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ORIGINAL ARTICLE

Evaluation of selective laser trabeculoplasty effectiveness in cases with pseudoexfoliation glaucoma and ocular hypertension

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Abstract

Purpose: The aim of the study was to evaluate and compare the effectiveness of a single-session of 180° selective laser trabeculoplasty (SLT) as primary treatment in newly diagnosed cases with pseudoexfoliation glaucoma (PEG) and ocular hypertension (OHT).

Methods: Thirty-six eyes of 36 PEG cases (PEG-group) and 32 eyes of 32 OHT cases (OHT-group) were included in the study. Intraocular pressure (IOP), central corneal thickness (CCT), and endothelial cell count (ECC) were noted at baseline and post-SLT 3rd month. IOP reduction and success rates were detected. Inter and intragroup comparisons were made

Results: At baseline, age and gender distributions of groups were similar (P>0.05). Baseline IOP was 26.7±1.6 in PEG-group and 27.2±1.2 mmHg in OHT-group (P=0.648). In both groups, there was a significant decrease in IOP at 3rd month compared to baseline (P<0.001). IOP at 3rd month was 18.9±1.1 in PEG-group and 19.6±0.6 mmHg in OHT-group (P=0.507). IOP reduction rate (29.2% vs. 27.9%, P=0.807) and success rate (69.4% vs. 75%, P=0.846) were similar in PEG-group and OHT-group. Baseline CCT was 541.4±25.3 in PEG-group and 543.3±22.1 µm in OHT-group (P=0.581), while baseline ECC was 2496.5±231.8 and 2512.3±242.7 cells/mm^2, respectively (P=0.324). In groups, no significant change was detected in CCT and ECC values at 3rd month compared to baseline (P>0.05). IOP, CCT, and ECC values of groups were similar at 3rd month (P>0.05).

Conclusion: We found that single-session of 180° SLT was similarly effective in reducing the IOP in newly diagnosed PEG and OHT cases. We also detected that it was safe for cornea and could be used as primary treatment in newly diagnosed cases.

Keywords: Cornea; intraocular pressure; ocular hypertension; pseudoexfoliation glaucoma; selective laser trabeculoplasty.

The only proven and effective approach for the treatment of open-angle glaucoma (OAG) and ocular hypertension (OHT) remains decreasing the intraocular pressure (IOP) to avoid further progression.[1] Ocular hypotensive drugs can be used as initial treatment to reduce IOP.[2,3] However, long-term use of these medications may weaken the patient compliance. In addition, drug-related side effects may occur. Moreover, long-term use of these drugs may be a risk factor for failure of future surgeries.[2-4] Due to these reasons, selective laser trabeculoplasty (SLT) application can be an attractive option for reducing the IOP in cases with open angle and high IOP.[2,3,5,6] In SLT treatment,

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laser beam is focused on pigmented part of trabecular meshwork. Due to possible mechanical, histopathological, cellular, and biological effects of SLT in trabecular meshwork and Schlemm's canal, the outflow of aqueous humor is facilitated, and the ocular hypotensive effect occurs.[3,7,8]

Pseudoexfoliation glaucoma (PEG) is one of the most common types of secondary OAG, and it is progressive if left untreated.[4,5] High IOP has been suggested as a risk factor for progression from OHT to glaucoma.[2,5] Therefore, lowering the high IOP without optic nerve damage in OHT may reduce the risk of glaucoma development.[2,5] For this purpose, SLT treatment can be used to achieve the target IOP in both PEG patients and OHT cases.[5] On the other hand, due to the accumulation of pseudoexfoliation materials in the angle region and other ocular structures, the responses of PEG patients to SLT treatment may be different from the responses of OHT cases whose angle region and other ocular structures are relatively preserved.[9] For this reason, examining this condition in newly diagnosed PEG and OHT cases is a subject worth researching. The aim of this study was to evaluate and compare the effectiveness of a single-session of 180° SLT as primary treatment in newly diagnosed PEG and OHT cases.

Materials and Methods

This study was conducted with the approval of our hospital ethics committee (approval number: 2020/9-17), adhering to the ethical principles of the Declaration of Helsinki. Written consent form was received from all individuals. Subjects were informed about the study. Newly diagnosed, previously untreated 36 early-stage PEG cases (PEG-group) and 32 OHT cases (OHT-group) with a positive family history of glaucoma in a first-degree relative were included in the study. A single-session of 180° SLT was applied as primary treatment. When the SLT was applied bilaterally, only one eye of the patient was randomly selected. The cases who had previously used ocular hypotensive drugs or received SLT treatment, the patients with a previous history of ocular surgery or ocular trauma, the individuals having corneal pathology, the patients using topical or systemic drugs that could affect ocular structures, and the cases who did not come to hospital visits regularly were not included in the study.

