The Assesment of Intraocular Pressure-Lowering Effect of Micropulse Laser Trabeculoplasty in Primary Open-Angle and Pseudoexfoliative Glaucoma

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ABSTRACT

Purpose: To determine the efficacy and reliability of micropulse laser trabeculoplasty (MLT) procedure in primary open-angle (POAG) and pseudoexfoliative glaucoma (PXG).

Materials and Methods: The medical records of 125 eyes of 125 glaucoma patients having uncontrolled high intraocular pressure (IOP) despite using topical anti-glaucomatous eye drops were included the study. Of all patients, 64 patients had POAG and 61 patients had PXG. MLT was applied to all cases with the aim of reaching the target IOP. The IOP were measured at 1st hour, 1st day, 1st, 3rd, 6th, and 12th months following MLT with Goldmann applanation tonometry. Those of measurements were compared to the baseline IOP measurements.

Results: The mean baseline IOPs was 22.4±1 mm Hg in eyes with POAG and was 22.5±2 mm Hg in eyes with PXG. The mean IOPs were significantly decreased in all follow-up sessions compared to baseline pre-laser values in both the POAG and PXG groups ($p<0.001$ for all sessions in both POAG and PXG patients). The success rate of the MLT procedure at the end of 12th moths, in terms of decresing IOP within the normal limit, was 68.8% in POAG and was 85.2% in PXG. Only one patient had developed a mild anterior chamber reaction after the procedure.

Conclusion: The lowering effect of the single-session MLT procedure on IOP in both POAG and PXG was more pronounced at the 1st week, and this effect continued at the 1st, 3rd, 6th and 12th months in both disease groups.

Keywords: Micropulse laser trabeculoplasty, pseudoexfoliative glaucoma, open-angle glaucoma.

INTRODUCTION

Different types of treatment modalities including topical anti-glaucomatous medications, penetrating and non-penetrating surgical procedures and laser therapies are available in the management of glaucoma disease. The first treatment option to control increased intraocular pressure (IOP) levels is to administrating topical anti-glaucoma medications. However, monotherapy or polytherapy with topical agents may fail to reduce intraocular pressure (IOP) within the targeted levels.[1,2] Ocular adverse reactions and systemic side effects of topical agents lead to diminished compliance of patients that is essential to control loss of retinal nerve fibers, deterioration of visual fields and decreasing visual acuity in glaucoma disease.[3]

Laser procedures can be considered an alternative method for those patients to control IOP levels before surgical intervention. The procedures consisting of argon laser trabeculoplasty (ALT), selective laser trabeculoplasty (SLT) and micropulse laser trabeculoplasty (MLT) can be applied as adjunct to medical therapies or initial treatment option for glaucoma.[4] Recently, MLT has been encouraged to replace ALT and SLT procedures due to less scarring formation on trabecular meshwork, corneal endothelial damage and pigment dispersion on endothelium.[3,5] The MLT also enables effective treatment by using subthreshold and pulsed laser energy in trabecular tissue. The accumulation of pseudoexfoliation materials causes hyperpigmentation on the trabecular tissue where the effect area of MLT; therefore the MLT provides a theoretical advantage over other laser therapies by eliminating pigmented cells in trabecular meshwork.[4,6]

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The purpose of the present study was to evaluate the IOP-lowering effect of MLT through consecutive sessions in patients with POAG and PXG.

MATERIALS AND METHODS

Study Design

This retrospective study was conducted between June 2017 and January 2020 at the Harran University Medical Faculty Ophthalmology Department. Informed consent was obtained from the each participant before the ophthalmological examination, and any measurements were performed. The study was approved by the Harran University Medical Faculty Research Ethical Committee (26/03/2020-E.14403) and was conducted in accordance with the Declaration of Helsinki.

Participants and examination

This study includes 125 eyes of 125 patients who are being followed in ophthalmology department. The records of 64 eyes of 64 patients with bilateral primary open-angle glaucoma (POAG) and 61 eyes of 61 patients with bilateral pseudoexfoliative glaucoma (PXG) were compiled from the patient's file.

