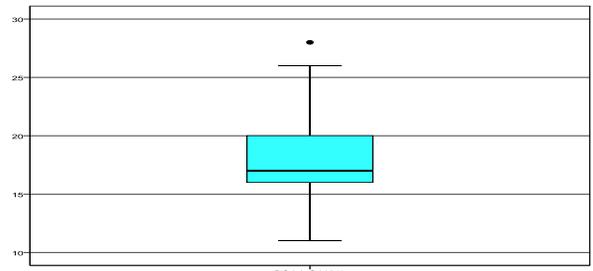


IOP - baseline
 Mean=22.94 mmHg
 SD=4.191 mmHg
 N=70

Fig. 4 Mean IOP - baseline

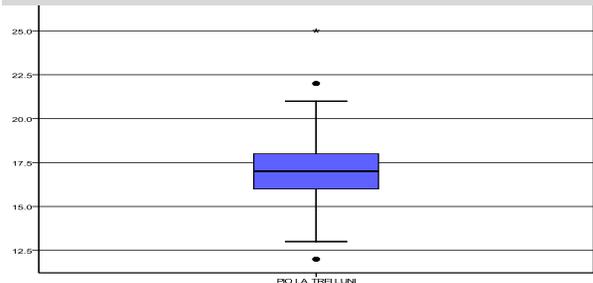


IOP < 19 mmHg IOP > 19 mmHg



IOP - 1 month
 Mean=17.79 mmHg
 SD=3.088 mmHg
 N=70

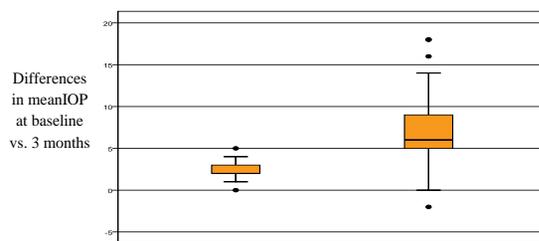
Fig. 5 Mean IOP - 1 month after SLT



IOP - 3 months
 Mean=16.84 mmHg
 SD=2.301 mmHg
 N=70

Fig. 6 Mean IOP - 3 months after SLT

Statistically, the Student Fisher test detected a negative correlation between the analyzed parameters (IOP level at baseline versus measured IOP/1 month or at 3 months after SLT), which clinically could be translated into a high practical importance: the higher IOP level was at baseline, the greater was the laser effect in IOP reduction; moreover the IOP dynamics maintained the same course both at 1 month and 3 months interval (Fig. 7).



IOP < 19 mmHg IOP > 19 mmHg

t	df	p
-3,797	68	.000

Pearson correlation = 0.378

p = 0.001

t	df	p
-3,860	68	.000

Pearson correlation = 0.558

p = 0.001

Fig. 7 Differences between mean IOP values at baseline compared to 1 month and 3 months

SLT efficacy was defined for a maximum IOP of 19 mmHg obtained after the procedure.

Percentile distribution in IOP reduction after the procedure was: 25% decrease with 2 mmHg, 50% with 5 mmHg, and 75% patients drop 7 mmHg from the IOP baseline level; at 3 months interval the same tendency in IOP dynamics was recorded, thus 25% subjects drop 3 mmHg, 50% - 5 mmHg and for 75% patients there was a 8.25 mmHg PIO reduction when compared to baseline. Overall the SLT procedure efficacy for 57 eyes (82%) showed that it was necessary to maintain the same topical glaucoma medication, whereas for 5 patients (7%) it was necessary to supplement the topical medication with an additional drug. In 3 eyes (4%) there was no need to add, but to reduce the number of topical medication and for 5 patients (7%) no topical medication was needed after trabeculoplasty at the 3 months visit.

In percent, the IOP reduction magnitude between baseline and the 1 month visit was 22.47%, while at 3 months there was an IOP decrease of 26.58%; between visits the intermediate IOP reduction value was 5.30% (p<0.05). Safety in this procedure was recorded after the visits by checking if any ocular inflammation, pain, vision decrease, tearing occurred. None of the above mentioned issues occurred in this study.