The patients' age and gender characteristics, medical, personal, and family histories were recorded. Best-corrected visual acuity of the cases was noted. Anterior segment structures were evaluated by slit-lamp biomicroscopy (Topcon KR-1, Topcon Company, Tokyo, Japan). IOP level was measured with Goldmann applanation tonometer. Iridocorneal angle was assessed by three-mirror Goldmann contact lens. Optic nerve head (ONH) and retina of the individuals were examined after pupil dilation. Retinal nerve fiber layer (RNFL) thickness was evaluated using an optical coherence tomography (OCT) device (Heidelberg spectralis; Heidelberg engineering, Heidelberg, Germany). Visual field (VF) test was made using an automated perimetry device (Humphrey field analyzer, 242 SITA standard strategy; Carl Zeiss Meditec, California, USA). Central corneal thickness (CCT) was measured by optical biometry device (LenStar LS900, Haag-Streit Diagnostic, Switzerland). Central corneal endothelial cell count (ECC) was determined by a Topcon noncontact specular microscopy device (Topcon SP-2000P, Tokyo, Japan). All measurements were made by the same researcher (HÖ) in a masked fashion between 10.00 and 12.00 a.m. The mean of three measurements was used for analyses.

PEG was diagnosed as follows: (a) IOP >21 mmHg by Goldmann applanation tonometry; (b) open anterior chamber angle on gonioscopy; (c) glaucomatous ONH appearance on fundoscopy, presence of RNFL changes on OCT and/or presence of glaucomatous VF defect on automated perimetry; and (d) presence of pseudoexfoliation material on ocular structures such as anterior lens capsule, pupillary margin or anterior chamber angle with the slit-lamp examination and gonioscopy.[5,10,11] OHT was diagnosed as follows: (a) IOP >21 mmHg by Goldmann applanation tonometry; (b) open anterior chamber angle on gonioscopy; and (c) normal ONH appearance on fundoscopy, presence of normal RNFL on OCT and/or normal VF on automated perimetry.[5,12] SLT application was performed by the same researcher (BÖ) under topical anesthesia (proparacaine HCl 0.5%), using a Ritch trabeculoplasty lens. SLT device (Lightmed SeLecTor Deux) was used for SLT treatment. Fifty laser shots were applied to the lower 180° angle area in a single session, with a power of 0.7–0.9 mJ. Energy level was adjusted according to microbubble observation. No topical anti-inflammatory medication was given after SLT. Individuals were observed in the hospital for 3 h after the laser for possible complications. IOP reduction rate was determined with a formula "IOP reduction rate (%) = ([baseline IOP – post-SLT IOP] × 100)/baseline IOP". The success of SLT treatment was defined as ≥20% IOP reduction from baseline IOP without the need for further intervention.[13] The success rate was calculated with a formula "success rate (%) = (number of successful cases × 100)/total case number". IOP, CCT, and ECC values of the groups were noted at baseline (pre-SLT)

and post-SLT 3rd month. Inter and intragroup comparisons were made for all parameters.

Statistical Analysis

Statistical Package for the Social Sciences version 22.0 (IBM Corp., Armonk, NY, USA) was used for the statistical analysis. Before beginning the study, power analysis revealed a sample size of 30 with 80% statistical power and 0.05 alpha error. Descriptive characteristics were shown as mean±standard deviation (minimum-maximum) values. Categorical variables were presented with percentage. The suitability of variables to normal distribution was evaluated with Kolmogorov–Smirnov test. Chi-square test was used for analysis of categorical variables. Independent sample t-test was used to compare two independent groups, while paired sample t-test was used to compare two dependent groups. $P < 0.05$ was thought statistically significant.

Results

In this study, there were 36 cases in PEG-group and 32 cases in OHT-group (P=0.729). At baseline, age (P=0.763) and gender (P=0.895) distributions of the groups were similar. Baseline IOP was 26.7±1.6 mmHg in PEG-group and 27.2±1.2 mmHg in OHT-group. Baseline CCT was 541.4±25.3 µm in PEG-group and 543.3±22.1 µm in OHT-group, while baseline ECC was 2496.5±231.8 cells/mm^2 and 2512.3±242.7 cells/mm^2, respectively. At baseline, IOP (P=0.648), CCT (P=0.581) and ECC (P=0.324) values of the groups were similar. Clinical and ocular features of the groups before SLT are given in Table 1.

