Study of The Effect of Cigarette Smoking on Tear film, Conjunctiva and Lacrimal System

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ABSTRACT

Background: The tear film covers the ocular surface, consisting of the conjunctival and corneal epithelia, and functions as the interface between the external environment and these epithelia. **Aim:** This study aimed to examine the impact of cigarette smoking on the tear film, conjunctiva, and lacrimal system and the correlation between dry eye severity level and cigarette smoking, aiming to improve quality of life and reduce morbidities arising from smoking.

Patients and methods: This case-control comparative research was performed on 100 eyes of cases attending Ismailia Outpatient Clinics. They have been classified into 2 groups: Group A: Smoker cases and Group B: Non-smoker cases (neither active nor passive smoker) in the Outpatient Clinic, Ophthalmology Department, Suez Canal University Hospital, Ismailia, Egypt, in 2020.

Results: A statistically significant variance was discovered among both groups regarding the Schirmer test, as it was greater in group A (p-value = 0.003). A statistically significant variance was discovered among both groups regarding the Tear Break Up Time Test (TBUT) (p value = 0.372).

Conclusion: Cigarette smoking negatively impacts tear film and ocular surface by decreasing tear secretion quantity, potentially leading to meibomian gland dysfunction and a risk factor for dry eye syndrome. Chronic smoking can cause ocular surface disorders, making it crucial to avoid smoking in cases of dry eye syndrome and ocular surface conditions, regardless of the severity of symptoms.

Keywords: TBUT, Cigarette smoking, Conjunctiva, Lacrimal system.

INTRODUCTION

The tear film covers the ocular surface, consisting of the conjunctival and corneal epithelia, and functions as the interface between the external environment and these epithelia. The tear film is crucial for the health and protection of conjunctival and corneal tissues and for maintaining clear vision, serving as 1st refractive surface of the eye ^[1]. Dry eye is a multifactorial disorder of the ocular surface marked by an absence of tear film homeostasis, which leads to ocular symptoms, where neurosensory abnormalities, ocular surface damage and inflammation, and tear film hyperosmolarity and instability contribute to its etiology ^[2].

Dry eye syndrome (DES), or keratoconjunctivitis sicca (KCS), is characterized by the presence of dry eyes. Additional correlated symptoms involve irritation, erythema, discharge, and easily fatigued eyes. Blurred vision can additionally happen. The symptoms may vary from mild and frequent to severe and persistent. Corneal scarring can happen in certain conditions without management ^[3, 4].

Dry eye manifests if the eye fails to generate sufficient tears or if the tears evaporate too rapidly ^[4]. Chronic conjunctivitis or infection can additionally result in the illness. Diagnosis primarily relies on the symptoms, although various additional tests can be utilized ^[5].

Cigarette smoke contains more than 4000 toxic compounds and is considered one of the top five risk factors of mortality, with more than five million deaths a year. Upon exposure to ocular tissues, these compounds are eventually poisonous and affect the eye through ischemic and oxidative mechanisms ^[6].

Many ophthalmologic syndromes are thought to be associated with tobacco smoking, involved age-related macular degeneration, tobacco–alcohol amblyopia, anterior ischemic optic neuropathy, cataract, and retinal ischemia ^[7]. Smokers are believed to complain of ocular surface symptoms more than non-smokers due to the irritant effect of smoke. Many studies have related smoking with dry eye, though reporting and documenting symptoms and signs, respectively, and using clinical tests like the Schirmer test. Results are still controversial, and further studies are required to clarify the topic. Smoking is regarded as a risk factor for ocular & intraocular surface inflammation ^[8].

The objective of research to examine the impact of cigarette smoking on the tear film, conjunctiva & lacrimal system and the correlation among dry eye severity level and cigarette smoking, aiming to enhance quality of life and reduce morbidities arising from smoking.

PATIENTS AND METHODS

This case-control comparative research has been performed on 100 eyes of cases attending Ismailia Outpatient Clinics. They have been classified into 2 groups: Group "A" included smoker cases and group "B" that included non-smoker cases (neither active nor passive smoker) in Outpatient Clinic, Ophthalmology Department, Suez Canal University Hospital, Ismailia, Egypt in 2020. We evaluated the effect of cigarette smoking for at least 1 year on the tear film, conjunctiva, and lacrimal system.

Inclusion criteria: Male patients, age group from 21 to 40 years. Smoker group where smoking must be for at least 1 year. Non-smoker group: Those who had never engaged in smoking and didn't have any smokers among their relatives in the first degree, thus removing the potential impact of passive smoking.

