Original Article

Cukurova Anestezi ve Cerrahi Bilimler Dergisi

From Smoke to Clarity: Evaluating Ocular Surface and Retinal Effects of Smoking and Cessation

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Abstract

Objective: To evaluate the impact of cigarette smoking on ocular surface parameters and inner retinal structure, and to explore the potential for reversibility following smoking cessation. **Material and Methods:** This cross-sectional study included 100 participants divided into four groups based on smoking status: Group 1 (non-smokers), Group 2 (current smokers <10 years), Group 3 (current smokers >10 years), and Group 4 (former smokers, >1 year cessation). All participants underwent detailed ophthalmic evaluation including tear film break-up time (TBUT), Schirmer test, Ocular Surface Disease Index (OSDI), meibography, noninvasive TBUT (NITBUT), and spectral-domain optical coherence tomography for ganglion cell complex (GCC) and retinal nerve fiber layer (RNFL) thickness. Correlations between daily cigarette consumption and ocular parameters were analyzed. **Results:** Current smokers (Groups 2 and 3) exhibited significantly lower TBUT, Schirmer, and NITBUT values, and higher OSDI scores compared to non-smokers (Group 1) and former smokers (Group 4) ($p < 0.01$). Meibomian gland loss was significantly elevated in current smokers, especially in Group 3. OCT analysis revealed thinner GCC and RNFL layers in chronic smokers ($p < 0.05$). Former smokers showed values closer to non-smokers, suggesting a possible improvement pattern. Among active smokers, daily cigarette intake negatively correlated with TBUT ($r = –0.41$, $p = 0.004$), Schirmer ($r = –0.35$, $p = 0.01$), GCC ($r = –0.38$, $p = 0.006$), and RNFL thickness ($r = –0.28$, $p = 0.045$). **Conclusion:** Chronic cigarette smoking is associated with significant ocular surface dysfunction and early retinal structural changes. These effects demonstrate a dose-dependent pattern and may be partially reversible upon cessation. Early screening and cessation counseling may mitigate long-term ocular damage in smokers.

Keywords: Dry eye; Meibomian glands; Retinal ganglion cells; Smoking; Tear film

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1. Introduction

Tobacco smoking remains one of the most preventable causes of morbidity and mortality worldwide, with over eight million deaths annually attributed to its direct and indirect effects[1]. Although smoking rates have declined in some high-income countries, the absolute number of smokers continues to rise globally due to population growth, particularly in low- and middle-income regions. Tobacco use exerts widespread harm beyond

the respiratory and cardiovascular systems, extending its effects to various organ systems through mechanisms such as oxidative stress, chronic inflammation, and vascular dysfunction[2]. In this context, the ocular system—despite its constant exposure to airborne toxins such as cigarette smoke—has received comparatively less attention. A better understanding of the ocular consequences of smoking may shed light on both local and systemic impacts of chronic tobacco exposure[2,3].

Increasing evidence has linked cigarette smoking to a range of ophthalmic disorders, including cataract formation, age-related macular degeneration, and ocular surface disease[4,5]. Chronic exposure to cigarette smoke has been shown to contribute to meibomian gland atrophy, orifice obstruction, and lipid layer abnormalities, ultimately destabilizing the tear film and exacerbating ocular surface pathology[6]. In addition to anterior segment effects, long-term smoking has also been associated with retinal structural changes. Optical coherence tomography (OCT) studies have reported significant thinning in the retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC), suggesting early subclinical neurodegenerative alterations likely due to oxidative damage, microvascular impairment, and mitochondrial dysfunction[7].

At the cellular level, cigarette smoke exposure has been shown to impair proteostasis and autophagy in human corneal epithelial cells, resulting in increased apoptosis, mitochondrial dysfunction, and accumulation of ubiquitinated protein aggregates[8]. These findings suggest that the ocular surface damage caused by tobacco smoke may extend beyond tear film disruption and inflammation to include deeper alterations in epithelial cell homeostasis.

Cigarette smoke is also a well-established modifiable risk factor in the development and progression of dry eye disease (DED). Tobacco-derived toxins negatively impact both the aqueous and lipid layers of the tear film, promoting excessive evaporation and triggering inflammatory damage to both the lacrimal and meibomian glands[9]. Nevertheless, data regarding the relationship between smoking intensity, duration, and the potential reversibility of ocular changes following cessation remain limited.

