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A cross-sectional study investigating the effects of argon laser retinal photocoagulation on lens clarity and corneal endothelial cells

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Abstract

Background: The mechanism of argon laser retinal photocoagulation (ALRP) treatment is to apply thermal-induced retinal pigment epithelium damage. Light passes through the anterior optical segments of the eye to reach the retina. Lens densitometry is a noninvasive and quantitative measurement providing information about corneal and lens clarity.

Objectives: This study aimed to investigate whether laser light affects lens clarity and corneal endothelial cells.

Design: This was a prospective, cross-sectional study.

Methods: Lens densitometric (LD) analysis and specular microscopy were performed before, after, and 1 month after ALRP treatment, by an expert ophthalmologist, blinded to the medical status of the patients. LD analysis was performed using a Pentacam HR (Oculus, Wetzlar, Germany) and a Specular Microscope CEM-530 (Nidek, Japan) was used for endothelial cell analysis.

Results: The evaluation was made on 81 eyes of 41 patients, with a mean age of 54.46 ± 6.7 years. LD, after ALRP, was significantly more than before ALRP ($p < 0.001$). There was no statistically significant difference in LD, before ALRP, and 1 month after ALRP ($p = 0.262$). There was a statistically significant increase in LD after ALRP compared to before ALRP, but it decreased after 1 month. There was an increase in the coefficient of variance (CV) after ALRP compared to before ALRP but it was not statistically significant ($p = 0.188$). There was no statistically significant difference in CV between before ALRP and 1 month after ALRP ($p = 1.000$). There was no statistically significant difference in the cell density, the hexagonality percentage between before ALRP, after ALRP, and 1 month after ALRP ($p = 0.993$, and 0.863, respectively).

Conclusion: ALRP may affect the lens densitometry temporarily during the procedure. Thermal damage may be the reason for increased lens densitometry.

Keywords: Argon laser retinal photocoagulation, corneal endothelial cell analysis, lens densitometry, topography

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Introduction

Decreased oxygen levels in ischemic retinal tissues result in the growth of abnormal neovascularization of the retinal surface mediated by an increase in vascular endothelial growth factor (VEGF) level within the vitreous cavity.[1] Argon laser retinal photocoagulation (ALRP) is a commonly employed treatment modality for ischemic retinal disorders that has been demonstrated to reduce VEGF levels and neovascularization.[2] The mechanism of ALRP treatment is to apply thermal-induced retinal pigment epithelium damage.

Figure 1. The pentacam image of the lens densitometric analyses.

However, this procedure may induce various retinal complications such as scotoma in macular and peripheral retinal areas, leading to central and peripheral vision loss, reduced night vision, and increasing macular edema and destructive changes in the retinal anatomy secondary to scarring due to this thermal injury.[3–7]

To reach the retina, light must pass through the anterior optical segments of the eye. Biologically active laser wavelengths of less than 300 nm are predominantly absorbed by the cornea, while wavelengths greater than 300 nm pass through the cornea and ultimately reach the lens and retina.[8] In this process, thermal energy may affect these optical structures of the eye.[9–11] Thermal damage to the cornea and the lens may result in protein denaturation and loss of clarity.

Lens densitometry is a noninvasive and quantitative measurement providing information about corneal and lens clarity. It can be measured by the Pentacam HR (Oculus, Wetzlar, Germany) using a rotating Scheimpflug camera that gives images of the anterior segment of the eye from the anterior corneal surface to the posterior lens capsule. Specular microscopy provides information about corneal endothelial cells such as cell counts and morphological features.

This study aimed to use topography and specular microscopy to investigate whether laser light affects corneal endothelial cells and the clarity of the lens.

Methods

Study design

This prospective cross-sectional study was conducted in the Ophthalmology Clinic of Pamukkale University Education and Research Hospital between January 2019 and December 2019. Initially, 89 eyes of 45 patients were included. However, three patients were excluded from the study because they continued their treatment in another center after the first laser treatment, and one patient was excluded due to herpetic keratitis. Thus, 81 eyes of 41 patients treated with ALRP for proliferative diabetic retinopathy were included in the study. Patients with a history of previous ocular trauma, corneal infectious diseases, corneal ectasia, dry eye, corneal or intraocular surgery, glaucoma, or autoimmune disease were excluded from the study. Laser burns were performed between 200 and 500 µm in size with a duration time of 0.20 s according to disease and ischemia severity using a laser (IRIDEX, Mountain View, CA, USA) by the same ophthalmologist Selen Akbulut (SA). A field of one burn size was left between two burns.