Exclusion criteria: History of using contact lenses, History of ocular operation e.g., refractive surgery, administration of eye drops containing preservatives for long durations, all patients with abnormalities in the cornea or conjunctiva or lid e.g., atopy, allergic diseases, or Sjogren's syndrome, diabetic patients, and patients with autoimmune disorders to avoid the secondary ocular effect. Pregnancy and lactation, outdoor workers, and prolonged exposure to air conditioning.

Ethical considerations: The investigation was executed following the acceptance of the protocol by The Local Research Committee, The Studies Committee, and the Research Ethics Committee of the Ophthalmology Department, Faculty of Medicine, Suez Canal University. Informed written consent was gathered from all cases, clearly outlining the research's objectives and methods. Throughout its implementation, the study complied with the Helsinki Declaration.

Sample type: The sample has been collected by a simple random technique.

$$n = 2 \left[\frac{\left(Z_{\alpha/2} + Z_{\beta} \right) * \sigma}{\mu_1 - \mu_2} \right]^2$$

Sample size and design: The sample size has been determined utilizing the following formula ^[9]:

Anywhere:

 $\mathbf{n} = \text{size of sample.}$

 $\mathbf{Z}_{\alpha/2} = 1.96$ (critical value that divides the central ninetyfive percent of the Z distribution from five percent in the tail).

 $\mathbf{Z}_{\beta} = 1.28$ (the critical value that separates the lower ten percent of the Z distribution from the upper ninety percent).

 σ = the estimation of SD of TBUT = 2.62 s. μ_1 = mean TBUT in smokers = 12.17 s^[10].

 μ_1 = mean TBUT in shokers = 12.17 s⁻¹. μ_2 = mean TBUT in non-smokers = 14.13 s^[10].

The calculated sample size was 50 eyes per group, accounting for a 10% drop-out proportion.

Methodology: All cases that fulfilled the exclusion and inclusion criteria have been enrolled in the research: History taking and examinations included refraction using an automated refractometer (NIDEK, AR-600, Japan). Best corrected visual acuity (BCVA) assessment using decimal notation. Examination of orbit and ocular motility. Measuring intraocular pressure using the Goldmann Applanation Tonometer (Haag Streit Tonometer, AT900, Switzerland). Fundus investigation utilizing Volk's non-contact double aspheric biconvex lens (power: +20) and indirect ophthalmoscope (Appasamy Associates, AAIO-7, India).

Slit-lamp biomicroscopic investigation (Topcon, SL-D, Japan): Full examination of the anterior segment performed (for: Lid examination: blepharitis, papillary reaction, and meibomian gland dysfunction). Lacrimal system examination: Assessment of the puncti. Corneal examination: Assessment of corneal filaments, erosions, and mucous plaques. Conjunctival examination: Assessment of tear meniscus height and tear particles. Examination of the sclera: Anterior chamber, iris, pupil, and lens. Schirmer II test, TBUT test, and RB staining.

Schirmer's II test: A single drop of Benox (Benoxinate hydrochloride 0.4 milligrams) was administered to the eye for topical anesthesia. This method assesses basic tear functionality. A standard sterile Schirmer's strip (5 millimeters x 35 millimeters) was folded at the notch and positioned in the inferolateral third of the lower eyelid, ensuring that the cornea wasn't contacted during the procedure. The following 5 minutes, the millimeter measurement of strip wetting was recorded. The test findings were regarded as positive when the wetting length measured below six millimeters within five minutes of the test ^[11].

Tear break-up time test: Conducted as a functional assessment of tear film stability. A fluorescein strip (Fluostrip, one milligram of fluorescein sodium) has been soaked with a single drop of Benox (Benoxinate hydrochloride 0.4 milligrams) and placed on the lower bulbar conjunctiva. Subjects have been given instructions to blink multiple times, and ocular structures have been examined with a slit lamp biomicroscope utilizing a broad beam and a cobalt blue filter. The interval from the last blink to the appearance of the first randomly distributed dry area on the cornea is termed the tear break-up time. The appearance of dry spots in below ten minutes is deemed abnormal. The operation was conducted 3 times, and the mean duration in sec has been documented for every eye ^[12]. A TBUT test value of less than ten seconds is deemed abnormal.

Rose Bengal (RB) staining: The procedure utilized rose Bengal strips containing 1.3 milligrams of RB stain each. RB is a crucial stain that identifies dead or degenerated epithelial cells in conjunctiva and cornea. It was applied to the lower bulbar conjunctiva. 3 fields were evaluated: Temporal conjunctiva, cornea & nasal conjunctiva. Each field is graded into 4 grades:

Overall grade up to 3.5 = normal finding. Overall grade > 3.5 = pathological ^[13].