The present study aims to bridge this gap by comprehensively evaluating the effects of chronic tobacco exposure and cessation on key parameters of ocular surface health—such as tear film stability, meibomian gland morphology, and conjunctival hyperemia—as well as retinal nerve fiber layer and ganglion cell complex thickness. By stratifying participants based on smoking status and duration, this study seeks to elucidate the dose–response relationship between tobacco exposure and ocular alterations, and to determine whether smoking cessation confers measurable anatomical or functional recovery in ocular tissues.

2. Material and Methods

2.1. Study Design and Participants

This cross-sectional study included a total of 100 participants divided equally into four groups based on their smoking status and duration. Group 1 comprised non-smokers with no history of active or passive smoking. Group 2 included current smokers who had smoked for less than 10 years, while Group 3 consisted of current smokers with more than 10 years of smoking history. Group 4 included individuals who had quit smoking for at least one year. Each group included 25 subjects. Both eyes of each participant were included in the analysis and treated as independent observations.

Inclusion criteria were: age between 18–65 years and absence of systemic or ocular diseases that may interfere with ocular surface parameters. Exclusion criteria included contact lens use within the past three months, ocular surgery or trauma, current use of ocular or systemic medications affecting tear film, pregnancy, and breastfeeding. Ethical

approval was obtained from the Clinical Research Ethics Committee of a tertiary care hospital, and all participants provided written informed consent.

2.2. Ocular Surface Assessment

2.2.1. Tear Break-Up Time (TBUT)

TBUT was measured after instillation of one drop of 1% sodium fluorescein in the inferior conjunctival sac. Three measurements were taken per eye, and the mean value was recorded. TBUT less than 10 seconds was considered indicative of tear film instability[10].

2.2.2. Schirmer Test

Schirmer I test was performed without topical anesthesia using standard 5×35 mm filter paper strips placed at the lateral third of the lower eyelid margin. After five minutes with closed eyes, the wetting length was measured in millimeters. A value below 10 mm was accepted as reduced aqueous tear production[10].

2.2.3. Subjective Symptom Assessment: OSDI

All participants completed the Ocular Surface Disease Index (OSDI) questionnaire, a validated 12-item instrument evaluating dry eye symptoms and their impact on vision-related quality of life. Scores range from 0 to 100: 0–12 (normal), 13–22 (mild), 23–32 (moderate), ≥33 (severe dry eye)[10].

2.2.4. Meibography and Meibomian Gland Loss (MGL)

Meibomian glands were assessed using meibography acquired with the Sirius corneal topographer/tomographer (CSO, Florence, Italy). The extent of MG loss was calculated as the ratio of the dropout area to the total tarsal plate area, and analysis was performed using ImageJ software. Glands were scored from 0 to 3 per eyelid based on the Arita et al. classification[11].

2.2.5. Corneal Epithelial Thickness Measurement

Anterior segment OCT (Optovue RTVue-XR Avanti) was used to map corneal epithelial thickness across central (0–2 mm), paracentral (2–5 mm), midperipheral (5–7 mm), and peripheral (7–9 mm) zones. Thickness values were reported in micrometers (μm).

2.3. Posterior Segment Imaging: OCT-Based Neural Layer Assessment

Spectral-domain OCT (Optovue RTVue XR Avanti) was used to assess ganglion cell complex (GCC) and retinal nerve fiber layer (RNFL) thickness. GCC parameters included average, superior, and inferior thickness. RNFL measurements included average, superior, inferior, nasal, and temporal values. Functional loss volume (FLV) and global loss volume (GLV) parameters were also recorded.

2.4. Statistical Analysis

All statistical analyses were conducted using IBM SPSS Statistics version 26.0. The normality of continuous variables was assessed with the Shapiro–Wilk test. Comparisons among four groups were performed using one-way ANOVA with Tukey post hoc test. Categorical variables were compared using the chi-square test. In active smokers (Groups 2 and 3), correlations between daily cigarette consumption and ocular parameters were evaluated using Pearson correlation analysis. A p-value of <0.05 was considered statistically significant.

