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EFFECT OF ELECTRONIC CIGARETTES ON TEAR FILM IN SAUDI ARABIAN POPULATION BY USING SMTUBE AND NON-INVASIVE KERATOGRAPH

Saleh Alshammeri[1]*

[1]Department of Optometry, College of Applied Medical Sciences, Qassim University, Qassim, Buraydah, Saudi Arabia, email: srshmry@qu.edu.sa

Abstract:

Objective: To investigate the effect of e-cigarettes on the tear film by evaluating the tear film parameters of smokers compared to smokers among Qassim University students and workers.

Methodology: A total of 60 males participants of the age group 20-38 years old divided into three groups were recruited to this cross-sectional single-visit study. All subjects underwent four different tests parameters through the Keratograph 5M JENVIS, the tests included are tear meniscus height TMH, nun-invasive tear break-up time NITBUT, ocular redness OR and lipid layer thickness LLT. Ocular redness OR degree was evaluated qualitatively on a scale of 1-4, as 1 being normal, 2 as mild, 3 as moderate and 4 as severe redness. Subjects were asked to open their eyes widely and an image of the eye was captured for the evaluation. Data were analyzed using Statistical Package for Social Sciences (SPSS) with p value of less than 0.05 was considered as significant. Also, One-Way ANOVA has been used which compares the means of the three groups in the study to determine whether there is statistical evidence that the associated population means are significantly different, and T-test was used as a post hoc analysis if there is a difference between the groups.

Results: For this study total of 40 smokers were recruited with mean age of 32.55 ± 9.25. For comparison, 20 nonsmokers were selected with a mean age of 33.85 ± 11.35. Comparing the ocular surface disease index score we observed high mean scores among smokers and vapors (10.85 ± 5.96 and 10.3 ± 7.67 respectively) than nonsmokers (4.25 ± 4.48) with a significant mean difference of 0.001. Tear meniscus height between the three groups was similar without any statistically significant difference (p-value 0.213). Our observations revealed that smoking affects the tear volume by decreasing the mean volume from 6.3 ± 1.41 to 3.2 ± 2.16. We reported a significant difference among the three groups when comparing tear volume through the strip meniscometry tube (SMTube) test (p=0.00001).

Conclusion: A strong positive alarming association has been found between tear breakup time and eye dryness. To understand the impact of e-cigarettes on the eyes more thoroughly, cellular and molecular research into the health of the ocular surface is necessary.

Keywords: Tear film breakup, E-cigarettes, Saudi population

Introduction:

Smoking is a global problem associated with many ocular conditions. Chemicals like nitrosamines, hydrocarbons, and heavy metals are widely used in cigarettes and can cause damage to the ocular tissues.[1] According to the World health organization, tobacco is a silent killer of its consumers. In recent times, a new type of cigarette named E-cigarette introduced in the market which does not

contain tobacco and is considered safe.[2] In 2014 definition of E-cigarettes was published by the Food and Drug Administration (FDA) which defines it as a nicotine and chemical supplier which operates with batteries and is different from traditional smoking habits.[3] Initially, E-cigarettes were considered safe however researchers provide strong evidence of vaping side effects on the respiratory system. Despite the hazardous effects, vaping is still popular with young adults and families having strong social status.[4] E-cigarettes deliver nicotine, designed in an aerosolized to provide the real experience of smoking to its users. Each E-cigarette contained 0 to 24 mg or more nicotine according to the user preferences. The chemical composition of E-cigarettes shows fewer toxicant levels than conventional cigarette smoke.[5] Since 2005, the E-cigarette market expands to three billion dollars in global business with 466 brands and almost 8,000 different flavors. This market opens the doors to nicotine addiction among the young population. In 2012, a study revealed two times high consumption of E-cigarettes in North America, the European Union, and the Republic of Korea from 2008.[6] The study by Zhang et al[7] found that nicotine delivery through E-cigarettes depends upon the vaping technique, particle evolution, and cloud effects. However, studies found that high E-cigarette exposure may lead to dry eye.[8,9] Study shows that e-cigarettes or vaping damage the lipid layer of the pre-corneal tear film resulting in dry eyes.[9] However, there are not enough studies have been published about the effect of e-cigarettes on the tear film, and none have been conducted in the Qassim region. So, we designed this research to investigate the effect of e-cigarettes on the tear film by evaluating the tear film parameters of smokers compared to smokers among Qassim University students and workers.