RESULTS

A statistically insignificant variance was discovered among both groups regarding age (p-value=0.32). Within group A, the average age was 30.84 ± 5.31 years, while within group B, the average age was 29.48 ± 6.12 years (Table 1).

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Group A	Group B	Р
		value
$30.84 \pm$	$29.48 \pm$	0.32
5.31	6.12	
	Group A 30.84 ± 5.31	Group A Group B 30.84 ± 29.48 ± 5.31 6.12

P-value > 0.05: Insignificant, p-value < 0.05 significant.

In group A, the mean duration of smoking was 8.62 ± 2.23 years, the mean number of cigarettes per day was 20.32 ± 3.67 cigarettes per day, and the mean smoking index was 172.66 ± 46.1 , as demonstrated in table (2).

 Table (2): Smoking characters in group A

	Group A
Period of smoking (years)	
Mean± SD	8.62 ± 2.23
Number of cigarettes per day	
Mean± Standard Deviation	20.32 ± 3.67
Smoking Index	
Mean± SD	172.66 ± 46.1

A statistically insignificant variance was discovered among both groups regarding BCVA (p value=0.071) (Table 3).

Table (3): BCVA in both examined	groups
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	Group A	Group B	P value		
Best corrected visual acuity					
1.00	45 (90%)	50 (100%)	0.071		
0.67	2 (4%)	0			
0.5	3 (6%)	0			

A statistically significant variance was discovered among both groups regarding tear meniscus height as it was higher in group B (p-value = 0.003). A statistically insignificant variance was discovered among both groups regarding particles (p value = 0.23) (Table 4).

 Table (4): Tear meniscus height and particles in both

 study groups

	Group A	Group B	Р
	_		value
Tear meniscus(millim	eter)		
Mean± Standard	0.46 ±	$0.74 \pm$	0.003
Deviation	0.17	0.26	
Particles			
	5 (10%)	2 (4%)	0.23

A statistically insignificant variance was discovered among both groups regarding corneal punctate erosions (p-value=0.15). A statistically significant variance was discovered among both groups regarding corneal filaments, as it was higher in group A (p-value = 0.02) (Table 5).

Table (5): Corneal punctate erosions and filaments in both examined groups.

	Group A	Group B	P value	
Corneal punctate erosions				
	25 (50%)	18 (36%)	0.15	
Corneal filaments				
	9 (18%)	2 (8%)	0.02	

A statistically significant variance was discovered among both groups regarding papillary reaction grade, as it was greater in group A, grade 0 (p-value > 0.001), grade one (p-value 0.01), and grade two (p-value 0.04). A statistically insignificant variance was discovered among both groups regarding blepharitis (p-value = 0.07) (Table 6).

Table (6): Papillary reaction grades and blepharitis in both examined groups

	Group A	Group B	P value	
Papillary reaction	on grades			
0	20 (40%)	38 (76%)	0.001	
1	16 (32%)	6 (12%)	0.01	
2	14 (28%)	6 (12%)	0.04	
Blepharitis				
	3 (6%)	0	0.07	

A statistically significant variance was discovered among both groups regarding the Schirmer II test, as it was higher in group A (p-value = 0.003). A statistically insignificant variance was discovered among both groups regarding TBUT (p value = 0.372).

 Table (7): Schirmer II test and average TBUT in both

 examined groups

	Group A	Group B	P-value	
Schirmer II test(mm)				
Mean± SD	24.1 ± 6.29	20.88 ± 4.1	0.003	
Average TBUT (secs)				
Mean± SD	9.86 ± 5.88	10.8 ± 4.52	0.372	

A statistically significant variance was discovered among smoking index and dry eye severity level regarding mild and moderate smoking index (p-value > 0.001), (p-value 0.007) respectively, while statistically insignificant variance was discovered regarding severe smoking index (p-value = 1).



Figure (1): Correlation between smoking index and dry eye severity level.

DISCUSSION

A statistically insignificant variance was observed among both groups regarding age (pvalue=0.32). Within group A, the mean age was 30.84 years \pm 5.31, while in group B, the mean age was 29.48 years \pm 6.12. Within group A, the mean period of smoking was 8.62 ± 2.23 years, the mean number of cigarettes per day was 20.32 ± 3.67 cigarettes per day, and the mean smoking index was 172.66 ± 46.1 . A statistically insignificant variance was observed among both groups regarding BCVA (p value=0.071). This finding is consistent with Shephard et al. [14] found visual acuity demonstrated similar age coefficients among ex-smokers, smokers, and non-smokers, with no independent impact from cigarette smoke exposure.

