The effect of smoking on the ocular surface and the precorneal tear film

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Conclusion

Smoking caused adverse effects on the precorneal tear film and there was strong association between smoking and tear film instability. Although a causative relationship could not be determined, there is a need for further longitudinal studies.

Key Words

Smoking, ocular surface, dry eye, tear stability, corneal and conjunctival sensitivity

What this study adds:

1. Tear stability of smokers is decreased
2. Punctate staining of the cornea is increased in smokers
3. Sensitivity of the cornea and conjunctiva is decreased in smokers

Background

Tobacco use kills more than five million people per year and is responsible for one in 10 adult deaths.¹ Among the five greatest risk factors for mortality, smoking is the single most preventable cause of death.¹ It is estimated that tobacco use will kill more than eight million people per year by 2030.¹ Although lung cancer is strongly associated with smoking, tobacco use also increases the risk of heart disease and other vascular diseases and leads to malnutrition, which will eventually result in increased health-care costs and premature death.² Smoking also affects the eyes, the toxins associated with smoking decrease blood flow or aid in the formation of clots within ocular capillaries, thus cutting off vital nutrients that are essential for eye health.³,⁴ Free radicals that are produced because of smoking impair the normal functionality of the cells and have been reported to cause ocular diseases.³

People who smoke cigarettes are at an increased risk of developing cataracts, age-related macular degeneration, diabetic retinopathy, glaucoma, Grave’s ophthalmopathy, and optic neuritis.⁴ Different epidemiological studies conducted shows that there is a dose response relation ship between smoking and development of nuclear cataract.¹⁵

Abstract

Background

Smoking, both active and passive, creates a plethora of health-related problems, which primarily affect the cardiovascular and respiratory systems. There is very little evidence on the effects of tobacco smoke on the eye, especially regarding anterior ocular surface related pathology. This study was undertaken to determine the effects of smoking on the ocular surface and the tear film in smokers.

Methods

A total of 51 (102 eyes) smokers and 50 (100 eyes) age- and gender-matched healthy non-smokers were included in this study. The ocular surface was evaluated by measuring tear film break-up time, surface staining with fluorescein, and corneal and conjunctival sensitivities, and by completing the Schirmer’s II test. Data was analysed using Statistical Package for Social Sciences (SPSS) version 11.5. A p value less than 0.05 was considered statistically significant.

Results

The smoker group had significantly lower tear film break-up time, and corneal and conjunctival sensitivity than the non-smoker group. Punctate staining was significantly higher in the smoker group than the non-smoker group. There was no statistically significant difference in Schirmer’s II test results between the smoker and non-smoker group.

RESEARCH

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Tobacco use kills more than five million people per year and is responsible for one in 10 adult deaths.¹ Among the five greatest risk factors for mortality, smoking is the single most preventable cause of death.¹ It is estimated that tobacco use will kill more than eight million people per year by 2030.¹ Although lung cancer is strongly associated with smoking, tobacco use also increases the risk of heart disease and other vascular diseases and leads to malnutrition, which will eventually result in increased health-care costs and premature death.²

Smoking also affects the eyes, the toxins associated with smoking decrease blood flow or aid in the formation of clots within ocular capillaries, thus cutting off vital nutrients that are essential for eye health.³,⁴ Free radicals that are produced because of smoking impair the normal functionality of the cells and have been reported to cause ocular diseases.³

People who smoke cigarettes are at an increased risk of developing cataracts, age-related macular degeneration, diabetic retinopathy, glaucoma, Grave’s ophthalmopathy, and optic neuritis.⁴ Different epidemiological studies conducted shows that there is a dose response relation ship between smoking and development of nuclear cataract.¹⁵
Studies have shown that the cessation of smoking reduces the risk of nuclear opacity, but these findings are not conclusive. Heavy smokers are at higher risk of developing exudative or atrophic age-related macular degeneration. The relationship between smoking and dry eye has not been studied extensively, but for those with dry eye, smoking is a significant irritant that leads to symptoms such as scratchiness, foreign body sensation, burning of the eyes and grittiness. These symptoms are suggestive of dry eye syndrome, and are caused by dysfunction in the thin precorneal tear film which covers the entire cornea and bulbar conjunctiva. This study was conducted to determine the effects of smoking on the ocular surface and the tear film in smokers.

**Methods**

Permission for conducting this study was obtained from the Institutional Review Board at the Manipal College of Allied Health Sciences, Manipal University, India. Ethics Committee approval was also obtained.