Measurement

LD analysis was performed using Pentacam HR (Oculus, Wetzlar, Germany) automatically and noncontactly (Figure 1). Pentacam Nuclear Staging software in the Pentacam HR (Oculus, Wetzlar, Germany) was used for the lens densitometry (LD) measurements. Pentacam HR uses Scheimpflug Camera that rotates around the eye, from 0° to 180°

Table 1. Comparison of mean lens densitometry and endothelial cell analysis results of the patients.

Measurement time	Lens densitometry	Cell density mean ± standard deviation (cells/mm²)	Coefficient of variance mean ± standard deviation (%)	Hexagonality percentage mean (*N*) ± standard deviation (%)
Before ALRP	8.8 ± 0.53	2478 ± 235	31 ± 5	66 ± 6
After ALRP	9.13 ± 0.78	2477 ± 224	32 ± 5	66 ± 6
1 month after ALRP	8.8 ± 0.56	2477 ± 242	31 ± 5	66 ± 4
p	<0.001	0.99	0.18	0.86

ALRP, Argon laser retinal photocoagulation.

to capture images. All measurements were performed between the same time zones of the day in the morning.[10,11] To prevent the effect of accommodation, pupil dilatation with cycloplegia using 1% tropicamide was performed prior to measurement. Low quality images were excluded from evaluation.

Endothelial cell analysis was applied using a Specular Microscope CEM-530 (Nidek, Japan). All the measurements were taken before ALRP, after ALRP, and 1 month after ALRP treatment, to show the effect of the laser treatment. Three measurements were made for all evaluations and the average of these three measurements was taken into consideration. All evaluations were made by an expert ophthalmologist blinded to the medical status of the patients.

Statistical analysis

The data obtained in the study were analyzed using IBM SPSS Statistics software version 21 (IBM Corporation, Armonk, NY, USA). The normality of data was assessed using the Kolmogorov–Smirnov Test, and the homogeneity of variances was evaluated using the Levene Test. Repeated measures Analysis of variance (ANOVA) was used to compare LD, cell density (CD), coefficient of variance (CV), and hexagonality percentage (HP) of patients before ALRP, after ALRP, and at 1 month after ALRP treatment. Missing data were not included in the study. A value of $p < 0.05$ was accepted as statistically significant.

Sample size

G*Power package program was used to determine the sample size. Assuming we can achieve a medium effect size (dz = 0.5), a power analysis was performed before the study. Accordingly, when at least 44 eyes were included in the study, that would result in 90% power with 95% confidence level (5% type 1 error rate). We included 81 eyes in the present study. For before ALRP and after ALRP results, we had a large effect size (dz = 0.478) and with this result we reached 98.9% power with 95% confidence level.

Results

The current study focused on evaluating the effect of ALRP on corneal thickness and volume. The results showed a statistically significant increase in LD after ALRP compared to before ALRP, but it decreased at 1 month after the procedure. There was also an increase in CV after ALRP compared to before ALRP, but it was not statistically significant. However, there were no statistically significant differences in CD and HP between before ALRP, after ALRP, and 1 month after ALRP.

The evaluation was made of 81 eyes of 41 patients (27 females and 14 males). Mean age of the patients was 54.46 ± 6.7 years. LD, after ALRP, was significantly more than before ALRP ($p < 0.001$). There was no statistically significant difference between LD, before ALRP, and 1 month after ALRP ($p = 0.26$) (Table 1). There was a statistically significant increase in LD after ALRP compared to before ALRP, but it decreased at the 1 month. There was an increase in CV after ALRP compared to before ALRP, but it was not statistically significant ($p = 0.18$). There was no statistically significant difference in CV between before ALRP and 1 month after ALRP ($p = > 0.99$). There was no statistically significant difference in CD and HP between before ALRP, after ALRP, and 1 month after ALRP ($p = 0.99$, 0.86, respectively) (Table 1).

