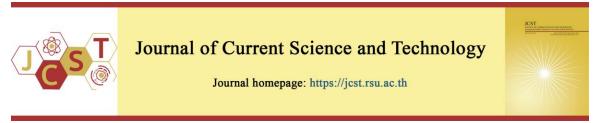
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Comparison of ocular parameters and dry eye measurements between Thai male smokers and non-smokers

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Abstract

We compared anterior and posterior ocular parameters, spherical refractive error, and dry eye measurements in smoking and non-smoking Thai men. This observational study included the left eyes of 145 male smokers and 147 agematched healthy male non-smokers. Subjects with systemic or ophthalmic diseases, use of any medications, history of ocular surgery or contact lens use were excluded. All participants underwent a medical history review, blood pressure, height, weight, and body mass index calculation. Spherical refractive error, corneal curvature, central corneal thickness, anterior chamber parameters, macular thickness, retinal nerve fiber layer (RNFL) thickness and cup to disc ratios were all measured. Additionally, dry eye was assessed by tear break-up time (TBUT) and Schirmer's test I. There were no significant differences found in anterior and posterior ocular parameters measure between smokers and non-smokers. The smokers in our study were 0.25 D less myopic than the non-smokers but this finding was not significant. The average TBUT among smokers was found to be two seconds less compared to non-smokers (5.00 seconds vs. 7.00 seconds, p < 0.001) and the average Schirmer I test finding among smokers was four millimeters less compared to non-smokers (10.00 mm vs. 14.00 mm, p = 0.044). Smoking > 5 yrs. vs. \leq 5 yrs. is associated with lower Schirmer I test results in those age 20-30 years old (16.00 mm vs. 22.52 mm, p = 0.05). It is concluded that smoking is significantly associated with loss of quality and quantity of tear film.

Keywords: dry eye; ocular parameters; Schirmer I test; smoking; spherical refractive error; tear break-up time; TBUT.

1. Introduction

Smoking is a serious global public health problem. The World Health Organization (WHO) reports that smoking annually kills more than 8 million people worldwide (World Health Organization, 2020). Smoking kills more than 72,000 people a year in Thailand (Southeast Asia Tobacco Control Alliance, 2019; The Nation Thailand, 2019), and tobacco-related illness costs the Thai economy 77.62 billion baht (approximately \$2.3 billion USD) annually (Bundhamcharoen, Aungkulanon, Makka, & Shibuya, 2016). Smoking is also associated with several ocular conditions that can cause visual loss or blindness including agerelated macular degeneration, glaucoma, Graves' disease and cataract (Cheng et al., 2000). According to the National Statistical Office of Thailand, among the 55.9 million Thai people age15 years or more, 10.7 million (19.1%) are smokers with men being much more likely to smoke than women (37.7% vs.1.7%) (National Statistical Office, 2017).

Tobacco smoking is a risk factor in the development of dry eye (Agrawal, Jharawal, Paharia, & Bansal, 2018; Koh, 2016). Cigarette smokers have higher levels of lipid peroxidation than nonsmokers and this can disrupt the precorneal tear film (Frei, Forte, Ames, & Cross, 1991; Pré & Le Floch, 1990). Tear protein patterns are different in smokers which were correlated with an increase of dry eye related to subjective symptoms in smokers (Grus, Sabuncuo, Augustin, & Pfeiffer, 2002). However, research of the effect of smoking on dry eye, refractive error, and ocular measurements has not been conducted in a Thai population.

Tobacco smoke contains oxidizing agents that produce free radicals that cause cell damage and may play an important role in ocular pathogenesis (Bertram, Baglole, Phipps, & Libby, 2009). Smoking is a risk factor for atherosclerotic related aortic, coronary and cerebral circulations difficulties (Sarin, Austin, & Nickel, 1974). Previous studies reported that cigarette smoking showed little effect on blood velocity in the optic nerve head (Tamaki, Araie, Nagahara, Tomita, & Matsubara, 2000) and that smoking was not found to be a risk factor for the onset of primary openangle glaucoma (Wang et al., 2012) however, one report has noted a loss of retinal nerve fiber layer (RNFL) thickness in chronic, healthy, heavy cigarette smokers (El-Shazly, Farweez, Elewa, Elzankalony, & Farweez, 2017).

2. Objectives

The objectives of this study are to compare anterior and posterior segment parameters measurements; spherical refractive error; and dry eye measurements in smoking and non-smoking Thai men.

