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Alterations in Biomechanical Properties of the Cornea After Selective Laser Trabeculoplasty

Selektif Laser Trabeküloplasti Tedavisi Sonrasında Korneanın Biyomekanik Özelliklerindeki Değişiklikler

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Abstract

Aim: To investigate changes in corneal biomechanical properties after selective laser trabeculoplasty (SLT).

Methods: Patients who have received SLT and underwent evaluation of corneal biomechanical properties by ocular response analyzer (ORA) in the preoperative period, one week, and one month after SLT were analyzed. Statistical analyzes were performed by examining pre- and post-SLT examination findings and ORA measurement values from the patients' files.

Results: The mean corneal compensated intraocular pressure (IOP) values were found to be significantly reduced one week and one month after the SLT than the values before the treatment (17.14±4.06 mmHg, and 16.91±3.55 mmHg, 19.96±5.00 mmHg; respectively; p=0.004). The mean corneal hysteresis (CH) measurements one week and one month after the SLT were not different from the preoperative measurements (9.89±2.17, 10.12±1.90, and 9.81±2.46, respectively) (p=0.662). The mean corneal resistance factor (CRF) measured prior to the SLT was higher than that in the first week and first month after SLT (11.09±2.08, 10.16±2.04 and 10.39±2.13, respectively) (p=0.002).

Conclusion: CH was found to be unchanged, while CRF was found to be decreased. The development of IOP reduction without statistically unaffected changes in CH and decreased CRF suggests that SLT does not have a significant side effect on the structural integrity of the cornea.

Keywords: Laser trabeculoplasty, cornea, corneal biomechanical properties, corneal hysteresis, corneal resistance factor

Öz

Amaç: Selektif laser trabeküloplasti (SLT) tedavisi sonrasında korneanın biyomekanik özelliklerinde meydana gelen değişiklikleri araştırmak.

Yöntemler: SLT tedavisi uygulanmış ve işlem öncesi, operasyon sonrası birinci hafta ve birinci ayda oküler cevap analizörü (OCA) ölçümleri yapılmış hastaların dosyaları tespit edildi. Hastaların dosyalarından SLT öncesi ve sonrasındaki muayene bulguları ve OCA ölçüm değerleri tespit edilerek istatistik analizleri yapıldı.

Bulgular: Korneal etkilerin düzeltildiği göz içi basınç (GİB) değerleri işlem sonrası birinci hafta ve birinci ayda işlem öncesi değerlere göre istatistiksel olarak anlamlı düzeyde azalmış bulundu (sırasıyla 17,14±4,06 mmHg, 16,91±3,55 mmHg, 19,96±5,00 mmHg; p=0,004). Ortalama korneal histerezis (KH) değerleri işlem öncesinde 9,81±2,46 bulundu. SLT sonrası ortalama KH değerleri birinci hafta ve birinci ayda istatistiksel olarak SLT öncesi ortalama değerlerden farklı değillerdi (sırasıyla 9,89±2,17; 10,12±1,90 ve 9,81±2,46; p=0,662). SLT öncesi ölçülen ortalama korneal rezistans faktör (KRF) değerleri ise işlem sonrasında birinci hafta ve birinci ayda ölçülen değerlerden istatistiksel olarak yüksek bulundu (sırasıyla 11,09±2,08; 10,16±2,04 ve 10,39±2,13; p=0,002).

Sonuç: Göz içi basınç (GİB) değerleri işlem öncesi değerlere göre birinci hafta ve birinci ayda KH değişmemişken KRF azalmıştı. GİB'deki düşüş ile KH'de istatistiksel olarak anlamlı etkilenme olmaması ve KRF'de azalma gelişmesi SLT'nin korneanın yapısal bütünlüğünde ciddi bir yan etki göstermediğini düşündürmektedir.