Anticipating a standard deviation of 1.75 for the tear film break-up time (TBUT) procedure and a clinically significant difference of two between the smokers and non-smokers, for a power of 90%, a minimum sample size of 25 people in each group was required.

Students from Manipal University and patients who came to the Outpatient Department of Ophthalmology over an eight month period were potential participants for the study. A total of 200 people were approached, which consisted of 120 smokers and 80 non-smokers.

Smokers and non-smokers were asked to complete a questionnaire that determined their eligibility to enrol in the study. The questionnaire included details on smoking status, such as duration and number of cigarettes per day, and ocular complaints of the participants. A total of 65 smokers and 55 non-smokers were eligible for further evaluation in the study. Smokers with a history of smoking more than six cigarettes per day for at least two years were included in the study with age- and gender-matched non-smokers. People with any of the following conditions were excluded from the study: any systemic or ophthalmic diseases, history of contact lens use, use of any medications, past ocular surgery, specific occupations associated with dry eye and high refractive errors.

Informed consent was obtained from each participant and examinations were carried out at the Optometry Clinic, Manipal. Visual acuity and refraction was performed in all participants, and all participants were examined thoroughly with a slit lamp biomicroscope to rule out any associated conjunctivitis or any other ocular problems that would fall into the exclusion criteria. A total of 51 smokers and 50 non-smokers met the inclusion criteria and were enrolled in the study.

In addition to a comprehensive assessment, the following examinations were also performed on all eligible participants: TBUT, punctuate staining of the cornea with fluorescein, corneal and conjunctival esthesiometry, and Schirmer’s II test. The values obtained from the smoker group were compared to those from age-matched non-smokers.

The first test performed was the TBUT, followed by superficial punctuate staining of the cornea. A fluorescein strip (Fluostrip, 1 mg fluorescein sodium, IP) was wetted with a single drop of Moisol (hydroxypropylmethylcellulose) and applied to the lower bulbar conjunctiva. Participants were asked to blink several times and the ocular structures were viewed with a slit lamp biomicroscope using the cobalt blue filter. The time between the last blink and the appearance of the first randomly appearing dark spot was measured. This procedure was repeated three times and the average value in seconds was recorded in each eye. Following TBUT, punctate staining was recorded using a grading system that was dependent on the area and density of staining in each eye. The staining area was graded on a numerical scale of 0–3, with 0 representing no punctate staining, 1 representing less than one-third staining, 2 representing one-third to two-thirds staining, and 3 representing more than two-thirds staining. The staining density was also graded on a numerical scale of 0–3, with 0 representing no punctate staining, 1 representing sparse density, 2 representing moderate density and 3 representing high density with overlapping lesions.

 Conjunctival and corneal sensitivity was measured using a Cochet-Bonnet esthesiometer (Luneau Ophthalmologie, France). The tip of the fully extended nylon filament was applied perpendicularly to the surface of the cornea, making sure the eyelashes were not touched, and pushed until the first visible bend of the filament. The length of the nylon filament was subsequently decreased until a blink response was induced in the participant. The participant was advised to blink normally. To ensure participant reliability, the nylon filament was advanced towards the cornea without actually touching it, and repeated measurements were also taken to increase reliability. The measurements were repeated four times and the length was recorded in millimetres. The average of the four measurements was taken as the corneal
sensitivity of that eye. The same procedure was used to measure the conjunctival sensation with the stimulus applied to the middle of the exposed temporal conjunctiva.

Schirmer’s test was the final assessment and was performed by placing a single drop of Paracaine (Proparacaine HCl, 0.5%) in each eye as topical anaesthesia. In a dimly lit room, a standard Schirmer’s strip (Graduated Tear Strips, Contacare Ophthalmics and Diagnostics, Vadodara, India) was placed in the inferolateral third of the lower lid, taking care not to touch the cornea in the process. After five minutes, the level of the strip wetting in millimetres was measured.

A single investigator enrolled the participants and performed all the tests in this study and another investigator did the data analysis. Both the investigators had sufficient knowledge to perform and interpret the tests.

Data was analysed and tabulated using Statistical Package for Social Sciences (SPSS) software version 11.5 for Microsoft Windows (SPSS Inc., Chicago, IL, USA). Statistical comparisons were done using the Student’s t-test for unpaired samples for TBUT, conjunctival and cornealesthesiometry, and Schirmer’s II test. Superficial punctuate keratopathy was compared using the chi-square test. Tamhane’s test for multiple comparisons was used to assess variance between those who had been smoking for 0 to 20 years and those who had been smoking for 21 to 40 years. A p value less than 0.05 was considered to be statistically significant.