Patients having increased IOP (>21 mmHg) with the normal anterior chamber depth , open-angle on gonioscopy (Schafer grade >2), glaucomatous visual field defect and optic nerve head retinal nerve fiber loss defined as POAG, and in addition to those findings, patients having exfoliation material on the anterior part of the crystalline lense and in the irido-corneal angle defined as PXG.

The inclusion criteria of patients were having a difficulty in compliance with topical administration, eyes with progressive nerve fiber loss and visual field defects despite using maximum anti-glaucomatous administration, patients developed any ocular or systemic side effects against the eye drops, the inadequate lowering effect of anti-glaucomatous agents on IOPs which were far from targeted values of IOP determined by international guidelines and patients having ≤ 25 mmHg IOP with maximum anti-glaucomatous medications.[7,8] The eye having severe visual field defects, worse visual detoriation and higher uncontrolled IOP was selected in each pair of eyes for the study.

Patients having an IOP > 25 mm Hg, while they have been using maximum treatment were referred to surgical operations in order to control the IOP levels were excluded from the study, likewise Kontić M.[7] The patients with history of uveitis, intraocular inflammation, a blunt trauma, undergone a laser trabeculoplasty procedures or an intraocular surgery and having a closed angle on gonioscopy, neovascularization on irido-corneal angle and corneal pathologies preventing complete visualization of angle were excluded from the study, as well.

Prior to MLT procedure, anterior segment and fundus examinations were performed using a slit-lamp biomicroscope, the IOP was measured using a Goldmann applanation tonometer, central corneal thickness was measured using ultrasonic biometry Pac-Scan 300p (Sonomed® Escalon, NY). The visual field of eyes was tested by using Standard Swedish Interactive Thresholding Algorithm (SITA)- standard 30-2 threshold strategy on the Humphrey Field Analyzer III (Carl Zeiss Meditec, Dublin, CA) with Goldmann size III stimulus on a 31.5 apostilb background intensity. Pattern standard deviations (PSD) and mean deviations (MD) were recorded. Peripapillary RNFL thicknesses were analyzed by Heidelberg Spectralis optical coherence tomography with volumetric scanning protocol using 3.4 mm circle scan size (Heidelberg Engineering, Heidelberg®, Germany). The anterior chamber angle was assessed with a Goldmann three-mirror goniolens in all patients. The degree of trabecular meshwork pigmentation (PTM) was recorded prior to laser application according to the international classification.[9]

Micropulse Laser Trabeculoplasty

The MLT was performed with a Supra Scan 577 nm micropulse yellow laser (Quantel Medical, Cedex, France). Topical proparacaine HCl 0.5% was used for local anesthesia before the laser application. The procedure was applied by the same ophthalmologist (MT). The same laser settings have been used at the beginning of procedure with 300 µm spot size diameter, a 15% duty cycle, and a duration of 300 ms. A laser goniolens with an integrated visible internal reference guide allowing the physician to deliver 10 laser shots per clock hour (Ocular Instruments, Bellevue, WA, USA). The laser was carefully focused on the anterior trabecular meshwork, and approximately 120 laser spots were evenly distributed around 360° a single session. Patients continued to receive the antiglaucoma treatment that was used prior to laser therapy.

Topical brimonidine tartrate 0.15% was administrated on each eye before the procedure and Dexamethasone 0.1% eye drops was prescribed four times daily for one week for one week for all patients.

Follow-up procedures

All patients were examined at 1 hour, 1 day, 1 week, and 1, 3, 6, and 12 months after MLT. Best-corrected visual acuity, split lamp biomicroscopy, the IOP measurements with Goldmann applanation tonometry, and retinal examination in dilated pupil were performed for each visit. The IOP was measured between at 09:00 and 12:00 a.m.

in order to minimize the diurnal variation.[10] The number of topical medication requirements was recorded. MLT complications such as pain, hyperemia, photophobia, anterior chamber inflammation, and sudden IOP elevation were recorded in each session. Increased IOP was defined as a rise of at least 5 mm Hg IOP after MLT. Cases in which IOP was reduced by 20% following MLT therapy were regarded as successful responses .[7]