IOP value at post-SLT 3rd month was 18.9±1.1 mmHg in PEG-group and 19.6±0.6 mmHg in OHT-group. CCT value at post-SLT 3rd month was 539.2±24.6 µm in PEG-group and 543.1±26.0 µm in OHT-group, while post-SLT ECC value was 2493.6±243.5 cells/mm^2 and 2511.2±218.9 cells/mm^2, respectively. In both groups, there was a significant decrease in IOP at post-SLT 3rd month compared to baseline (P<0.001). At 3-month follow-up, IOP reduction rate (29.2% vs. 27.9%, P=0.807) and success rate (69.4% vs. 75%, P=0.846, respectively) of SLT were similar in PEG-group and OHT-group. In both groups, no significant change was detected in CCT and ECC values at post-SLT 3rd month compared to baseline (P>0.05). PEG and OHT groups' ocular features before and after SLT are shown in Table 2. At

Table 1. The comparison of clinical and ocular features of the groups before and after SLT

Clinical and ocular features	PEG group (n=36)	OHT group (n=32)	P-value
Age (years)	45.1±2.6 [42–48]	43.8±2.1 [40–47]	0.763[a]
Gender (Male/Female)	16/20	15/17	0.895[b]
Baseline IOP (mmHg)	26.7±1.6 [24–29]	27.2±1.2 [26–30]	0.648[a]
Baseline CCT (µm)	541.4±25.3 [508–572]	543.3±22.1 [514–573]	0.581[a]
Baseline ECC (cells/mm^2)	2496.5±231.8 [2064–2927]	2512.3±242.7 [2089–3106]	0.324[a]
Post-SLT IOP (mmHg)	18.9±1.1 [17–22]	19.6±0.6 [19–23]	0.507[a]
Post-SLT CCT (µm)	539.2±24.6 [506–571]	543.1±26.0 [512–573]	0.316[a]
Post-SLT ECC (cells/mm^2)	2493.6±243.5 [2058–2924]	2511.2±218.9 [2087–3105]	0.285[a]

Descriptive characteristics were shown as mean±standard deviation (minimum-maximum) values. SLT: Selective laser trabeculoplasty; PEG: Pseudoexfoliation glaucoma; OHT: Ocular hypertension; n: Number of cases; IOP: Intraocular pressure; CCT: Central corneal thickness; ECC: Endothelial cell count. [a]Independent sample t-test, [b]Chi-square test, P<0.05 statistically significant.

Table 2. PEG and OHT groups' ocular features before and after SLT

	PEG group (n=36)			OHT group (n=32)		
Ocular features	Baseline value	Post-SLT value	P	Baseline value	Post-SLT value	P
IOP (mmHg)	26.7±1.6 [24–29]	18.9±1.1 [17–22]	<0.001[a]	27.2±1.2 [26–30]	19.6±0.6 [19–23]	<0.001[a]
CCT (µm)	541.4±25.3 [508–572]	539.2±24.6 [506–571]	0.436[a]	543.3±22.1 [514–573]	543.1±26.0 [512–573]	0.802[a]
ECC (cells/mm^2)	2496.5±231.8 [2064–2927]	2493.6±243.5 [2058–2924]	0.792[a]	2512.3±242.7 [2089–3106]	2511.2±218.9 [2087–3105]	0.876[a]

Descriptive characteristics were shown as mean±standard deviation (minimum-maximum) values. PEG: Pseudoexfoliation glaucoma; OHT: Ocular hypertension; SLT: Selective laser trabeculoplasty; n: Number of cases; IOP: Intraocular pressure; CCT: Central corneal thickness, ECC: Endothelial cell count. [a]Paired sample t-test, P<0.05 statistically significant.

post-SLT 3rd month, IOP (P=0.507), CCT (P=0.316), and ECC (P=0.285) values of the groups were similar. Ocular features of the groups after SLT were given in Table 1. Transient conjunctival hyperemia was observed in 6 (16.7%) cases of PEG-group and 5 (15.6%) cases of OHT-group within 3 h after SLT treatment (P=0.852). In addition, a temporary IOP increase was detected in 2 (5.6%) cases of PEG-group. This pressure increase and conjunctival hyperemia returned to normal at post-SLT 1st day. Hyphema, anterior chamber reaction, and/or corneal edema did not develop in any case.