Methodology:

A total of 60 males participants of the age group 20-38 years old divided into three groups were recruited to this cross-sectional single-visit study, 20 non-smokers, 20 tobacco smokers, and 20 vapors were enrolled in this cross-sectional study, ethical approval was obtained from Qassim University Ethics Committee for this study. Subjects who use contact lenses, eye lubricants, or any medications that could affect the eyes adversely, and passive smokers were excluded from the study. Chronic smokers and healthy individuals were included in the study. Tests were conducted during the morning and afternoon (8 am - 2 pm) and all subjects were given a written consent form prior to conducting the tests, dry eye symptoms questionnaire also has been given to the participants (Ocular surface disease index OSDI). The sample size was calculated based on the differences in tear breakup time in nonsmokers (11.28±1.27 seconds) and tobacco cigarette smokers (7.26±1.86 seconds),[10] which showed that four subjects in each group were sufficient to detect significant differences with a 95% confidence interval and 80% power. Data were analyzed using Statistical Package for Social Sciences (SPSS) with p-value of less than 0.05 was considered significant. Also, One-Way ANOVA has been used which compares the means of the three groups in the study to determine whether there is statistical evidence that the associated population means are significantly different, and the t-test was used as a post hoc analysis if there is a difference between the groups. All subjects underwent four different test parameters through the Keratograph 5M JENVIS, the tests included are tear meniscus height TMH, nun-invasive tear break-up time NITBUT, ocular redness OR, and lipid layer thickness LLT. TMH test was conducted by

measuring the tear height at the lower lid margin three times and taking the average of the three, subjects were asked to focus on a red dot of light, a height of more than 0.20 mm was considered as normal TMH, and less than 0.20 mm was considered as low TMH. NITBUT was also measured quantitively through K5M, subjects were asked to focus on the red dot of light and not to blink for about 25 seconds while recording, then the average was measured by the K5M. TUBT of 10 seconds or more was considered as normal BUT, and less than 10 seconds as low BUT. Ocular redness OR degree was evaluated qualitatively on a scale of 1-4, with 1 being normal, 2 as mild, 3 as moderate, and 4 as severe redness. Subjects were asked to open their eyes widely and an image of the eye was captured for evaluation. Assessment of LLT was done qualitatively in grading by a scale of 1-4 grades based upon the color hue of the corneal tear film layer that appears in the video recording [1 yellowish- grayish hue: lipid at equilibrium (normal), 2 reddish to bluish hue: high lipid abundance (mild), 3 grayish to whitish hue: mild lipid deficit (moderate), 4 very pale-whitish hue: significant lipid deficit (severe)], the subject is asked to blink multiple times during the recording, first two blinks are for the adjustment of focus for the rings reflected from the subject cornea. OSDI questionnaire score results of the answers were collected for each subject, the questionnaire consists of 12 multiple choice questions related to dry eye symptoms, each question has 5 answers and each answer has a score (all the time "4 score", most of the time "3 score", half of the time "2 score", some of the time "1 score", none of the time "0 score"). OSDI questionnaire score results were gathered and the average was taken for each group. The new strip meniscometry tube (SMTube) was used in this study as a test of tear production.

Results:

For this study total of 40 smokers were recruited. Out of these forty, 20 were using vaping with a mean age of 32.55 ± 9.25. For comparison, 20 nonsmokers were selected with a mean age of 33.85 ± 11.35. However, no significant difference was observed between the ages of these three groups (p-value 0.85) Comparing the ocular surface disease index score we observed high mean scores among smokers and vapors (10.85 ± 5.96 and 10.3 ± 7.67 respectively) than nonsmokers (4.25 ± 4.48) with a significant mean difference of 0.001. Tear meniscus height between the three groups was similar without any statistically significant difference (p-value 0.213). The mean tear meniscus height in nonsmokers was reported as 0.272 ± 0.04, while in the smokers and vapors group we observed mean tear meniscus height of 0.255 ± 0.05 and 0.244 ± 0.04 respectively. The average tear breakup time was significantly decreased in both smokers and vapors group (10.15 ± 1.92 and 10.25 ± 2.65 respectively) than in nonsmokers (13.35 ± 2.36). A statistically significant difference was found when comparing the tear breakup time among the three groups (p=0.000041). Eye redness was increased in vapors (2 ± 0.83) however no significant difference was found among the three groups (p=0.071). Meanwhile, we observed that lipid lt increased from 1.45 ± 0.51 to 1.85 ± 0.48 after vaping. Our observations reported high lipid lt values in the vapors group (1.85 ± 0.48). However, no significant differences were found among the three groups (p=0.065). For the evaluation of tear volume, we performed a strip meniscometry tube (SMTube) test. Our observations revealed that smoking affects the tear volume by decreasing the mean volume from 6.3 ± 1.41 to 3.2 ± 2.16. We reported a significant difference among the three groups when

comparing tear volume through the strip meniscometry tube (SMTube) test (p=0.00001). Table 1 reflects the detailed clinical outcomes.