Discussion

There are studies highlighting the potential risks and side effects of ALRP treatment on the cornea. Some of them are case reports, including corneal burns[12,13] and corneal perforation,[14] both secondary to ALRP treatment. Also, corneal sensitivity changes have been investigated as a side-effect of ALRP on the cornea in the literature. Corneal burns and perforation are serious complications that can result from the use of laser therapy. Changes in corneal sensitivity and subbasal nerve plexus parameters may also occur as a result of thermal damage to the corneal sensory nerve. Additionally, ALRP may cause endothelial cell loss, although the degree of damage appears to be small and may not be significant in all cases.

Neira-Zalentein *et al.*[15] found that diabetic patients receiving ALRP treatment had aggravation in corneal sensitivity disturbances, which was thought to be a result of thermal damage from laser light on the corneal sensory nerve. Similarly, Bitirgen *et al.*[16] reported a decrease in subbasal nerve plexus parameters measured by confocal microscopy following ALRP, which suggests damage to corneal nerves. These findings highlight the potential adverse effects of ALRP treatment on corneal nerves and sensitivity. Pardos and Krachmer[17] investigated endothelial cell loss after ALRP and found that a small fraction of endothelial cells may be destroyed by the high dosage of an argon laser. In contrast, Mäkitie *et al.*[18] did not find any significant endothelial cell changes in diabetic patients treated with ALRP. In a study by Panek *et al.*,[19] the effect of argon laser iridotomy on the corneal thickness and corneal endothelial cell count was investigated and no statistically significant difference was determined between preoperative and postoperative measurements.

In a study, Kanagaratnam and Ong[20] investigated the effects of selective laser trabeculoplasty (SLT) and ALRP on the corneal endothelial cells and found a decrease in corneal endothelial CD recovery at the first month, after SLT. They found a minor increase in polymegathism after ALRP but they concluded that neither SLT nor ALRP has a clinically significant effect on the corneal endothelium. In an experimental study, Hirst *et al.*[21] found deposits on the corneal endothelium of monkey corneas by scanning electron microscopy after argon laser iridotomy and panretinal photocoagulation. Robin and Pollack[22] found a significant loss of central endothelial cells after argon laser iridotomy.

In our study, we observed a nonsignificant increase in CV, while CD and HP remained unaffected by ALRP treatment. Based on our findings, we conclude that ALRP does not significantly impact corneal endothelial cells.

Few studies in the literature have investigated the effect of ALRP on lens clarity, and no study could be found which had examined the effect of ALRP on lens clarity of adults. There are only studies reporting cataract development following argon laser treatment in infants.[23–25] The association between heat and development of cataracts has been investigated. In a study, authors concluded that thermal energy related to laser light may lead to cataracts.[26] Other studies in the literature have reported a potential association between increased temperature and the development of cataracts.[27,28] Additionally, studies have reported that high ambient temperatures increase the risk of nuclear cataract development.[28,29]

In the current study, we investigated the effect of ALRP on lens clarity and found a temporary increase in LD after the procedure, which may be a result of thermal injury. The potential causes of thermal damage include the iris, possible iris pigments on the surface of the lens, and burned retina absorbing laser energy. However, one limitation of this study is that the ocular surface temperature was not measured to demonstrate the thermal effect of ALRP on the anterior chamber. Furthermore, longer follow-up periods and larger sample sizes would be necessary to better understand the effects of ALRP on lens clarity.

In conclusion, to the best of our knowledge, there has been no previous study investigating the effect of ALRP treatment on lens clarity with densitometric analysis. The results suggest that ALRP treatment increases lens densitometry temporarily after the procedure, possibly due to thermal injury. However, endothelial cells were not affected by ALRP treatment. Further, long-term studies with larger sample sizes are needed to investigate the potential long-term effects of ALRP on the lens and to confirm these findings.

Declarations

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research

committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from all individual participants and their guardian included in the study prior to study initiation. The study was approved by the Institutional Review Board of Pamukkale University, School of Medicine with the approval number 60116787-020/59581 on 19/10/2018.

Consent for publication

Not Applicable.

Author contributions

Uğur Yılmaz: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Writing – original draft; Writing – review & editing.

Hüseyin Kaya: Data curation; Formal analysis; Investigation; Methodology.

Selen Akbulut: Data curation; Formal analysis; Investigation.

Yasin Durkal: Data curation; Formal analysis.

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Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author [U.Y.], upon reasonable request.

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