Anahtar Sözcükler: Laser trabeküloplasti, kornea, korneal biyomekanik özellikler, korneal histerezis, korneal rezistans faktör

Introduction

Glaucoma is a chronic disease in which the rate of progression can be slowed down by reducing intraocular pressure (IOP) with appropriate treatments, and the visual function and quality of life must be maintained at a reasonable cost (1). It is a difficult art to measure IOP

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and decrease IOP with different treatment methods (2,3). Goldmann applanation tonometry (GAT) remains the gold standard for IOP measurement, but new methods such as those using ocular response analyzer (ORA) are being developed for more accurate IOP measurements (4-6). In addition to anti-glaucoma eye drops used to reduce IOP, treatment methods such as selective laser trabeculoplasty have been used in recent years (3,7).

ORA evaluates the biomechanical properties of the cornea and attempts to reduce erroneous measurements due to cornea-related factors during IOP measurement. ORA evaluates corneal biomechanics by calculating corneal hysteresis (CH) and corneal resistance factor (CRF) accordingly. Basically, every substance having elasticity holds hysteresis, and Young's modulus is used for calculating its hysteresis (8,9). Hysteresis is found by calculating the amount of alterations in elasticity and viscosity of the cornea which is the cornea's ability to dampen and dissipate applied energy (10). When the air is applied to the cornea 400 times a second by the ORA device, a depression occurs and then the cornea returns to its original state. Two sets of IOP values are measured in the form of the depression and the transition to the old state. At this time, the energy that is emitted and absorbed in the cornea is analyzed as CH. CRF is mathematically calculated with the help of a constant coefficient.

Since the definition of selective laser trabeculoplasty (SLT) by Latina and Park (7), it has taken its place as an important method for the treatment of glaucoma disease all over the world. SLT is a preferred method because of minor side effects, easy feasibility, and temporary effectiveness in reducing IOP (11,12). There have been recent studies showing that SLT usually makes temporary and clinically negligible changes on corneal topography and corneal specular microscopy findings (13-16). In addition, anterior segment interventions are known to affect the cornea (17). However, as far as we can reach, there is not enough literature on the effects of SLT treatment on corneal biomechanics. In this retrospective study, we investigated the effects of SLT therapy on ORA findings in patients undergoing SLT therapy for primary open angle glaucoma (POAG) and ocular hypertension (OHT).

Methods

In this retrospective study, the files of patients who were followed in a tertiary training and research hospital glaucoma unit were scanned. The files of POAG and OHT patients, who were previously treated with SLT, were collected. These files were further inspected for revealing ORA measurements before and after the SLT treatment. This study protocol was approved by the Bağcılar Training and Research Hospital Ethics Committee (date: 24.11.2017, approval no: 2017.11.1.06.004.r1.014). All the authors worked according to the Helsinki declaration. Informed consent forms were provided.

Patient Selection

The files of 2458 patients followed in the glaucoma unit were reviewed. Since the ORA device was provided to our clinic in 2015, the records of patients who underwent SLT treatment between January 2015 and March 2016 were provided. Among these dates, 133 patients who received SLT treatment were identified.

Clinical characteristics and demographic data of patients and anamnesis of systemic disease, were recorded. Preoperative and postoperative examinations notes including best corrected visual acuity results, biomicroscopy and retinoscopy examination findings, and IOP measurement with GAT were checked (IOP_{gat}). Patients with a spherical equivalent above +5.00 diopter and below -5.00 diopter were not included in the study.

Selective Laser Trabeculoplasty Technique

An Ellex™ solo (Adelaide, Australia) device was used for SLT application. The treatment method that we routinely apply in our patients is as follows: one drop of sterile topical anesthetic eye drop (Alcaine™, proparacaine hydrochloride, 0.5%) is instilled into both eyes of the patients. Before the procedure, iridocorneal angles are examined again with gonioscopy and SLT therapy is applied between 90 and 100 shots until 360 degree of the trabecular meshwork is treated. The initial energy level is selected to be 0.8 mJ as described by Latina and Park (7) and is gradually increased to 1.3 mJ until the bubble formation at the angle is observed after laser application. After treatment, a non-steroidal anti-inflammatory drop is prescribed (Nevenac™, Nepafenac 1%, four drops per day). All patients continue to use antiglaucomatous drops initiated before SLT.