Results

This study comprised of 101 participants: 51 smokers and 50 healthy age-matched non-smokers. The mean age of the smoker group was 35.14 ± 14.5 years and the mean duration of smoking was 6.20 ±10.12 years. The mean age of the non-smokers was 36.4 ± 12.3 years. All the study participants were males because smoking was uncommon among females in this area.

Smokers had a lower mean TBUT (7.26 ± 1.86 s) than the non-smokers (11.28 ± 1.27 s; p=0.0001). This indicates that there is a certain amount of tear film instability in smokers compared with non-smokers.

The mean Schirmer’s II test value was not significantly different in the smokers (20.21 ± 6.62 mm/5 min) compared with the non-smokers (19.12 ± 5.93 mm/5 min; p=0.22). This shows that there is no relationship between tobacco smoking and aqueous production.

The average corneal sensitivity recorded was significantly lower in smokers (47.23 ± 8.68 mm) than in non-smokers (57.66 ± 2.76 mm; p=0.0001). The average conjunctival sensitivity was also significantly lower in smokers (31.16 ± 7.44 mm) than in non-smokers (36.4 ± 5.02 mm; p=0.0001). Superficial punctuate staining of cornea was seen among 56.9% of smokers (Figure 1) while there was no staining observed in the control group (Figure 2). When a chi-square test was done, the difference between groups was found to be statistically significant (χ²=39.88; p<0.0001).

The assessment of ocular surface and tear film changes according to daily smoking amount is given in Table 1.

Table 1: Relation of ocular surface and tear film changes to smoking amount

| Variable                  | ≤1 pack per day (mean ± SD) | >1 pack per day (mean ± SD) | p value |
|---------------------------|-----------------------------|-----------------------------|---------|
| Corneal Esthesiometry (mm) | 48.2 ± 8.65                 | 45.3 ± 8.55                 | 1.52    |
| Conjunctival Esthesiometry (mm) | 31.6 ± 7.61             | 30.2 ± 7.12                 | 0.869   |
| Schirmer’s II (mm/5min)    | 20.3 ± 7.09                 | 20.1 ± 5.63                 | 0.137   |
| TBUT (s)                  | 7.49 ± 2.01                 | 6.83 ± 1.41                 | 0.197   |

The comparison between the ocular surface and tear film changes by years of smoking is given in Table 2.
Table 2: Relation of ocular surface and tear film changes to years of smoking

| Variable                      | 0–20 years (mean ± SD) | 21–40 years (mean ± SD) | Non-smokers (mean ± SD) |
|-------------------------------|------------------------|-------------------------|-------------------------|
| Corneal Esthesiometry (mm)    | 48.38 ± 8.94           | 42.56 ± 5.52            | 57.66 ± 2.75            |
| Conjunctival Esthesiometry (mm)| 31.43 ± 7.66           | 30.06 ± 6.49            | 36.36 ± 5.02            |
| Schirmer's II (mm/5 min)      | 21.24 ± 6.6            | 16 ± 4.87               | 19.12 ± 6.2             |
| TBUT (s)                      | 7.57 ± 1.85            | 6.00 ± 1.26             | 11.28 ± 1.26            |

Table 3 presents the results of Tamhane’s test, which was performed to identify significantly different group means; it is based on the t-test for unequal variances for those who have smoked for more or less than 20 years.

Table 3: Tamhane’s Test of Multiple comparisons for smoking years

| Variable                      | I          | J          | 95% CI for the difference in mean (I–J) | p value |
|-------------------------------|------------|------------|----------------------------------------|---------|
| Corneal Esthesiometry        | 0–20 years | 21–40 years| 5.87 (0.65, 11.09)                     | 0.44    |
|                               | Non-smokers|           | 9.27 (–12.36, 0.00)                     | 0.0001  |
| Conjunctival Esthesiometry   | 0–20 years | 21–40 years| 1.77 (–5.09, 9.06)                      | 0.888   |
|                               | Non-smokers|           | –4.92 (–8.31, –1.52)                    | 0.02    |
| Schirmer’s II                 | 0–20 years | 21–40 years| 4.88 (–0.89, 10.65)                     | 0.110   |
|                               | Non-smokers|           | 2.58 (–0.64, 5.80)                      | 0.153   |
| Schirmer’s II                 | 0–20 years | 21–40 years| 1.17 (–0.44, 2.38)                      | 0.061   |
|                               | Non-smokers|           | –3.71 (–4.51, –2.84)                    | 0.0001  |

Discussion

Dry eye is one of the most common ophthalmic medical problems, causing complaints of burning, itching, or even dryness. The treatment modalities available are in the form of tear substitutes, which provide a modicum of relief from symptoms for a short period of time, but require frequent application.