Discussion

In recent years, SLT has been increasingly used as adjuvant or primary therapy in reducing the IOP.[2,3,5,6,8] In literature, most of the studies related to SLT were investigated the SLT application as an adjuvant treatment choice, such as for OAG patients responding insufficiently to topical drugs or using medications irregularly, or for delaying the glaucoma surgery.[3,8,14] The number of studies evaluating the SLT as primary therapy was relatively low.[3,8,14] Gracner applied the 180° SLT as adjuvant treatment to uncontrolled PEG cases. The authors reported an IOP reduction of 22.9% at 3rd month in eyes with a baseline IOP of 23.6 mmHg. In these cases, they determined the success rate as 64% at 18-month follow-up.[15] In another study, IOP reduction rate was found to be 25% at 1st month after adjuvant SLT in PEG patients with a baseline IOP of 24.8 mmHg.[16] Kara et al. made adjuvant 180° SLT treatment to PEG eyes with 22.4 mmHg baseline IOP. The authors stated a significant IOP decrease of 27.7% at the end of the 3rd month. They detected 78.4% success rate after 1 year.[17]

Belitsky et al. applied the SLT as adjuvant therapy in some cases and as primary therapy in others. The authors examined all cases together in the same group. They showed a significant IOP reduction of 17.7% at 100th day after 180° SLT in PEG eyes with a baseline IOP of 24.2 mmHg.[18] Similarly, Soboka et al. evaluated the patients who underwent SLT as adjuvant or primary treatment together in the same group. The authors determined 21.1% IOP reduction rate at 3rd month in PEG eyes with a baseline IOP of 24.7 mmHg. They reported 72.7% success rate in these cases at 1-year follow-up.[19] On the other hand, Shazly et al. performed primary 180° SLT to PEG individuals with a baseline IOP of 25.5 mmHg. The authors found a significant IOP decrease of 26.3% at 3rd month after the laser. They stated 74% success rate at 13-month follow-up.[20] Consistent with the literature, in PEG-group, we detected 29.2% IOP reduction rate and 69.4% success rate at 3rd month after SLT.

In some previous studies, SLT was also applied to OHT cases.[8,13,19,21] Goyal et al. included OHT and OAG patients together in the same group. The authors reported 24% IOP reduction rate and 72% success rate at 1-month follow-up after primary 180° SLT.[21] In another study, the cases undergoing adjuvant or primary SLT were assessed together in the same group. IOP reduction rate in OHT eyes with a baseline IOP of 24.1 mmHg was found to be 19.1% at 3rd month.[19] Garg et al. determined a significant IOP decrease of 29.7% at 2nd month after primary SLT in OHT individuals with a baseline IOP of 26.5 mmHg. The authors showed 72.8% success rate in these cases at the end of the 3rd year.[13] Consistent with the literature, in OHT-group, we detected 27.9% IOP reduction rate and 75% success rate at 3rd month after SLT.

In previous comparison studies about the effects of SLT in literature, PEG patients were mostly compared with primary OAG (POAG) patients.[15-18,20] Kara et al. found significantly higher IOP reduction rate in PEG patients (27.7%) compared to POAG cases (18.9%) at 3rd month after adjuvant 180° SLT. The authors also stated a significantly higher success rate in PEG eyes (78.4%) compared to POAG eyes (54.2%) at the end of the 1st year. They considered that the tendency for heavier angle pigmentation in PEG patients resulted in higher SLT efficacy.[17] On the other hand, most of the previous comparison studies detected similar IOP reduction rate in PEG and POAG individuals after SLT treatment.[15,16,18,20] Gracner reported that IOP reduction rate in PEG eyes (22.9%) did not significantly differ from the rate in POAG eyes (26.8%) at 3rd month after adjuvant 180° SLT. The authors also showed that success rate in PEG patients (64%) was similar to the rate in POAG cases (78%) at 18-month follow-up.[15] In addition, Shazly et al. stated similar IOP reduction rate in PEG (26.3%) and POAG (25.9%) individuals at 3rd month after primary 180° SLT. They determined similar success rate in PEG (74%) and POAG (77%) cases at 13-month follow-up.[20] In the literature, there were also some studies comparing OHT and OAG patients about the effects of SLT.[13,19] Garg et al. found no significant difference between OHT (29.7%) and OAG (26.1%) eyes in terms of IOP decrease at 2nd month after SLT. The authors also detected similar success rate in OHT (72.8%) and mild OAG (64.3%) individuals at 36-month follow-up.[13] In a study evaluating the patients who underwent SLT as adjuvant or primary therapy together in the same group, no significant difference was reported between OHT (19.1%) and PEG (21.1%) eyes in terms of IOP reduction rate at 3rd month after SLT.[19] Similarly, we