3. Materials and methods

3.1 Studied subjects

This observational study used a crosssectional design that included smokers and nonsmokers. Potential subjects were recruited from Rangsit University and the neighboring community of Patumthani by posters and social media. All subjects were Thai men because smoking is unusual among Thai women. Those with systemic, ophthalmic diseases, use of any medications, history of ocular surgery or contact lens use were ineligible for the study. Participants were not involved in the design of this research.

3.2 Data collection

All smokers were requested to complete a smoking history questionnaire that determined their eligibility to participate in the study. The questionnaire captured the duration of smoking in years and the typical number of cigarettes smoked per day. Those with a history of smoking cigarettes less than two years were excluded. Those who smoked for at least 2 years before the time of study were included with age-matched nonsmokers. A total of 145 smokers and 147 healthy non-smokers were included in the study.

All participants underwent a physical examination including blood pressure, height, weight and medical history by questionnaire, conducted by one optometrist who was blind to the smoking status of all participants. The body mass index (BMI) was calculated as weight in kilograms divided by the height in meters squared. Refractive error and corneal curvature were measured by an autorefractometer (model: PRK-5000; Potec, Daejeon, South Korea). Intraocular pressure (IOP) was measured by using a non-contact tonometer (model: TX-20P, Canon, Japan). The central corneal thickness (CCT), anterior chamber depth (ACD), anterior chamber angle (ACA), anterior chamber volume (ACV), macular thickness, retinal nerve fiber layer (RNFL) thickness and cup to disc ratio were measured with a High Definition Optical Coherent Tomography (HD-OCT, model: CIRRUS 5000 Zeiss, Germany).

Dry eye parameters were determined by tear break-up time (TBUT) and Schirmer's test I. TBUT was determined first by using a fluorescein strip wetted with a single drop of saline solution and applied to the lower bulbar conjunctiva. Participants were asked to blink several times and the cornea surface was viewed on a biomicroscope with the cobalt blue filter. The duration between the last blink and the appearance of the first dark spot was measured in seconds by stopwatch. The Schirmer test I was measured by Schirmer strips without using anesthetic. A Schirmer strip was placed per manufacture instructions and left in place for 5 minutes before measuring the length of wetting in millimeters.

All steps of the examination were conducted and recorded on right eyes and then left eyes respectively. Several optometrists collected data. Each optometrist was responsible for one instrument or measurement and each measurement was made by one optometrist only. All optometrists where blind to the participant's smoking status.

3.3 Data analysis

Data were double entered. Descriptive statistics were determined by the Kolmogorov– Smirnov test and shown as mean \pm standard deviation (SD) or median \pm interquartile range (IQR). As there were no significant differences between the measurements of right and left eyes, left eye data is presented here. The comparisons between smokers and non-smokers in reference to demographic data, dry eye and ocular parameters were assessed with an independent t-test or Mann-Whitney U test. The statistical significance was *P*-value \leq 0.05. All data analyses were performed in the SPSS 17.0 software.

3.4 Ethical approval

This study adheres to the tenets of the Declaration of Helsinki and was approved August 2017 by the Ethical Committee form the Institutional Review Board at the Research Institute of Rangsit University in Thailand (Project No. RSEC 03/2560). Participants were given full verbal and written explanations about the purpose of the study and its consequences, with confirmation regarding the confidentiality of data. A signed informed consent was obtained from all participants.

4. Results

No significant differences were found between the 145 smokers and the 147 non-smokers in age, weight, height, BMI, systolic or diastolic blood pressure (Table 1). Among the smokers, the average number of years smoked was 18.63 (SD \pm 12.09) and the average number of cigarettes smoked per day was 9.05 (SD \pm 5.65).

Table 1	Demographic and he	ealth profile of	participating Thai ma	ale smokers and non-smokers

Parameters	Smokers	Non-smokers	P value
Number of subjects	145	147	
Age (years old)	36.00 ± 23.00	37.00 ± 24.00	0.573ª
Weight (kg)	70.00 ± 16.75	70.00 ± 17.50	0.520ª
High (cm)	170.00 ± 9.00	170.00 ± 9.00	0.983ª
Body mass index; BMI (km/m ²)	24.97 ± 4.01	24.71 ± 4.00	0.610 ^b
Systolic blood pressure (mmHg)	130.00 ± 15.41	129.29 ± 15.32	0.690 ^b
Diastolic blood pressure (mmHg)	86.21 ± 13.09	85.28 ± 12.35	0.516 ^b
Smoking duration (years)	18.63 ± 12.09		
Number of cigarette (day)	9.05 ± 5.65		