Cigarette smoking has been reported to be one of the factors in a multitude of clinical conditions that cause a dysfunctional tear film, resulting in dry eye.7,9,13 In this study, we have shown that smoking has statistically significant detrimental effects on the precorneal tear film and ocular surface.

There are many theories about the mechanisms by which smoking causes the breakdown of the precorneal tear film. Of those, the effect of lipid peroxidation of the outer layer of the precorneal tear film is the most probable cause of tear film breakdown that leads to dry eye symptoms.5 The ocular surface is exposed to over 1E+14 short-lived radicals in the gas phase per puff and even more in the tar phase during which the radicals are long lived.6 Altinors et al7 assessed the lipid layer of the tear film in smokers and reported damage in the lipid layer which prevents the even spreading of tear film over the corneal surface, rendering it unwettable. According to them, smoking damages the precorneal tear film lipid layer by lipid peroxidation process and causes dry eye symptoms.7 Cigarette smokers also have higher levels of lipid peroxidation than non-smokers.6 The chemical composition of cigarette smoke is complex, with many free radical species, aldehydes, peroxides, epoxides, nitrogen oxides, peroxyl radicals, and other pro-oxidants being present.8 There is growing evidence that these oxidant species may contribute to the disease process associated with smoking. The tar and gas phases of smoking contain many oxidising substances.5 Smoking can also cause ocular surface epithelial damage because the smoke comes
into direct contact with the ocular surface. Satici et al\(^9\) reported that there was a higher amount of squamous metaplasia in the conjunctival surface epithelium in smokers than in controls. This could be caused by increased inflammation due to the toxic irritants present in cigarette smoke, which results in the absence of growth factors required for epithelial differentiation. Polymorphonuclear leukocytes and squamous epithelium cell counts were increased in tobacco workers before and after shifts. Kjaergard et al\(^{10}\) reported a higher degree of ocular irritation among tobacco workers who came in contact with a high concentration of the substance. The presence of toxins and irritants in smoke causes a conjunctival reaction that leads to eye redness.

Cigarette smoking also causes a change in the tear protein patterns of smokers compared with non-smokers. By performing electrophoretic analysis of tear proteins, Grus et al\(^{11}\) observed that changes in tear proteins were greater and more severe in smokers than in controls. They noted significantly more protein peaks in severe smokers than in non-smokers. They correlated the changes with the increase in dry-eye-related subjective symptoms in smokers.

Doane\(^{12}\) reported that the lipids, aqueous portion, and mucin components of the tear film interact with each other to achieve an even spread of the lipid layer in the tear film, rendering the cornea wettable and allowing tear stability within the normal limits. Matsumoto et al\(^{13}\) reported that chronic smoking induced distinctive quantitative and qualitative disturbances of the ocular surface health. The results of our study confirmed that smoking is deleterious to the precorneal tear film and the ocular surface, which is consistent with many other study findings.\(^{5-13}\)

Yoon et al\(^{14}\) observed no significant difference in TBUT, corneal staining, or symptom scores between smokers and non-smokers, which is not consistent with our study results. This difference may be because of the smaller sample size in their study. However, basal tear secretion and corneal sensitivity was reduced in the smokers group. Deterioration of ocular surface was related to amount of smoking according to Yoon et al, which was noted also in our study.

We have not assessed the exposure to indoor air pollution or any other exposures at the work place, such as passive smoking in either of the groups, which could have been a confounding factor for some of the participants.

These study results confirmed and emphasised the fact that chronic smoking does have adverse effects on the precorneal tear film and the ocular surface, which worsens with increased duration of smoking years.

**Conclusion**

Smoking causes tear film instability and leads to decreased TBUT, decreased corneal and conjunctival sensitivity, and increased superficial punctate staining. Although smoking bans and smoking cessation programs focus on cardiovascular and respiratory problems, tear film dysfunction can cause ocular discomfort and thus affect the quality of life of patients. The current study adds more evidence for the ill effects of tobacco use. In order to control this global health issue, there is a dire need to increase knowledge and create more awareness about mortality risks and provide support and motivation towards cessation of tobacco use.

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CONFLICTS OF INTEREST
None.

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ETHICS COMMITTEE APPROVAL
The protocol was approved by the Institutional Review Board for research proposals, Manipal College of Allied Health Sciences, Manipal University.