also found no significant difference between PEG and OHT cases in terms of IOP reduction rate (29.2% vs. 27.9%) and success rate (69.4% vs. 75%) at 3rd month after primary 180° SLT. However, compared to Soboka's study mentioned above,[19] we determined higher IOP reduction rates in both PEG and OHT patients in our study. The reason for this may be that the entire population in our study consisted of the individuals to whom SLT was applied as primary therapy. In the literature, it was stated that in PEG cases, the accumulation of pseudoexfoliation material in the drainage angle might inhibit the adequate laser-tissue interaction in SLT application.[15,22] The inhibition of the adequate laser-tissue interaction might result in a relatively lower than expected response to SLT application in PEG patients, contrary to what was theoretically thought. The reason why we found similar IOP reduction and success rates in PEG and OHT eyes may be related to the mechanism mentioned above.

The laser beam applied in SLT passes through the cornea and reaches the trabecular meshwork. Laser may affect the corneal function by causing an increase in the production of inflammatory cytokines, matrix metalloproteinases, and free oxygen radicals in tissues.[3,8,23] Therefore, the effects of SLT on CCT and ECC were also examined in the literature.[6,24-26] Kanagaratnam and Ong determined a transient increase in CCT and a transient decrease in ECC at 20th min after adjuvant 180° SLT in OAG patients. The authors reported that these changes in CCT and ECC nearly returned to baseline values at 1st month after SLT. They attributed these changes to the transient endothelial cell dysfunction that might occur in early period due to laser effect, and the resulting temporary corneal edema.[24] Gedik and Gulseren included PAOG and OHT cases undergoing adjuvant 180° SLT together in the same group. The authors detected similar CCT and ECC values before and after SLT at 6-month follow-up.[25] Some other studies also stated that CCT and ECC did not differ during monthly follow-ups after adjuvant 180° SLT in POAG and PEG patients.[6,26] Similarly, in both groups, we found that CCT and ECC values did not change at 3-month follow-up after primary 180° SLT.

In the literature, some complications such as transient conjunctival hyperemia, temporary IOP increase, photophobia, headache, anterior chamber reaction, hyphema, corneal edema, and corneal abrasion were mentioned after SLT.[3,8] In the previous studies, transient conjunctival hyperemia was reported as 9–24.5%,[6,27,28] while temporary IOP elevation was stated as 2.9–16% at 1st h after 180° SLT.[6,22,29] Consistent with the literature, in our study, transient conjunctival hyperemia was observed in 16.2% of all cases, while temporary IOP increase was detected in 3% of all cases within 3 h after SLT treatment. Transient conjunctival hyperemia may be associated with local irritant effects of the trabeculoplasty lens and the preservatives of gels used at the interface, while temporary IOP elevation may be related to the inflammation occurring in the early period.[3,6,8] In our study, IOP elevation and conjunctival hyperemia returned to normal at 1st day. In addition, hyphema, anterior chamber reaction, and/or corneal edema did not develop in any case.

There were some limitations in this study. It had relatively small case number and follow-up period. Although the possibility of PEG occurrence increases with aging, the majority of elderly cases, in whom we detected PEG, had moderate or advanced-stage PEG requiring multiple interventions at the time of diagnosis. In addition, some of the newly-diagnosed elderly patients, in whom we detected PEG, had a previous history of ocular surgery, trauma, and/or systemic drug usage that might affect eye structures. Therefore, we could not include these cases in our study. In our study, the young age of the newly diagnosed, previously untreated, early-stage PEG patients may be due to the above reasons. Planning the future studies with larger case numbers and longer follow-up periods, in which other imaging methods are used in addition to pachymetry and specular microscopy for detecting the corneal changes, may provide more comprehensive data about the effects of primary SLT on newly diagnosed PEG and OHT patients.

Conclusion

We found that single-session of 180° SLT was similarly effective in reducing the IOP in newly-diagnosed PEG and OHT cases. We also detected that it was safe for cornea and could be used as primary treatment in newly diagnosed cases.

Ethics Committee Approval: This study was approved by Izmir Tepecik training and Research Hospitals Ethics Committee (23.07.2020 date; number 2020/9-17).

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