Statistical Analysis

Statistical analysis was performed on IBM SPSS 15.0 software (SPSS Inc., Chicago, IL, USA). Normality of distribution was assessed using the Kolmogorov-Smirnov test. Normally distributed numerical variables were expressed as mean +/- standard deviation, and non-normally distributed numerical variables as median (min-max), while categorical variables were expressed as frequencies (percentage). Differences between two independent groups were analyzed using the independent samples t test for normally distributed numerical variables, the presence of a significant difference between two dependent measurements was assessed using the dependent t test, and relationships between categorical values were evaluated using Pearson's chi-square test and Fischer's exact test. p values <0.05 were regarded as statistically significant. The G*Power programme 3.1 version was used to determine the sample size of groups prior to the study. The power of the study with 64 participants including 0.05 type a error, 0.5 effect size was 80%.

RESULTS

The mean age was 57.3±7 years for POAG patients and was 56.16±5 years for patients with PXG. The characteristic of patients, the visual field and peripapillary optic nerve head parametere with 95% confidence interval were demonstrated in Table 1.

The mean initial IOP values before the MLT procedures was 22.41±1 mmHg in POAG patients and 22.52±2 mmHg in the PXG patients. The mean IOPs at 1 hour, 1 day, and 1,

Table 1: *Demographic characteristics and clinical features of patients with 95% Confidence interval for mean.*

	POAG	95% confidence interval		PXG	95% confidence interval	
		Lower Bound	Upper Bound		Lower Bound	Upper Bound
Sex (F/M)	29/35	-	-	28/33	-	-
Age, years	57.13±7.06	55.36	58.89	56.16±5.36	54.79	57.54
MD, dB	-2.46±1.29	-2.75	-1.91	-2.44±1.42	-4.17	-2.84
Mean IOP, mmHg	22.41±1.04	21.76	22.21	22.52±2.15	22.04	23.14
Mean c/d ratio	0.50±0.13	0.47	0.53	0.51±0.13	0.47	0.54
Mean RNLF, µm	96.44±6.84	94.73	98.15	95.08±14.82	86.77	94.77
Angle pigmentation	1.25±0.43	1.14	1.36	2.46±0.80	2.25	2.67

POAG= primary open-angle glaucoma; PXG = pseudoexfoliative glaucoma; MD= median deviation, c/d= cup/disc; RNFL= retinal nerve fiber layer.

Table 2: *Mean IOP values at baseline and different time points up to one year.*

	POAG	P1	PXG	P2	P3
Initial	22.41±1.035	-	22.52±2.15	-	0.698
1 hour	21.75±0.87	<0.001	21.72±1.82	<0.001	0.910
1 day	19.56±0.89	<0.001	19.00±1.38	<0.001	0.007
1 week	18.64±0.88	<0.001	17.08±1.02	<0.001	<0.001
1 month	18.30±0.77	<0.001	16.54±0.87	<0.001	<0.001
3 months	18.17±0.73	<0.001	16.30±0.78	<0.001	<0.001
6 months	18.16±0.80	<0.001	16.59±0.99	<0.001	<0.001
12 months	18.09±0.79	<0.001	16.95±1.18	<0.001	<0.001

- POAG= primary open-angle glaucoma; PXG = pseudoexfoliative glaucoma
- P1= Difference between initial and other measurements in the POAG group
- P2= Difference between initial and other measurements in the PXG group
- P3 = Difference in measurements between the POAG and PXG groups

3, 6, and 12 months were significantly reduced compared to pre-laser IOP measurements in both POAG and PXG patients ($p<0.001$ for all visits in POAG and PXG). Table 2 provides data about the mean IOP measurements compared to pre-laser values in each visit during the follow-up period and the mean IOP courses in patients with POAG and PXG are shown in Figure 1.