3. Results

A total of 100 participants (200 eyes) were evenly distributed across the four study groups. There was no statistically significant difference in mean age between groups

(p = 0.159), and sex distribution was also comparable (p = 0.140), ensuring demographic homogeneity (Table 1).

Table 1. Demographic characteristics of study participants

Group	Age Mean±SD (range)	Female	Male
Group 1 (Non-smokers)	45.52 ± 13.89 (18–65)	18	32
Group 2 (Smokers <10y)	45.44 ± 13.82 (18–64)	20	30
Group 3 (Smokers ≥10y)	45.88 ± 11.12 (18–65)	28	22
Group 4 (Former smokers)	46.08 ± 7.67 (35–65)	26	24
p-value	0.159*	0.140**	

** ANOVA; ** chi-square test. G1: non-smokers, G2: <10 years smokers, G3: ≥10 years smokers, G4: former smokers.*

3.1. Ocular Surface Parameters

TBUT and NITBUT values were significantly lower in Groups 2 and 3 compared to Group 1, with the most pronounced reductions in Group 3 (TBUT: G1–G3 p = 0.0037, G3–G4 p = 0.0056; NITBUT: G1–G3 p < 0.0001, G3–G4 p < 0.0001). Schirmer test values followed a similar pattern (all p < 0.001). OSDI scores were significantly higher in Group 3 than in Groups 1 and 4, indicating more severe subjective symptoms among chronic smokers. Former smokers (Group 4) showed comparable or better scores than non-smokers in all parameters, suggesting partial recovery. Meibomian gland loss (MGL) upper eyelid scores were significantly higher in Groups 2 and 3 compared to Group 1; only Group 3 showed significantly higher lower eyelid MGL scores compared to Group 4 (p = 0.0007) (Table 2).

Table 2. Comparison of tear film stability, ocular surface symptoms, and meibomian gland loss between study groups

Parameter	G1	G2	G3	G4	Overall p	G1-G2	G1-G3	G1-G4	G2-G3	G2-G4	G3-G4
TBUT (s)	8.41±2.08	6.80±2.11	6.64±2.04	8.44±2.34	0.0020	0.0090	0.0037	0.9689	0.7822	0.0124	0.0056
NITBUT (s)	12.8±2.1	7.1±1.9	6.2±2.0	11.9±2.2	<0.001	0.0012	<0.001	0.6254	0.2746	0.0009	<0.001
Schirmer (mm)	16.76±4.54	10.48±2.71	7.84±2.13	17.90±5.31	<0.001	<0.001	<0.001	0.4175	0.0004	<0.0001	<0.0001
OSDI score	13.38±3.59	16.55±4.66	16.77±3.75	11.14±4.09	<0.001	0.0098	0.0020	0.0447	0.8521	0.0001	<0.001
MGL Upper	1.80±0.96	2.84±1.34	2.36±0.95	1.60±0.79	0.0002	0.0027	0.0435	0.4246	0.1501	0.0002	0.0035
MGL Lower	1.91±1.33	2.59±1.18	2.51±1.11	1.41±1.04	0.0014	0.0606	0.0897	0.1477	0.7969	0.0005	0.0007

Data are mean ± SD. TBUT: tear break-up time; NITBUT: noninvasive TBUT; OSDI: Ocular Surface Disease Index; MGL: meibomian gland loss. G1: non-smokers, G2: <10y smokers, G3: ≥10y smokers, G4: former smokers. One-way ANOVA + Tukey post hoc.

There were statistically significant differences in corneal epithelial thickness across all quadrants between groups (all p < 0.0001). The thinnest epithelial profiles were observed in Group 3, with significantly lower values in every region. No significant differences were observed between Groups 1 and 4 across most zones, supporting epithelial remodeling after quitting (Table 3).