Ocular Response Analyzer Technique

Biomechanical properties of the cornea were evaluated with an ORA (Reichert Ophthalmic Instruments, Buffalo, New York, USA). Analysis of corneal biomechanical properties with ORA device has been described in detail in the literature (10,18). However, briefly, ORA sends a short stream of air to create a depression in the cornea. In this applanation process, as the shape of the cornea changes, an electro-optic sensor processes and examines two independent IOP values called P1 and P2. The value of CH is obtained by subtracting P2 from P1. CRF is detected with the help of another software registered in the main memory of the device. This software uses the following formula for CRF detection:

$CRF = P1 - kP2$

In the formula, k is a constant coefficient and is obtained after analysis of the relationship of P1 and P2 with central corneal thickness. As another important data, the ORA device outputs two different IOP measurement results. The first of these is IOP_g which is correlated with the IOP measured by GAT. The second result is called IOP_{cc}. It is the corrected IOP value of the corneal effects which is obtained as a result of the calculation of the linear combination of P1 and P2 (19). In addition, the device has software that analyzes the measurement quality and extracts it as data called wave score. Measurements with ORA device are performed at least three times in our clinic. For statistical reasons, the study included only eyes with the best wave scores at pre-SLT measurements. In addition, only patients with a wave score over six were included, taking into account the guideline of the ORA device. In our clinic, all ORA measurements are made before instilling any drops. The measurements were made between 10:00 and 16:00 with diurnal variation in mind.

Statistical Analysis

Analysis of the data was done with Statistical Package for the Social Sciences 21.0. The Kolmogorov-Smirnov test was used to analyze whether the data fit the normal distribution. The Bonferroni correction for the analysis of pre-SLT, first-week post-SLT, and first-month measurements was performed using the ANOVA test for repeated measures. Statistical significance level was taken as p=0.05.

Results

Only 22 of 133 patients had suitable pre-SLT, first-week and first-month post-SLT ORA measurements, and met all of the inclusion criteria, therefore, the information of these 22 patients was analyzed. Sixteen of the patients were female (72.7%) and six were male (27.3%). Nineteen of the patients were treated for POAG and three for OHT (86.4% and 13.6%, respectively). Normal distribution of IOP_{gat}, CH, CRF, IOP_{cc}, and IOP_g was analyzed by the Kolmogorov-Smirnov test and yielded p values over 0.05. The basic descriptive data for the studied patients are shown in Table 1.

Mean CH values did not show a statistically significant difference at pre-SLT, first week, and first month (p=0.662). The mean CRF values were significantly decreased in the first week and the first month after SLT treatment (p=0.002). IOP_{gat}, CH, CRF, IOP_{cc}, IOP_g and values of the patients before and after SLT are shown in Table 2.

Correlation analysis was performed between IOP_{gat}, CH and CRF (Table 3). There was a statistically significant positive correlation between mean IOP_{gat} and CRF. However, there was a statistically insignificant correlation between IOP_{gat} and CH.

Discussion

SLT is an important and effective treatment in patients with PAAG and OHT to reduce IOP (20). Previous investigations examining the efficacy of SLT therapy reported positive results with regard to this treatment method, although temporary and mild side effects, such as eye pain, conjunctivitis, corneal edema and blurred vision were observed (11,12,21). This study examined the early effects of SLT therapy on corneal biomechanics and found that CRF decreased statistically significantly in the early period (p=0.002).

Table 1. Basic descriptive data of patients

	n	Minimum	Maximum	Mean	Standard deviation
Age	22	27	74	53.32	12.144
C/D[a]	22	0.1	0.9	0.4545	0.21762
RNFL[b]	22	58	112	93.55	14.272
MD[c]	22	-18.1	0.7	-6.588	5.6017

C/D[a] : Cup/disk ratio, RNFL[b] : Retinal nerve fiber layer, [c]: Computerized visual field mean deviation value, MD: Mean deviation