^aIndependent Student's *t*-test

^bMann-Whitney U test

Table 2 provides ocular and dry eye parameters in smokers and non-smokers. Average spherical refractive error findings differed by one quarter of a diopter between smokers -0.13 D (SD \pm 1.38) and non-smokers -0.38 D (SD \pm 1.88) but this finding was not found to be significant (p = 0.068). No significant differences were found between smokers and non-smokers in IOP, corneal curvature, CCT, anterior chamber measurements,

macular thickness, RNFL or cup to disc ratio. The average TBUT among smokers was found to be two seconds less compared to non-smokers (5.00 seconds vs. 7.00 seconds, p < 0.001) and the average wetting found in the Schirmer test I among smokers was four millimeters less than compared to non-smokers (10.00 mm vs. 14.00 mm, p = 0.044).

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Parameters	Smokers (<i>n</i> = 145)	Non-smokers (<i>n</i> = 147)	P value
Ocular parameters			
Spherical equivalent (diopters)	-0.13 ± 1.38	-0.38 ± 1.88	0.068 ^b
Intraocular pressure (mm Hg)	13.00 ± 4.30	<i>13.10</i> ± <i>4.90</i>	0.460^{a}
Corneal curvature (mm)	7.79 ± 0.25	7.77±0.27	0.530 ^a
Central corneal thickness (µm)	547.22 ± 51.08	545.83 ± 38.50	0.888^{b}
Anterior chamber right-angle (degree)	34.00 ± 12.0	32.00 ± 13.00	0.095 ^b
Anterior chamber left-angle (degree)	30.35 ± 9.44	28.59 ± 8.83	0.100 ^a
Anterior chamber depth (mm)	2.97 ± 0.31	2.93 ± 0.45	0.825 ^b
Anterior chamber volume (mm ³)	22.65 ± 5.43	23.11 ± 4.17	0.689ª
Macular thickness (µm)	255.00 ± 21.00	255.00 ± 21.00	0.155 ^b
RNFL (µm)	99.00 ± 12.00	98.00 ± 13.00	0.377 ^b
Cup to disc ratio	0.57 ± 0.18	0.57 ± 0.19	0.394 ^b
Dry eye parameters			
TBUT (s)	5.00 ± 3.00	7.00 ± 3.00	$< 0.001^{b*}$
Schirmer test I (mm)	10.00 ± 20.00	14.00 ± 20.00	0.044 ^b *

 Table 2 Ocular parameters and dry eye in left eyes of Thai male smokers and non-smokers

RNFL = retinal nerve fiber layer

TBUT = tear bleak-up time

^aIndependent Student's *t*-test

^bMann-Whitney U test

*Statistically significant

As TBUT and Schirmer's Test I results both reduce with age, Table 3 provides a comparison of these values between smokers and non-smokers by 10-year age groups. The mean TBUT was lower for smokers compared to nonsmokers, in every 10-year age strata. These differences were significant in all strata except the 41-50 years age group. The mean millimeters of wettability found in the Schirmer I Test was also consistently lower in the smokers compared to the non-smokers in each 10-year strata, but none of these differences were found to be significant.

Table 3 Comparison of TBUT and Schirmer test I between Thai male smokers and non-smokers by 10-year age groups

Age range	TBUT (S)			Schirmer test I (mm)		
(years)	Smokers (n)	Non-smokers (n)	P value	Smokers (n)	Non-smokers (n)	P value
20 - 30	$5.69 \pm 1.76\ (54)$	$7.24 \pm 1.60\ (54)$	$< 0.001^{a*}$	$18.54 \pm 11.73 \ (54)$	$20.72 \pm 11.61 \ (54)$	0.333 ^a
31 - 40	5.47 ± 1.83 (36)	$7.24 \pm 1.60\ (27)$	0.004^{a*}	14.25 ± 11.67 (36)	16.67 ± 11.61 (27)	0.418ª
41 - 50	$5.50 \pm 2.74 \; (34)$	$6.16 \pm 2.29~(38)$	0.272ª	12.62 ± 11.19 (34)	16.71 ± 11.58 (38)	0.133ª
51 - 60	4.81 ± 2.25 (21)	$6.57 \pm 2.91 \ (28)$	0.026 ^a *	8.14 ± 9.00 (21)	9.36 ± 7.41 (28)	0.607ª

TBUT = tear break-up time

^aIndependent Student's *t*-test

*Statistically significant

Among smokers in the 20-30 years age group, there was no difference in TBUT for those who have smoked 5 years or less compared to those who have smoked more than 5 years (5.86 ± 1.46)

sec. vs. 5.58 ± 1.94 sec., respectively, p = 0.57) but there was a significant difference in the wettability of the Schirmer I test between those have smoked 5 years or less compared to those who smoked more than 5 years (22.52 ± 10.75 mm vs. 16.00 ± 11.77 mm, respectively, p = 0.05). This analysis was not possible in the older age groups due to lacking participants who have smoked 5 years or less.

