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The Effects of Smoking on Anterior Segment Parameters, Retinal Nerve Fiber Layer, and Pupillary Functions

Sigaranın Ön Segment Parametreleri, Retinal Sinir Lifi Tabakası ve Pupil Fonksiyonları Üzerine Etkileri

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Summary

Objectives: To evaluate the alterations in the anterior segment parameters, retinal nerve fiber layer, and pupillary functions in smokers.

Materials and Methods: In this case-control study, 45 eyes of 45 smokers and 45 eyes of 45 non-smoker control subjects were evaluated. All patients underwent measurement of anterior segment parameters with optical low coherence reflectometry (OLCR), mesopic and photopic pupillary diameter with an aberrometer device, retinal nerve fiber layer thickness with optical coherence tomography, and dry-eye assessment with Schirmer's test. The results were compared with independent t-test by SPSS 16.0 Inc., and a p-value lower than 0.05 was determined as significant.

Results: There was a significant difference between both groups in terms of mesopic pupil diameters that were measured with both OLCR and aberrometer device (p=0.03 and 0.02, respectively). Schirmer scores were also significantly decreased in smokers (p=0.001). The other measured parameters demonstrated no difference between smokers and non-smokers (p>0.05 for all).

Conclusion: Smoking may affect pupillary functions, especially the mesopic pupillary diameter, and may cause a deficiency in pupil response under dark circumstances. *(Turk J Ophthalmol 2014; 44: 11-4)*

Key Words: Autonomic neuropathy, dry eye, pupillary response, retinal nerve fiber thickness, smoking

Özet

Amaç: Sigara içenlerde ön segment parametreleri, retinal sinir lifi tabakası ve pupil fonksiyonlarını değerlendirmek.

Gereç ve Yöntem: Bu vaka-kontrol çalışmasında sigara içen 45 kişinin 45 gözü ve sigara içmeyen 45 kontrol bireyin 45 gözü değerlendirildi. Tüm hastalarda düşük koheranslı optik reflektometre (DKOR) ile ön segment parametreleri, aberometre cihazı ile mezopik ve fotopik pupil çapları, optik koherans tomografi ile retina sinir lifi kalınlığı ölçümleri ve Schirmer testi ile kuru göz değerlendirmesi yapıldı. Sonuçlar SPSS 16,0 kullanılarak bağımsız t-testi ile karşılaştırıldı ve 0,05'in altında p değeri anlamlı kabul edildi.

Bulgular: İki grup arasında hem DKOR hem de aberometre cihazı ile elde edilen mezopik pupil çapları arasında anlamlı fark vardı (sırasıyla p=0,003 ve 0,02). Schirmer değerleri de sigara içenlerde belirgin olarak azalmıştı (p=0,0001). Ölçülen diğer parametreler açısından sigara içen ve içmeyen grup arasında fark bulunmadı (hepsi için p>0,05).

Sonuç: Sigara içmek pupil fonsiyonları özellikle mezopik pupil çapını etkileyebilir ve karanlık ortamlarda pupil cevabında yetersizliğe yol açabilir. *(Turk J Ophthalmol 2014; 44: 11-4)*

Anahtar Kelimeler: Otonomik nöropati, kuru göz, pupil cevabı, retina sinir lifi tabakası, sigara

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Introduction

Smoking is related to various systemic and ocular diseases.[1] It is accepted as a risk factor for several ophthalmic diseases, particularly with regard to age-related macular degeneration (AMD), Graves'ophthalmopathy, cataract, and dry eye.[2-7]

When considering AMD, smoking has been accused for increased oxidative stress, the reduction of macular pigments, and an increased amount of inflammatory mediators that play a role in the pathogenesis of especially wet type AMD.[2,3] In Graves'ophthalmopathy, the exaggerated disease has been related to the increased sympathetic activity due to nicotine and benzpyrene, thus further stimulating the thyroid follicle cells and increasing thyroxine secretion. Increased amounts of inflammatory cytokines in smokers further accelerate the disease progression.[4] In addition, smokers are reported to have nuclear cataracts. Cataract formation in these subjects was related to the accumulation of reactive oxygen species and iron deposition in the lens. Moreover, the smoke itself was proposed to cause cataractogenesis by increasing the temperature of the lens.[5] Dry eye has also been investigated in smokers and has been reported to have deteriorating effects on the lipid layer of the precorneal tear film.[6,7]

Aside from cataract formation, the cornea can also be affected by smoking. Nishitsuka et al. have reported that smoking is related to increased corneal thickness, and Spoerl et al. proposed that cigarette smoking is negatively associated with keratokonus.[8,9]

In this study, we have evaluated the anterior segment parameters and pupillary functions in heavy smokers, with optical low coherence reflectometry and a corneal-topography-aberrometer device respectively. Dry eye evaluation with Schirmer's test was also performed in these patients, and the results were compared to those in age-and gender-matched healthy control subjects.