Post-Hoc Analysis:

ANOVA test shows a significant difference in ocular surface disease index, tear breakup time, and tear volume among the three groups. On these three variables, we performed Tukey's HSD test for post hoc analysis. For the ocular surface disease index, we observed Tukey's HSD value of 4.70. A pairwise comparison of the ocular surface shows a significant difference between nonsmokers versus smokers (p value= 0.00375) and nonsmokers versus vapors (p value= 0.00845). These results indicate that ocular pressure increases due to nicotine consumption which causes vision dysfunction. Meanwhile, tear breakup time and volume were also reduced in nonsmokers vs smokers and nonsmokers vs vapors group (p value= 0.00018, 0.00028) and (p value= 0.00001 and 0).

Logistic regression analysis:

In logistic regression analysis, we observed a negative correlation between smokers and nonsmokers in terms of age, OSDI, redness, and lipid Lt (r= -0.02,-0.53,-0.3, and -0.13). A low positive correlation of tear meniscus height was observed between smokers and nonsmokers (r=0.18). However, comparing the results of nonsmokers and vapors, a negative correlation was observed in terms of the ocular surface index and eye redness. Cohen's d was measured to evaluate the mean difference between groups. Adjusted odd ratios were observed at a 95% confidence interval. Tables 5 and 6 enlisted the logistic regression analysis of Non-Smokers vs Smokers and non-smokers vs vapers.

Table 1: Demographic and Clinical characteristics of participants

Variables	Non-Smokers	Smokers	Vapors	F-ratio (Annova)	P-value
Age	33.85 ± 11.35	34.35 ± 11.09	32.55 ± 9.25	0.1534	0.85
Ocular Surface Disease Index (OSDI)	4.25 ± 4.48	10.85 ± 5.96	10.3 ± 7.67	7.01	0.001
Tear meniscus height (TMH) mm	0.272 ± 0.04	0.255 ± 0.05	0.244 ± 0.04	1.58	0.213
Tear breakup time (TBUT)	13.35 ± 2.36	10.15 ± 1.92	10.25 ± 2.65	12.13	0.000041
Redness	1.55 ± 0.51	1.95 ± 0.75	2 ± 0.83	2.766	0.071
Lipid Lt	1.45 ± 0.51	1.6 ± 0.59	1.85 ± 0.48	2.855	0.065
SMTube	6.3 ± 1.41	3.2 ± 2.16	3.1± 1.91	19.13	0.00001

Table 2: Post-Hoc Analysis of Ocular Surface Disease Index

Pair wise comparison	Tukey's HSD (C.I at 0.05 = 4.70)	Value for Q (C.I at 0.05 = 3.40)	P-value
Non smokers Vs smokers	6.60	4.77	0.00375
Non smokers Vs vapers	6.05	4.38	0.00845
Smokers Vs vapers	0.55	0.40	0.957

Table 3: Post-Hoc Analysis of Tear breakup time (TBUT)

Pair wise comparison	Tukey's HSD (C.I at 0.05 = 1.7771)	Value for Q (C.I at 0.05 = 3.40)	P-value
Non smokers Vs smokers	3.20	6.13	0.00018
Non smokers Vs vapers	3.10	5.94	0.00028
Smokers Vs vapers	0.10	0.19	0.98

Table 4: Post-Hoc Analysis of SMTube

Pair wise comparison	Tukey's HSD (C.I at 0.05 =1.4154)	Value for Q (C.I at 0.05 = 3.40)	P-value
Non smokers Vs smokers	3.10	7.45	0.00001
Non smokers Vs vapers	3.20	7.69	0.0000
Smokers Vs vapers	0.10	0.24	0.98

Table 5: Logistic regression analysis of Non-Smokers vs Smokers

Variables	Cohen's d	Pearson correlation	Adjusted odd ratio (95% C.I)
Age	-0.04	-0.02	-0.08 (-1.24, 1.08)
Ocular surface disease index	-1.25	-0.53	-2.27 (-3.54, -1)
Tear meniscus height (TMH) mm	0.38	0.18	0.68 (-0.49, 1.85)
Tear breakup time (TBUT)	1.49	0.6	2.7 (1.39, 4.01)
Redness	-0.62	-0.3	-1.13 (-2.32, 0.06)
Lipid Lt	-0.27	-0.13	-0.49 (-1.66, 0.67)
SMTube	1.7	0.65	3.08 (1.73, 4.44)

Table 6: Logistic regression analysis of Non-Smokers vs Vapers

Variables	Cohen's d	Pearson correlation	Adjusted odd ratios (95% C.I)
Age	0.13	0.06	0.23 (-0.93, 1.39)
Ocular surface disease index	-0.96	-0.43	-1.75 (-2.97, -0.52)
Tear meniscus height (TMH) mm	0.7	0.33	1.27 (0.07, 2.47)
Tear breakup time (TBUT)	1.24	0.53	2.24 (0.97, 3.51)
Redness	-0.65	-0.31	-1.18 (-2.38, 0.01)
Lipid Lt	-0.81	-0.37	-1.47 (-2.67, -0.26)
SMTube	1.91	0.69	3.46 (2.06, 4.86)