5. Discussion

To the best of our knowledge this is the first study to assess possible associations between anterior and posterior ocular parameters, and spherical equivalent refractive error in any population. To the best of our knowledge this is the first study to assess dry eye measurements among smokers and non-smoking Thai men.

We found no difference in the CCT between Thai smokers and non-smokers, similar to a study conducted in Turkey (Yildirim, 2015). We found no difference in the thickness of RNFL between smokers and non-smokers. This is in line with the findings of El-Shazly et al. who reported the average RNFL thickness to be similar between active smokers and passive smokers excluding for the superior and inferior of RNFL thickness (El-Shazly et al., 2017). Teberik related the thickness of temporal and inferonasal quadrants less than in smoker when compared with controls, but no difference in the average RNFL thickness (Teberik, 2019). Differences in the thickness of RNFL of our study and others may be because of instrumentation and software differences and as axial length was not considered. We found no significant difference in the macular thickness and cup to disc ratio between groups, similar to the findings of others (Teberik, 2019).

To the best of our knowledge, this is the first study to investigate smoking and anterior chamber measurements in any population. We found no difference in anterior chamber angles, depth or volume between smokers and nonsmokers.

The smokers in our study were 0.25 D less myopic than the non-smokers but this finding was not significant. Yildirim et al., 20215, also found no differences in the spherical equivalent refractive error between smokers and non-smokers (Yildirim, 2015) but Khalaj et al., 2014, found the onset of presbyopia among smokers was earlier compared to nonsmokers (Khalaj, Gasemi, Barikani, Ebrahimi, & Rastak, 2014). If a hyperopic shift does occur among smokers, this may help account for earlier onset of presbyopia.

The literature is not consistent on the association between smoking and IOP. It has been

suggested that nicotine can cause rising blood pressure and IOP (Timothy & Nneli, 2007). It has also been suggested that smoking associated elevation of IOP is caused by increasing of blood viscosity and decreasing of peripheral ocular circulation due to an increasing of outflow resistance of episcleral vein affected to rise of aqueous humor outflow (Yoshida et al., 2014). However, several studies shown no difference in the IOP between smokers and non-smokers and that smoking is not a risk factor for primary open angle glaucoma (POAG) (Wang et al., 2012).

Thai men who smoke had significantly shorter TBUT (2.00 seconds, p < 0.001) and significant lower Schirmer test finding (4.00 mm, p)= 0.044) compared to non-smoking Thai men. The duration of smoking affected tear production in the youngest participants. In those age 20-30 yrs. those who smoked \geq 5 yrs. had an average 6.52 mm lower Schirmer I test result compared to those who smoked < 5 yrs (p = 0.05). In this study, the TBUT of both the smoking and non-smoking Thai men (5.00 and 7.00 seconds, respectfully) was found to be deficient (<10 seconds) (Yildirim, 2015) but the average Schirmer test result for both the smoking and non-smoking Thai men (10.00 and 14.00 mm, respectfully) were within the normal range of > 5mm (Yildirim, 2015).

Strengths of this study were that all examiners were masked to the smoking status of participants and with the exception of TBUT, all items were objectively measured in a standardized manner. Weaknesses of this study include that participants were all self-selected Thai men thus caution would be needed in extrapolating findings to a broader population. Our TBUT measurements were reliant upon subjective observations and thus may be difficult to reproduce with precision. Another limitation of this study was lack of the axial length and amplitude of accommodation measurements, which might provide further insight into possible ocular parameters or refractive error values difference between groups. Although the association between smoking and dry eye has previously been reported (Aktas et al., 2017; Altinors et al., 2006; Frei et al., 1991; Masmali et al., 2016; Thomas, Jacob, Abraham, & Noushad, 2012; Yoon, Song, & Seo, 2005) our study confirms this finding among Thai men.

Additional research is needed. Studies with larger samples sizes need to be conducted to determine if any association exists between smoking and refractive error. These studies should include axial length measurements and should take into account amplitude of accommodation. Studies on ocular parameters that affect refractive error are needed that include measurement of plasma nicotine levels or plasma free radicals.

6. Conclusion

Smoking is significantly associated with loss of quality and quantity of the tear film in Thai men. Eye care providers have a public health role to play in informing smokers about the negative impacts of smoking on health and the eye.

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