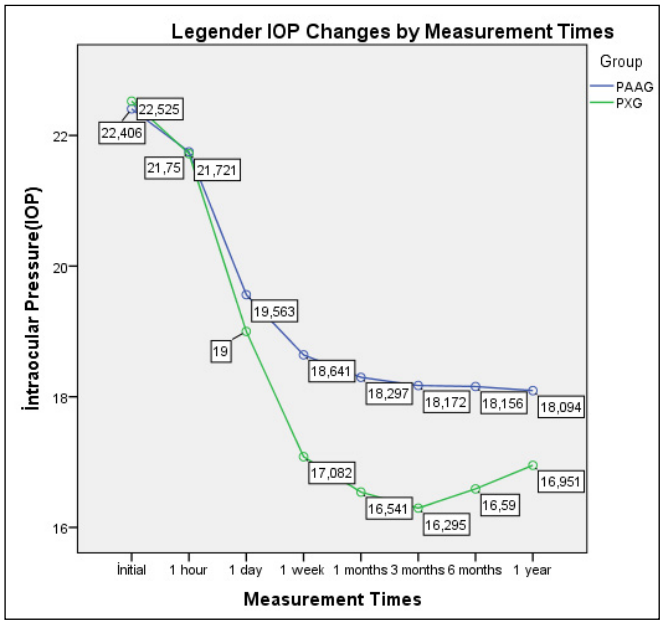

Figure 1: *Time-dependent IOP courses for POAG and PXG.*

The mean IOP decreased by 16.8 % for POAG and 24.2% for PXG predominantly at the end of 1st week of laser procedure. At the end of 12th month, the decrease in the mean IOP measurements was 4.32±0.02 mmHg in POAG patients (19.3%) and 5.57±0.02 mmHg PXG patients (24.7%) compared to initial values. At the end of 12th month, 68.8% of eyes with POAG and 85.2% of those with PXG were achieved to control within the target levels (Figure 2). Table 3 provides data regarding the percentage

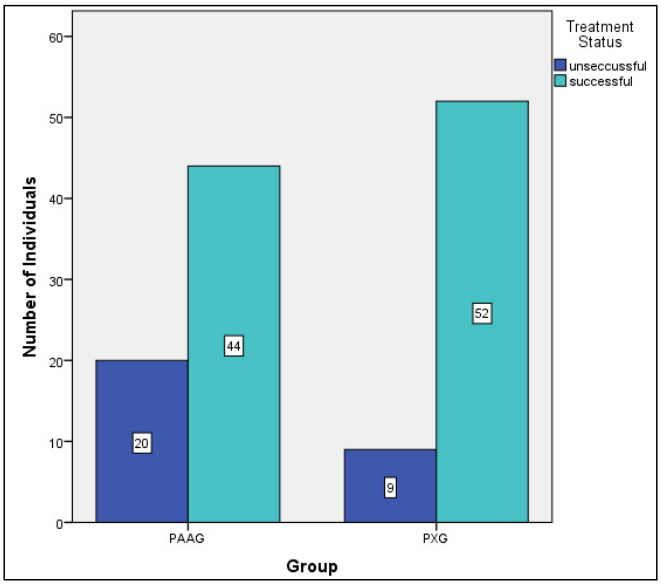

Figure 2: *Treatment status numbers in the groups.*

of reduction rates in the mean IOPs compared to initial measurements in POAG and PXG patients.

The mean number of drugs used before treatment was 2.8 in the POAG group and 2.9 in the PXG group. One year after treatment, the mean number of drugs was 2.7 in the POAG group and 2.7 in the PXG group.

During the follow up period, only one patient with PXG developed a mild anterior chamber reaction treated with topical dexamethasone 0.1% in four times/daily in one week.

DISCUSSION

In this study, the MLT procedure was found to be an effective method to control IOP levels for POAG and PXG. The MLT displayed its IOP-lowering effect more pronounced at the end of 1st week; However, the IOP-lowering effect of MLT nearly remained constant in the 1st,

Table 3: *Amount and percentage of reduction of intraocular pressure values at various time points relative to baseline.*

	POAG (mmHg)	%	PXG (mmHg)	%
Initial	22,41±1,035		22,52±2,15	
1 hour	0.66 ±0.01	% 2.9	0.80 ±0.02	% 3.6
1 day	2.85±0.02	% 12.7	3.52±0.02	% 15.6
1 week	3.77 ±0.02	% 16.8	5.44± 0.02	% 24.2
1 month	4.11 ±0.02	% 18.3	5.98 ±0.02	% 26.6
3 months	4.24±0.02	% 18.9	6.22±0.02	% 27.6
6 months	4.25±0.02	%19.0	5.93±0.02	% 26.3
1 year	4.32±0.02	% 19.3	5.57±0.02	% 24.7

POAG= primary open-angle glaucoma; PXG = pseudoexfoliative glaucoma; *Independent samples t test.