Table 2. Corneal biomechanical parameters and intraocular $pressure_{gat}$ values before and after selective laser trabeculoplasty treatment

	n	Pre-SLT		Post-SLT 1st week		Post-SLT 1st month		p*
		Range	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD	
IOP_{gat} (mmHg)	22	12-28	19.64±4.293	10-22	16.18±3.157	10-29	16.91±3.951	0.000
CH	22	4.5-14.4	9.81±2.46	4.8-14.3	9.89±2.17	4.8-13.0	10.12±1.90	0.662
CRF	22	7.2-15.8	11.09±2.08	4.9-15.0	10.16±2.04	4.9-14.7	10.39±2.13	0.002
IOP_{cc} (mmHg)	22	13.9-33.4	19.96±5.00	12.6-30.6	17.14±4.06	11.8-25.4	16.91±3.55	0.004
IOP_g (mmHg)	22	13.8-28.4	19.39±4.11	11-26	16.20±3.54	11.6-25.4	16.24±3.78	0.000

SLT: Selective laser trabeculoplasty, IOP: Intraocular pressure, CH: Corneal hysteresis, CRF: Corneal resistance factor, GAT: Goldmann applanation tonometry SD: Standard deviation, *p: Significance level for repeated measures ANOVA test after Bonferroni correction

Table 3. Analysis of correlation between intraocular pressure$_{gat}$, corneal hysteresis and corneal resistance factor

		Pre SLT IOP$_{gat}$	IOP$_{gat}$ 1st week	IOP$_{gat}$ 1st month	Pre SLT CH	CH 1st week	CH 1st month	Pre SLT CRF	CRF 1st week	CRF 1st month
Pre SLT IOP$_{gat}$	r*	1	0.638	0.778	0.052	0.257	0.134	0.491	0.476	0.441
	p*		0.001	0.000	0.817	0.248	0.552	0.020	0.025	0.040
IOP$_{gat}$ 1st week	r*	0.638	1	0.700	0.240	0.154	0.163	0.578	0.498	0.322
	p*	0.001		0.000	0.283	0.494	0.469	0.005	0.018	0.144
IOP$_{gat}$ 1st month	r*	0.778	0.700	1	0.311	0.447	0.415	0.636	0.717	0.660
	p*	0.000	0.000		0.158	0.037	0.055	0.001	0.000	0.001
Pre SLT CH	r*	0.052	0.240	0.311	1	0.732	0.697	0.825	0.637	0.711
	p*	0.817	0.283	0.158		0.000	0.000	0.000	0.001	0.000
CH 1st week	r*	0.257	0.154	0.447	0.732	1	0.787	0.679	0.858	0.839
	p*	0.248	0.494	0.037	0.000		0.000	0.001	0.000	0.000
CH 1st month	r*	0.134	0.163	0.415	0.697	0.787	1	0.644	0.753	0.852
	p*	0.552	0.469	0.055	0.000	0.000		0.001	0.000	0.000
Pre SLT CRF	r*	0.491	0.578	0.636	0.825	0.679	0.644	1	0.805	0.831
	p*	0.020	0.005	0.001	0.000	0.001	0.001		0.000	0.000
CRF 1st week	r*	0.476	0.498	0.717	0.637	0.858	0.753	0.805	1	0.899
	p*	0.025	0.018	0.000	0.001	0.000	0.000	0.000		0.000
CRF 1st month	r*	0.441	0.322	0.660	0.711	0.839	0.852	0.831	0.899	1
	p*	0.040	0.144	0.001	0.000	0.000	0.000	0.000	0.000	

*r: Represents the Pearson's correlation coefficient, p: Represents the statistical significance level, Statistically significant values are shown in bold, SLT: Selective laser trabeculoplasty, IOP: Intraocular pressure, CH: Corneal hysteresis, CRF: Corneal resistance factor, GAT: Goldmann applanation tonometry

The effects of SLT on the cornea have been investigated by various investigators using different methods because of the cornea forming the upper wall of the iridocorneal angle, and conflicting results have been obtained (13-16,22).