Discussion

SLT efficacy in open angle glaucoma was earlier described in many studies in ophthalmology literature, but the conclusion widely accepted is that its effect decreases in time (3). Glaucoma Laser Trial [3,4] shows that in 5 years, 32% from the subjects treated with ALT had still an acceptable level of IOP control, with no other methods to decrease the intraocular pressure. Smaller studies conclude

that SLT efficacy is similar to ALT (IOP decreased between 12.1-39.9% vs. baseline) [7-11], but the effect is shorter in time and decreases rapidly on the way [6]. Latina et al. considered that in his experience and practice SLT was still successful at 5 years follow up (50-60%) [1].

Clement et al. (SLT/MED study) reported in 2012 that SLT efficacy, if applied on 360 degrees and compared to prostaglandin analogues (latanoprost) is comparable (82% vs. 90%) after 12 months. Of course, the therapeutic response differed from case to case, but for both methods a drop of more than 20% from the baseline IOP level could be considered efficient [12]. Similarly, McIlraith et al. finds that IOP was reduced equally when used either PGA (prostaglandin analogues) or SLT (83% vs. 84% patients) at 12 months [13].

Theories responsible for losing the SLT effect in time recollected no changes in the trabecular meshwork histology and architecture, offering thus the possibility of re-treatment, which is in complete opposition to the ALT mechanism that produces actual burns in the trabeculum, with no possibility of re-treatment. Different methods of applying the SLT impacts include either 2 sessions, each performed on 180 degrees, or a single session applied on 360 degrees. Hong demonstrated in one of his studies that SLT efficacy at 5 years is higher when applied in sequences, on 180 degrees versus a single sequence on 360 degrees(6). Still, Nagar et al. proved that the most effective SLT regimen was on 360 degrees, in a single laser session [14].

One of the determinant factors responsible for a greater IOP reduction after SLT could be a higher level in the IOP baseline levels [15-16], fact also confirmed by this study.

Conclusion

The present study shows that SLT represents a safe and efficient procedure for

mid-term control of IOP (3 months). Additionally, laser treatment (trabeculoplasty) in open angle glaucoma or ocular hypertension could successfully be considered as alternative to topical medication, mostly when thinking costs or compliance.

IOP reduction after SLT was significant at 1 month, but the hypotensive effect continued until later, at 3 months, although not in the same impressive manner. Moreover there was found a negative correlation between the initial IOP level (baseline) and the quantitative aspect of the IOP drop (the higher IOP at baseline was, the greater the reduction was after SLT).

Knowing the fact that most patients (85%) maintained the same topical medication in our study, we can conclude that SLT *enhances* IOP control, but rarely manages to cut off the patient from medication (7%) and seldom reduces the number of topical active agents (7%) which concurred with the existed and cited literature data [4]. It is also highly possible that the IOP reduction induced by SLT could also reduce the amplitude of IOP fluctuation during 24 hours (glaucoma progression element).

The authors intend to extend the follow up period, increase the number of subjects for having a better view on IOP dynamics and changes in SLT treated patients. In a small prospective data, recent literature data show that after 30 months the SLT failure reaches 16% in POAG and 22% in PXG [17].

Also it would be interesting to establish whether there is a statistical significant relationship between the total energy delivered by SLT and the amount of IOP reduction for a correct and efficient treatment.

In conclusion, SLT applied in a single regimen, on 360 degrees, offers around 25% IOP reduction, both at 1 month and 3 months follow-up interval. The higher the IOP baseline level is, the greater the reduction proves to be. The procedure appears safe as no moderate or severe side effects were reported. There is still a need to confirm the present results with longer studies with larger number of patients in order to properly place the SLT in the armamentarium used to treat open angle glaucoma.

Contributors: AC and AP were involved in manuscript preparation, design and execution of the study, also in data collection process, statistical analysis and manuscript writing. DC was involved in all the steps and mentored the other authors.

Competing/ financial interest: none.

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