Table 3. Comparison of corneal epithelial thickness (μm) in different quadrants among study groups

Zone (μm)	G1	G2	G3	G4	Overall p	G1-G2	G1-G3	G1-G4	G2-G3	G2-G4	G3-G4
Central	52.86±1.52	52.55±1.60	51.30±1.54	52.89±1.59	<0.0001	0.82862	0.00004	0.07785	0.00002	0.11783	<0.0001
Superior	50.28±1.68	50.28±1.89	48.16±1.45	50.01±2.02	<0.0001	0.45126	<0.0001	0.68246	0.00000	0.73536	<0.0001
Inferior	50.53±1.96	49.80±1.79	48.80±2.07	49.83±2.08	<0.0001	0.06548	<0.0001	0.17904	0.00029	0.60154	0.00005
Nasal	50.07±1.85	50.07±1.84	48.42±1.90	50.05±2.04	<0.0001	0.94015	<0.0001	0.60623	<0.0001	0.53756	<0.0001
Temporal	50.63±2.03	50.01±2.20	48.52±1.70	50.20±1.88	<0.0001	0.82862	0.00004	0.07785	0.00002	0.11783	<0.0001

Data are mean ± SD. G1: non-smokers, G2: <10y smokers, G3: ≥10y smokers, G4: former smokers. One-way ANOVA + Tukey post hoc.