Discussion:

According to the National Eye Institute, dry eye is classified into Aqueous tear deficiency (ATD) which is characterized by inadequate aqueous production by the lacrimal gland, and Evaporative tear deficiency (ETD) in which tears are evaporated easily due to insufficient lipid layer production by the Meibomian glands, ETD comprises the majority of dry eye patients.[11] The Tear film is a critical component part for the anterior ocular segment, it comprises a protective shield for the eye from any foreign bodies or bacterial infections, tear film also functions as a nutrient provider for the cornea and as a lubricant for the anterior ocular surface.[12] The tear film consists of three layers; mucus, aqueous, and lipid layers, any disturbances to these layers could cause an abnormality called Dry Eye, which is a condition defined as a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface.[13] There are many factors that could cause any of the symptoms associated with the dryness of the ocular surface, such as high-temperature weather, low humidity, chronic allergies, aging, and even smoking. Active and passive smoking "the exposure to the cigarette smoke in a smoking environment" has been proven that it could cause affect tear film stability. Smoking is considered one of the factors that could lead to dry eye symptoms. Many toxic substances are there in a single cigarette that may be related to the effect of the cigarette on systemic & ocular health, and since the emergence of the electronic cigarette fifteen years ago, it has been used widely around the world that fact they contain less nicotine and other toxic substances.[14]

This study was conducted to evaluate the effect of E-cigarettes on the tear film of the Saudi Arabian Population. To our knowledge, this is the first Saudi study using Smtube And Non-Invasive Keratograph. A previous study by Althobaiti[15] revealed 26.3% consumption of E-cigarettes among Saudi citizens. Their study revealed a significantly high prevalence of smoking tobacco (p value=0.002) in between 18 to 24 years age group.

The ocular surface of the human eye is fully covered with the tear film. This tear film plays a crucial role in the nutritional route for corneal epithelium. A Study revealed that smoking contains more than 4000 toxic minerals and matters which cause ophthalmological disorders especially dry-eye disease.[16] In our study, we observed that the majority of the smokers lie in the mean age group of 32.55 years similar to the previous study of Agrawal[17]. A meta-analysis highlights the several pathogeneses of dry eye including chronic inflammation of the ocular surface, low sensitivity of the cornea, and low production of tears and. stability.[18] A study by Kjaergard and colleagues[19] conducted a study on tobacco workers. They found a high degree of ocular irritation among them. In the current study Keratograph the 5M, JENVIS test was performed to evaluate the OSDI score. We observed that the ocular surface disease index score increases up to 40% among smokers and vapors with a significant mean difference (p-value = 0.001).

In the past, several studies demonstrate an association between tear instability and smoking.[10,11,12] The majority of the studies found a strong association between tear instability in smokers. A study by Satici et al[9]., explores the effect of smoking on the ocular surface. They observed ocular surface epithelial damage in smokers groups due to direct contact of smoke with the ocular surface. Jetton's study[20] found that smoking interrupts the corneal wound healing process. However, Munsamy's study[21] found no effect of vaping on the pre-corneal tear film and corneal epithelial thickness. In our study, we observed a significant reduction in tear breakup time and tear volume among smokers and vapors than non-smokers. A previous study by Etter et al[22] found that e-cigarette users vaped an average of 175 puffs. Variations in the results may occur due to several puffs and the efficacy of the nicotine delivery per day. A recent study of Nishitsuka[23] found an increase in corneal thickness among Japanese smokers. Meanwhile, the study of Du et al[24] revealed that corneal epithelial thickness appears stable during the daytime. A study by Isa et al[13] observed mild to moderate eye dryness (25.0 [interquartile range, 14.6 to 43.7) in vapors as indicated by the ocular surface disease index. However, in our study, only 6 vapors reported mild to moderate eye dryness (Median IQ= 12.5).

This study has certain limitations in terms of a small sample size and missing demographic information. In this study, the number of E-cigarette puffs was not mentioned, along with missing information on vaping techniques. The corneal thickness of patients was not mentioned to construct reasonable results. There is a need to fulfill these gaps.

Conclusion:

In conclusion, we found that vaping effect the tear lipid layer of users which causes low tear breakup time, less tear volume, and may cause high incidents of dry eye. A strong positive alarming association has been found between tear breakup time and eye dryness. There is a need for strict checks and balances on E-cigarette consumption for controlling cases of vision impairments.

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