The effects of SLT on the corneal endothelium have been investigated by some researchers using specular microscopy (13,14). In a study conducted by Ong et al. (13) and colleagues in 147 eyes of 94 patients, it has been reported that the number of endothelium decreased in the first month after SLT, although not statistically significantly (p=0.1), and the corneal dark spots were reversibly increased. These authors advised to be careful with SLT applications in patients with recurrent SLT and endothelium pigment accumulations. Another study by Lee et al. (14) and colleagues found that 111 eyes had a statistically significant decrease in endothelial counts at the first week after SLT but did not show a statistically significant decrease when compared to pretreatment values at the end of the first month. It has been noted by Lee et al. (14) that increased dark areas observed in the first week may be associated with decreased endothelial numbers. Both Ong et al. (13) and Lee et al. (14) have reported that inflammatory triggering effects of SLT may help explain the change in specular microscopy findings. This inflammatory effect has been associated with corneal edema and refractive changes in the literature (23). Although the above studies have indicated that there was a change in endothelial measurements after SLT, the effect of these changes on the corneal biomechanics may be limited due to the fact that in our retrospective study the CH did not change.

Scheimpflug corneal topography is an important method used to examine the cornea and anterior segment (24). In a study conducted by Guven Yilmaz et al. (16) and his colleagues, the central corneal thickness increased in the first month after SLT and the anterior chamber depth decreased, but in the third month, normalization was detected in both parameters. In addition, a study by Atalay et al. (15) and colleagues found a statistically significant but clinically insignificant decrease in central corneal thickness in the third month post-SLT. Both authors have proposed extensive investigations to investigate the effects of SLT on corneal topography. Corneal thickness is a factor that can affect CH and CRF (10,25). In normal and naive eyes, the viscous damping capacity of the cornea increases as the corneal thickness increases. This increase is eventually recorded as a high CH and CRF. However, transient increases in corneal thickness and changes in corneal biomechanical properties with reduced

CH and CRF values were observed after surgery, such as transparent corneal cataract surgery, which had effects on the number of endothelium and anterior chamber inflammation (26,27).

In a study of determining the effect of corneal biomechanics on the outcome of SLT therapy in medically uncontrolled glaucoma, CH and CRF together with pretreatment IOP values predicted a good modeling of the outcome of treatment (22). The data obtained by Hirneiß et al. (22) were obtained by using linear regression analysis of OCA measurements performed one year after SLT treatment in medically uncontrolled patients, as the authors have indicated. In a study conducted by Pillunat et al. (28) and colleagues on high pressure glaucoma and normal pressure glaucoma patients, the IOP_g and IOP_{cc} adjusted measurements of CH and CRF mean values were not statistically different before and after SLT. They also included patients with an uncomplicated cataract surgery, wave scores above 3.5, and reviewed measurements at least four weeks later (13.6±7.0 weeks). In our study, we planned to investigate the early effects of SLT therapy on ORA data and found that CH did not change in the early period, but CRF changed statistically significantly (p=0.662 and p=0.002, respectively). Our study differs from the study of Pillunat et al. (28) and colleagues in that there was a significant difference in CRF value probably due to early inflammation and IOP spikes after SLT. An insignificant correlation between mean IOP_{gat} and CH values after SLT may be due to the formula CH = P1-P2 used in the calculation of CH, although CH values were affected by corneal thickness. In addition, the use of corneal thickness in the calculation of CRF may have led to a decrease in CRF, which correlates positively with IOP_{gat} reduction, because of temporary changes in corneal thickness and structure early in the course of SLT therapy. The lack of significant correlation between decreased IOP_{gat} and CH, and the significant positive correlation of CRF with IOP_{gat} may have been obtained as a result of transient changes in the early post-SLT period, which was noted in previous studies examining the corneal endothelium and corneal structure.

Our study has important limitations to be emphasized. First, our study was not randomized and prospective. CH and CRF are known to have some changes with age (29). Although the average age of our patients was 53.3, the fact that PAAG has an increasing frequency with age restricts the results of our study to adaptation to different age groups.

Conclusion

SLT therapy maintains its important place in the treatment of PAAG and OHT. We believe that comprehensive, prospective, randomized trials investigating early and long-term effects of this treatment method on corneal biomechanics will be an important contribution to the treatment and follow-up plans in PAAG and OHT patients.

Authorship Contributions

Surgical and Medical Practices: K.A. Concept: K.A. Design: K.A. Data Collection or Processing: K.A., A.K. Analysis or Interpretation: K.A., A.K. Literature Search: K.A., A.K. Writing: K.A.

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