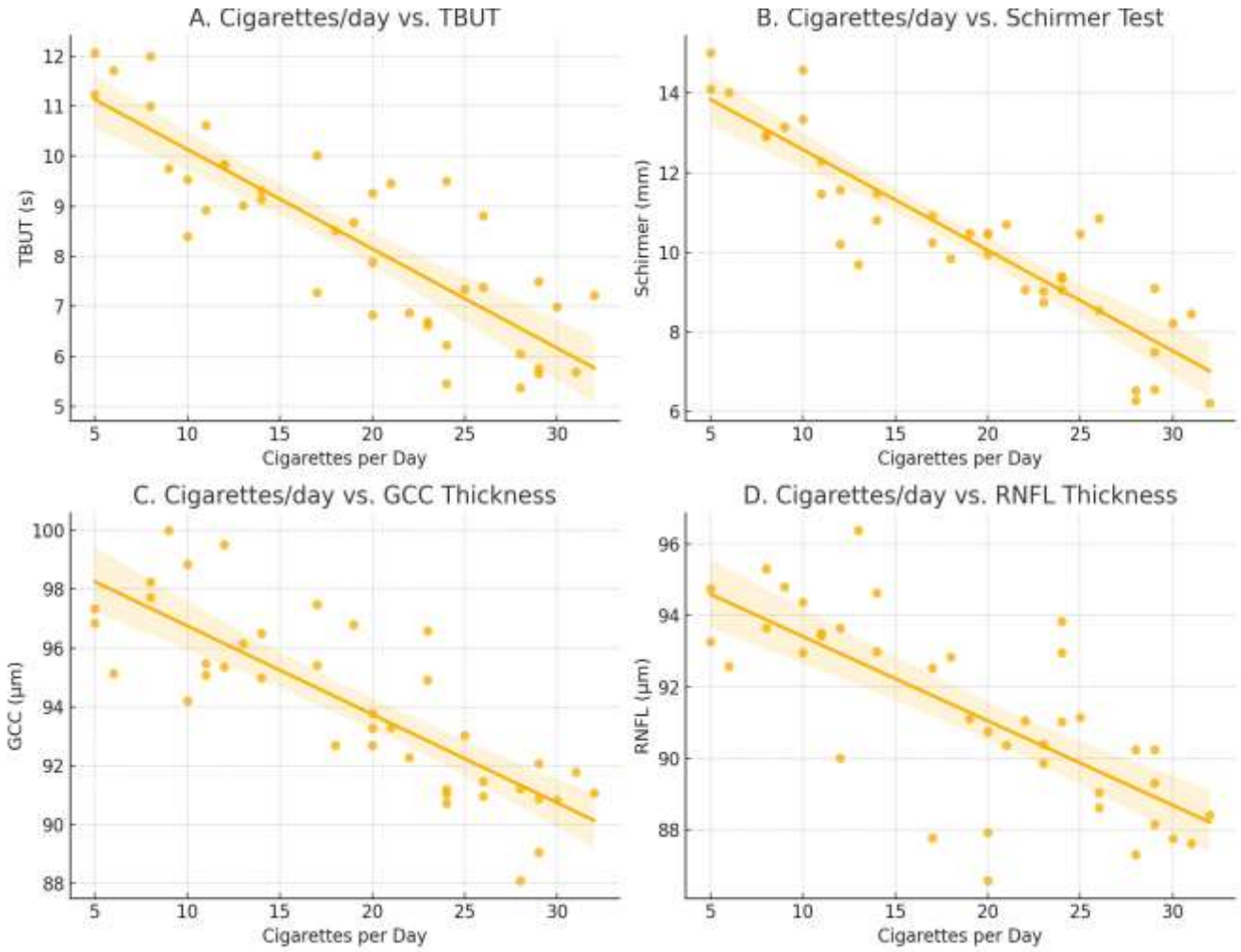

Figure 1. Dose-dependent associations between daily cigarette consumption and ocular parameters in active smokers. (A) Negative correlation between cigarettes smoked per day and TBUT. (B) Negative correlation between daily cigarette consumption and Schirmer test values. (C) Inverse association between cigarette intake and GCC thickness. (D) Negative correlation between cigarette consumption and RNFL thickness.

3.2. Retinal Structural Parameters

Group 3 exhibited the most pronounced thinning in both GCC and RNFL measurements. GCC average thickness was significantly reduced in Group 3 (94.63 ± 3.30 µm) compared to all other groups ($p < 0.0001$). RNFL average thickness was also lowest in Group 3 (88.53 ± 4.33 µm), with significant differences when compared to Groups 1 and 2 ($p < 0.001$). Former smokers demonstrated intermediate GCC and RNFL values, often not statistically different from non-smokers, suggesting partial structural recovery (Table 4).

Table 4. Comparison of retinal structural parameters (GCC and RNFL thicknesses) among study groups

Thickness (µm)	G1	G2	G3	G4	Overall p	G1-G2	G1-G3	G1-G4	G2-G3	G2-G4	G3-G4
GCC Average	99.88±3.34	98.75±4.41	94.63±3.30	98.51±3.62	<0.001	0.7006	<0.001	0.5568	0.0009	0.9957	0.0019
GCC Nasal	102.64±3.37	101.32±4.68	97.79±3.91	101.4±4.14	0.0004	0.6599	0.0003	0.7055	0.0140	0.9999	0.0112
GCC Temporal	96.80±3.44	95.95±4.75	91.41±3.57	95.48±4.07	<0.001	0.8750	<0.001	0.6452	0.0007	0.9750	0.0028
GCC Superior	99.47±3.41	98.44±4.83	94.67±3.71	99.00±3.81	0.0001	0.7928	0.0003	0.9754	0.0064	0.9576	0.0012
GCC Inferior	100.07±4.12	98.43±4.74	94.93±3.93	99.05±3.77	0.0002	0.5014	0.0002	0.8206	0.0190	0.9510	0.0038
RNFL Average	93.28±4.33	92.92±4.67	88.53±4.33	90.81±4.74	<0.0001	0.6226	<0.0001	0.0979	0.0019	0.6764	0.0530
RNFL Nasal	98.52±5.09	98.28±4.34	93.21±5.07	96.05±5.57	0.0017	0.2466	0.0010	0.0347	0.1799	0.8137	0.6538

RNFL Temporal	88.66±4.45	87.48±5.33	82.9±4.65	85.71±5.0	<0.0001	0.0989	<0.0001	0.0677	0.0616	0.9984	0.0906
RNFL Superior	93.31±4.27	91.70±4.46	88.88±4.79	91.81±4.50	0.0143	0.1267	0.0185	0.8845	0.8671	0.4514	0.1160
RNFL Inferior	93.17±3.58	91.53±4.01	89.02±4.77	91.61±4.38	<0.0001	0.0025	<0.0001	0.1451	0.7063	0.4484	0.0570

Data are mean ± SD. GCC: Ganglion Cell Complex; RNFL: Retinal Nerve Fiber Layer. G1: non-smokers, G2: <10y smokers, G3: ≥10y smokers, G4: former smokers. One-way ANOVA + Tukey post hoc.