3rd, 6th, and 12th months for both POAG and PXG patients.

The reliability and effectiveness of MLT procedure in PXG remains unclear, while that is used for the treatment of open-angle glaucoma.[2,6] In the present study, the mean IOP was decreased by 24.7% of patients and 85.2% of eyes with PXG were within the normal limits at the end of following period. Rantala and Valimaki et al. stated a decrease by 17.4% in the mean IOP with MLT (180°-810nm) in POAG and PXG.[11] Makri et al. investigated the effect of MLT performed with 360° and 532 nm for one year period and they noted significantly lower IOP compared to baseline 1st, 3rd, 6th and 12th months after MLT. Decreases in IOP ≥ 20% compared to baseline were observed in 52.17% of eyes with PXG.[12,13] The success rate of procedure might demonstrate a fluctuation according to changing in laser parameters and the degree of trabecular meshwork where MTL is applied.

In the current study, the mean IOP was reduced by 19.3 %, furthermore 68.8% of eyes with POAG was benefited to MLT procedure at the end of 12th month. The effectiveness of MLT in open-angle glaucoma ranges between 12% and 21%.[14,15] In compliance with our study, Lee et al. reported a 19.5% decrease in the mean IOP levels in POAG patients and 75% of them benefited to MLT.[16] Hong et al. stated a 19.9% decrease in the mean IOP measurements following the procedure for POAG patients.[17] Fea et al. (810 nm) determined a mean 22.1% decrease in the IOP at 12 months with 180°-810 setting, with decreasing greater than 20% being achieved in 60% of patients.[18] Babaola et al. observed a 17.2% decrease in the IOP with same laser settings.[19] The MLT treatment, even at different laser parameter settings (577-877 nm) appears to be a useful method to decrease IOP in patients with POAG.

In the present study, the mean IOPs decreased by 3.52 mmHg, 5.93 mmHg and 5.57 mmHg on 1st day, 6th months and 12th months of the MLT procedure in patients with PXG, respectively; Furthermore, those of decreased by 2.85 mmHg, 4.25 mmHg and 4.32 mmHg on 1st day, 6th months and 12th months of the MLT procedure in patients with POAG.

Consistent with previous studies, the outcomes of the present study suggest that MLT may have a higher IOP-lowering effect and success rates in the PXG than POAG. The obstruction of trabecular meshwork by pigments and exfoliation materials is regarded as the most likely cause of increased IOP in PXG.[6,20,21] It is hypothesis that the pigmentation in the angle tends to be more severe in eyes with pseudoexfoliation. Laser used in MLT exerts a selective effect on the trabecular meshwork, and that energy released by laser is absorbed by melanin granules inside the trabeculum due to the fact that the IOP-lowering effect of MLT may be associated with the density of pigmentation.[22-24] In contrast to the view, Hirabayashi et al. reported that trabecular pigment density had no impact on success in SLT or MLT.[9] Gracner et al. reported a negative correlation between successful SLT and pigmentation of the trabecular meshwork.[25] In the present study, the significant reduce in the IOP level during the early period in PXG patients to may be caused by an intensive effect of micropulse laser on melanin in trabecular tissue, and increased fluid passage promoted by inflammation in trabecular meshwork. The gradually decrease in the effectiveness of MLT at the first week may be associated with redepositing PEX material preventing fluid passage in trabecular tissue.

The study has several limitations. Patients are using different topical antiglaucoma agents in order to achieve targeted IOP levels. Studies with larger sample sizes are needed to confirm these results.

CONCLUSION

Settings with 360° 577 nm yellow laser MLT was an effective and reliable therapeutic modality to control IOP in POAG and PXG patients. The favorable role of single-time MLT procedure on the decreasing IOP maintained its effect as long as 12 months of follow-up period in POAG and PXG. The MLT exhibited its IOP-lowering effect more markedly at the end of 1st week ; However, the lowering effect slightly remained constant in the 1st, 3rd, 6th, and 12th months for both POAG and PXG patients.

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