Materials and Methods

This comparative study adhered to the tenets of the Declaration of Helsinki, and the study protocol was approved by the local ethics committee. All patients gave their informed consent to take part in the study.

The study recruited 45 cigarette smokers (27 men, 18 women) who were smoking at least one pack per day for the last 5 years (heavy smokers) and 45 age-and gender-matched healthy control subjects (25 men, 20 women). The subjects in the smoker group were enrolled from the public health department, and among them were patients who have admitted to quitting smoking. Exclusion criteria included having any ocular or systemic disease, and history of intraocular surgery.

The patients were requested to abstain from smoking for 2 hours prior to examination and measurements. All patients underwent a complete ophthalmic examination including anterior segment evaluation with slit lamp biomicroscopy, intraocular pressure measurement with Goldmann applanation tonometer, and fundus examination.

The measurements of anterior segment parameters were performed with an OLCR (Lenstar LS 900, Haag-Streit, Switzerland). LenStar uses an 820 µm superluminescent diode with a Gaussian-shaped spectrum to provide high axial resolution, and the effect of time-domain interferometric or coherent superposition of light waves to measure ocular distances. In the examination with Lenstar, the patients were requested to sit, place their chin on the chin rest, and lean their forehead against the head-rest of the device. The patients were then asked to gaze into the round circle in front of them and not to blink during the measurement, which was recorded and interpreted. Each control subject that was measured by one examiner (technician) underwent a five serial measurement with Lenstar LS 900 and a mean value was gained. All the measurements were taken under native pupil conditions, without any medication under a dim illumination (3 lux).

Photopic and mesopic pupil measurements were also performed with a corneal topography-aberrometer device (OPD Scan, Nidek, Japan) for all cases. For measurements of the retinal nerve fiber layer (RNFL) thickness, an optical coherence tomography (Stratus OCT, Carl Zeiss Meditec, Inc., Germany) was used. After all these procedures, Schirmer's test was performed with topical anesthesia (propacaine HCl 5%). The right eye of each patient was chosen for statistical evaluation.

Statistical analysis was performed in SPSS for Windows 11.6 (SPSS Inc., Chicago, IL). The descriptive statistics were shown as mean ± standard deviation. For the comparison between smokers and non-smokers regarding central corneal thickness, pupil diameters, RNFL thickness and Schirmer's test scores, independent-t test was used; a p-value lower than 0.05 was accepted as statistically significant.

Results

The mean age of patients in the smoker group was 40.3±9.9 years (range 21-58 years), and the mean age of the non-smoker group was 39.7±12.2 years (range 19-58 years). In the smoker group, 27 (60%) were men and 18 (40%) were women. In the non-smoker group, there were 25 (55%) men and 20 (45%) women. Demographic data of the patients are summarized in Table 1.

Among the anterior segment parameters, mean pachymetry measurements in smokers were 544.5±39.9 µ, while it was measured as 533.2±26.1 µ in non-smokers. There was no statistically significant difference between these results (p=0.18).

Table 1. Demographic data of the patients

Patients	Smokers	Non-smokers
N	45	45
Age of patients (years)		
Mean±SD	40.3±9.9	39.7±12.2
Range	21-58	19-58
Gender (M/F)	27/18	25/20

Mesopic pupil diameter measured in a dimly-lighted room with OLCR was 5.87±0.85 mm and 6.29±1.00 mm in smokers and non-smokers, respectively. There was a significant difference in terms of mesopic pupil diameter between smokers and non-smokers (p=0.03). Smokers tended to have 0.42 mm smaller pupils or 0.42 mm less dilatation response in mesopic environment as compared to non-smokers.

The pupil diameter measurement was also performed by a corneal topography-aberrometer device (OPD Scan, Nidek, Japan) that could measure both photopic and mesopic pupil diameters. In the comparison of photopic pupil diameters, no significant difference was observed between smokers and non-smokers. The mesopic pupil diameter was 5.77±0.83 mm and 6.19±0.86 mm in smokers and non-smokers, respectively (p=0.02). Again, there was 0.42 mm difference between the two groups. The mean mesopic pupil diameter was smaller in smokers than in non-smokers.

The mean results of RNFL measurement by OCT were 103±10.7 µ and 100±8.86 µ in smokers and non-smokers, respectively. No significant difference was found for the RNFL thickness between the two groups (p=0.06).

The Schirmer's test results were significantly different among smokers and non-smokers (p=0.001). The scores were approximately 4.5 mm lower in smokers, with a mean value of 5.7±3.9 mm, which may be accepted within the limits of dry eye.

All the parameters that were compared between the two groups are summarized in Table 2.

Discussion

The effects of smoking on the anterior segment of the eye have been partially reviewed in literature. The increased rigidity, due to induced cross-linking by products of cigarette smoke such as nitrogen oxides, nitrite and formaldehyde, was proposed in the study of Hafezi.[10] The authors claimed that tobacco smoking represents a source of advanced glycosylation products (AGEs), similar to diabetes mellitus. Also, in the study of Spoerl et al.[9] smoking was found to be negatively associated with keratoconus due to increased cross-linking in the cornea.