3.3. Dose-Dependent Associations in Active Smokers

Among active smokers (Groups 2 and 3), significant inverse correlations were observed between daily cigarette consumption and multiple ocular parameters. Specifically, TBUT was negatively correlated with cigarette consumption ($r = –0.41$, $p = 0.004$), as were Schirmer test values ($r = –0.35$, $p = 0.01$) and average GCC thickness ($r = –0.38$, $p = 0.006$). A weaker but still significant negative correlation was also detected between cigarette consumption and average RNFL thickness ($r = –0.28$, $p = 0.045$) (Figure 1).

4. Discussion

This study represents one of the most comprehensive evaluations to date exploring the dose-dependent and potentially reversible ocular effects of cigarette smoking. By integrating both anterior and posterior segment analyses, our findings offer a holistic view of smoking-induced ocular pathology. In accordance with Ağın et al.[12], our study revealed significant thinning in both GCC and RNFL thicknesses among current smokers, particularly in inferior and temporal quadrants. Importantly, the structural indices of former smokers approached those of non-smokers, suggesting a potential improvement pattern rather than definitive recovery.

The impact of cigarette smoking on tear film and ocular surface parameters has been extensively reported. Latif & Naroo[13] demonstrated that acute smoking significantly decreased TBUT, likely due to oxidative damage to the lipid layer and ocular surface epithelium. In alignment, our data showed a pronounced reduction in TBUT and Schirmer test scores in active smokers—especially those with longer exposure—together with elevated OSDI scores, reinforcing the notion of progressive tear film instability and inflammation.

Ibrahim et al.[14] further emphasized a dose-dependent deterioration of ocular surface parameters, including increased staining scores and reduced tear production. Our study integrated meibography and epithelial thickness mapping, revealing structural loss of meibomian glands and corneal epithelium, confirming that tobacco-related damage encompasses both functional and morphological domains of the ocular surface.

Our results also resonate with those of Mohidin and Jaafar[15], who reported significantly decreased NITBUT and TBUT values even among light smokers. Likewise, Bhutia et al.[16] found that OSDI and Schirmer values were compromised in smokers, further supporting the presence of dose-related tear film instability.

Inner retinal involvement has also been reported by Karimi et al.[18], who documented peripapillary and macular thinning among smokers due to chronic ischemia and oxidative injury. In accordance, our study found significantly lower RNFL and GCC values in active smokers, with the extent of thinning correlating negatively with daily cigarette consumption.

Additional support comes from Matsumoto et al.[4], who demonstrated oxidative damage to the tear film and goblet cell loss among chronic smokers. In our study, both TBUT and OSDI scores were significantly impaired in smokers, and this deterioration pattern paralleled increasing meibomian gland loss and epithelial thinning, especially in long-term smokers.

Finally, the work by Carreira et al.[19] highlights that while tear film dysfunction in smokers may partially improve with lipid-based lubricants, meibomian gland loss and

corneal epithelial thinning remain largely irreversible. Our results support this finding, as we observed substantial recovery in functional indices in former smokers, but persistent deficits in structural metrics.

Strengths and Limitations

A key strength of this study lies in its comprehensive and multimodal assessment of both ocular surface and inner retinal structures across well-defined smoking subgroups. The inclusion of a former smoker subgroup offers valuable insights into the potential reversibility of smoking-induced changes. However, the cross-sectional design precludes direct conclusions about causality or temporal progression. Smoking exposure was not quantified using standardized measures such as pack-years. Additionally, inflammatory markers and tear film composition were not evaluated, limiting insights into underlying pathophysiology. The relatively small sample size may restrict generalizability.

5. Conclusion

This study demonstrates that cigarette smoking is significantly associated with both ocular surface dysfunction and neuroretinal structural compromise, with the severity of changes correlating with smoking duration and intensity. Chronic smokers exhibited markedly reduced TBUT and Schirmer values, increased meibomian gland dropout, and thinning of both GCC and RNFL layers. Former smokers displayed partial recovery in several parameters, suggesting a pattern of improvement associated with smoking cessation; however, due to the cross-sectional design, causal relationships and true reversibility cannot be confirmed. These findings underscore the importance of early ophthalmologic evaluation in smokers and provide further support for smoking cessation as a critical measure in preserving ocular health.

Conflict of Interest: The authors declare that they have no conflict of interest related to this study.

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