A statistically significant variance was observed among both groups regarding tear meniscus height, as it was higher in group B (p-value = 0.003). A statistically insignificant variance was observed among both groups regarding Particles (p value = 0.23). This finding is in agreement with **Bhutia** *et al.*^[15] as they stated that the mean values of all dry eye variables were statistically variance between smokers and nonsmokers regarding tear meniscus height (p-value < 0.0001). **Bhutia** *et al.* ^[15]. As far as we know, there are no studies about tear particles to compare our results with.

In our study, a statistically insignificant variance was observed among both groups regarding corneal punctate erosions (p-value = 0.15), while a statistically insignificant variance was observed among both groups regarding corneal filaments (p-value = 0.02). In the research of **Thomas** *et al.* ^[16], superficial punctate staining of the cornea has been found in 56.9% of smokers, whereas no staining was detected in the controls. A Chi-square test revealed a statistically significant variance among groups (χ^2 =39.88; p-value<0.0001). As far as our knowledge, there were no studies done before regarding corneal filaments in smokers.

The present study showed that as regards papillary reaction grade in group A, 40% were grade zero, 32% were grade one, and 28% were grade two, while in group B, 76% were grade zero, 12% were grade one, and 12% were grade two. Statistically significant variance was discovered among both groups as grade zero (p-value > 0.001), grade one (p-value 0.01) and grade two (p-value 0.04), while statistically insignificant variance was discovered among both groups according to blepharitis (p-value = 0.07). Our outcomes are supported by research of **Wang** *et al.* ^[17] as they stated that eyelid edge abnormalities have been detected to be statistically significantly greater in the smokers.

The present research demonstrated that in group A, the mean Schirmer test was 24.1 ± 6.29 mm, while in group B, the mean Schirmer test was 20.88 ± 4.1 mm. A significant variance was discovered among both groups regarding the Schirmer test (p-value = 0.003). In group A, the mean TBUT was 9.86 ± 5.88 secs. in group B, the mean TBUT was 10.8 ± 4.52 secs. Insignificant variance was discovered among either group regarding TBUT (pvalue = 0.372). Our findings are supported by the research conducted by Uchino et al. [18], which showed an average tear break-up time of 4.3 ± 2.7 s, specifically 4.5 ± 3.0 s in males and 3.9 ± 2.1 s in females. No notable variance was observed in the average Tear Break-Up Time across the four age groups: 1) twenty to twenty-nine years, 2) thirty to thirty-nine years, 3) forty to forty-nine years, and 4) fifty years of age and older. The mean Schirmer test value for present smokers $(13.3 \pm 11.5 \text{ mm})$ was significantly below that for non-smokers $(19.0 \pm 11.7 \text{ mm}, \text{ P-}$ value = 0.016). The difference between this study and ours as regards Schirmer test results may be explained by the large sample size (sample = 145 eyes). While, in the study of Thomas et al. ^[16] smokers showed a reduced mean tear break-up time of 7.26 ± 1.86 seconds compared to non-smokers, who had a mean TBUT of 11.28 ± 1.27 sec (p-value = 0.0001). This suggests that smokers

demonstrate an amount of tear film instability relative to non-smokers; the difference between this study and ours as regards TBUT results may be explained by the large sample size (102 eyes). The mean Schirmer's II test value was insignificantly variant between smokers (20.21 \pm 6.62 mm per five minutes) and non-smokers (19.12 \pm 5.93 mm per five minutes; p-value = 0.22). This indicates that there is no correlation between aqueous production and tobacco smoking ^[16].

In our research, a statistically significant variance was discovered among the smoking index and dry eye severity level regarding the mild and moderate smoking index, while statistically insignificant variance was discovered regarding the severe smoking index. Our results are supported by several studies. In the study of **Tank & Kulkarni** ^[19] the mean values of the dry eye score (9.75; 3.42) were significantly more impacted in smokers (p-value 0.000).

CONCLUSION

Cigarette smoking adversely affects the tear film and ocular surface by reducing the quantity of tear secretion. Smoking may cause meibomian gland dysfunction, becoming a potential risk factor for dry eye syndrome. Ocular surface conditions associated with chronic smoking are considered the potential damage to the meibomian glands. Consequently, it is advisable for cases suffering from dry eye syndrome and ocular surface conditions to prevent smoking, regardless of the severity of their dry eye symptoms.

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