The corneal thickness was reported as being increased in the presence of smoking in the Japanese population. Nishitsuka et al have evaluated the risk factors and determinants of corneal thickness in the Japanese population and concluded that impaired glucose tolerance, diabetes, obesity, and current smoking were associated with an increase in corneal thickness.[8] In our study, we evaluated the effects of smoking on some of the anterior segment parameters including corneal thickness. However, no significant difference was found between smokers and non-smokers in terms of central corneal thickness.

The most significant difference between smokers and non-smokers regarding the anterior segment parameters was the mesopic pupil diameter, when measured with both the Lenstar LS 900 and OPD Scan II. Smokers tend to have smaller pupils than non-smokers, while in darkness. This phenomenon is also reported as reduced dark-adapted pupil size in long-standing diabetics.[11] In diabetes, this deficient response was related to autonomic dysfunction, mainly in the sympathetic innervations of the iris sphincter. However, in diabetes, the photopic response

Table 2. Comparison of all measured parameters among smokers and non-smokers

Parameters	Smokers	Non-smokers	p
Pachymetry (Lenstar LS 900)			
Mean±SD (µ)	544.5±39.9	533.2±26.1	0.18
Range (µ)	457-621	476-592	
Pupil diameter (Lenstar LS 900)			
Mean±SD (mm)	5.87±0.85	6.29±1.00	0.03
Range (mm)	3.62-6.99	4.34-8.33	
Photopic pupil diameter (OPD Scan II)			
Mean±SD (mm)	3.95±0.86	4.15±0.73	0.25
Range (mm)	2.28-5.95	2.56-5.74	
Mesopic pupil diameter (OPD Scan II)			
Mean±SD (mm)	5.77±0.83	6.19±0.86	0.02
Range (mm)	3.84-6.99	4.26-8.00	
RNFL (Stratus OCT)			
Mean±SD (µ)	103±10.7	100±8.86	0.06
Range (µ)	75-127	80-123	
Schirmer's test			
Mean±SD (mm)	5.7±3.9	10.2±4.3	0.001

in the pupils is also decreased which was not observed in our study. The photopic pupil diameters were not significantly different between smokers and non-smokers.

Sobaci et al.[12] proposed that chronic smoking might dilate the pupil. The authors reported larger photopic pupil sizes in smokers and they associated this finding as a result of nicotine-induced autonomous neuropathy. In their study, the smoker patients were required to abstain from tobacco for 12-14 hours prior to measurements. In our study, the patients were told not to smoke only 2 hours before the assessment. This might explain the conflict of our results with the results of Sobaci et al. Therefore, our patients might have been still under the acute effects of smoking, considering their pupil diameter comparison.[13]

The deficiency of the pupil to dilate in darkness is hypothesized to be due to relatively sympathetic denervation of the iris and may be called as autonomic neuropathy.[14,15] The deficient mydriasis in darkness may be due to the increased rigidity of the iris, similar to the cornea, in smokers. Still, then the pupillary photopic response should also be affected.

The retinal vascular function is also impaired by smoking, and this is mostly related to an altered endothelial function in chronic smokers.[16] Moura et al.[17] have evaluated the RNFL thickness in three patients with tobacco-alcohol-induced toxic optic neuropathy and found increased RNFL thickness in some quadrants, although their findings were not concurrent with the visual field changes of the patients. We have evaluated the RNFL thickness by OCT in smokers and non-smokers. Although the smokers had thicker RNFL, the difference was not statistically significant.

Smoking causes several changes in the ocular surface including decreased tear break-up time, alterations in the lipid layer of the tear film, reduced basal secretion, reduced corneal and conjunctival sensitivity, reduced tear lysozyme concentration and it may precipitate the development of squamous metaplasia in the conjunctiva.[6,7] In this study, we have evaluated the basal tear secretion by performing Schirmer's test (with topical anesthesia). The smokers had reduced basal tear secretion with lower scores of Schirmer's testing, compared to non-smokers. This result was consistent with previous studies.

There were some limitations in our study. Firstly, we have not classified the precise amount of smoking within the smoker group, which may demonstrate the correlation between the amount of smoking and the observed changes in the measured parameters. The second limitation was the near-response which was not examined in either group. If the mechanism of the deficit in the pupil was similar to that in diabetes, the near-light dissociation should be observed. Also, in diabetes there are many studies on the denervation hypersensitivity.[18] We have not performed any pharmacological tests regarding this manner. The final limitation may be the absence of pharmacological dilatation of the pupil in both groups and subsequent comparison of the results. Again, this may indicate a reason of response deficit in darkness-the rigidity of the iris or sympathetic denervation?

Smokers have a reduced pupil dilatation in darkness, compared to non-smokers. This deficit may be due to an autonomic neuropathy, as in diabetes. Moreover, dry eye is clinically significant in smokers. Further studies are necessary to investigate the etiology of dark response deficit of the pupil.

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