EVALUATION OF DRY EYE PARAMETERS AMONG ELECTRONIC CIGARETTE SMOKERS

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DISCLAIMER

I hereby certify that the work in this dissertation is my own except for the quotations and summaries which have been duly acknowledged.

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ABBREVIATIONS

ACM	Aerosol collected mass
CDC	Centers for Disease Control and Prevention
CEDARS	Cornea, External Disease and Refractive Society
DED	Dry eye disease
DEQ-5	Dry Eye Questionnaire
DEWS	Dry Eye Workshop
E-cigarette	Electronic cigarette
ETS	Environmental tobacco smoke
FDA	Food and Drug Administration
HTAA	Hospital Tengku Ampuan Afzan
HUSM	Hospital Universiti Sains Malaysia
IQR	Interquartile range
JEPeM	Jawatankuasa Etika Penyelidikan Manusia
MREC	Medical Research Ethics Committee
NEI	National Eye Institute
NMRR	National Medical Research Registry
OCT	Optical coherence tomography

OSD	Ocular surface disorder
OSDI	Ocular Surface Disease Index
PS	Power and Sample Size
SANDE	Symptoms Analysis in Dry Eye
SD	Standard deviation
SPEED	Standard Patient Evaluation of Eye Dryness
SPSS	Statistical Package for Social Sciences
TBUT	Tear break-up time
TFOS	Tear Film and Ocular Surface Society
TMH	Tear meniscus height
TPM	Total particulate matter
W	Watt

Abstrak

Pengenalan

Kemunculan rokok elektronik sebagai versi merokok yang “lebih sihat” kian menjadi sebutan baru-baru ini, terutamanya dalam kalangan dewasa muda. Walaubagaimana pun, pengetahuan mengenai potensi kesan rokok elektronik pada structure okular adalah terhad. Kajian ini menyiasat tentang kesan rokok elektronik pada parameter penyakit mata kering.

Objektif

Untuk menilai perubahan dalam purata parameter penyakit mata kering membandingkan pengguna rokok elektronik dengan bukan perokok, dan mengenalpasti korelasi antara parameter penyakit mata kering dan output kuasa rokok elektronik.

Methodologi

Kajian ini telah dijalankan secara keratan rentas dan lawatan tunggal daripada Januari 2021 hingga Jun 2022 di klinik mata Hospital Tengku Ampuan Afzan (HTAA) and Hospital Universiti Sains Malaysia (HUSM). 85 pengguna rokok elektronik yang berusia dalam ringkungan 18 hingga 45 tahun, menghadiri klinik berhenti merokok di HTAA dan HUSM atau kedai rokok elektronik sekeliling Kuantan, Pahang dan Kubang Kerian, Kelantan, serta memenuhi kriteria inklusi and exklusi telah dipilih. Satu lagi kumpulan merangkumi 85 peserta bukan perokok telah dipilih sebagai kumpulan kawalan. Pengguna rokok elektronik telah ditemubual mengenai tempoh penggunaan rokok elektronik, bilangan sedutan yang diambil setiap hari dan output kuasa rokok elektronik. Seterusnya, semua peserta menjalani penilaian parameter penyakit mata kering, yang termasuk soal selidik Ocular Surface Disease

Index (OSDI), ketinggian meniskus air mata, tear break-up time (TBUT), pewarnaan fluorescein pada kornea dan Schirmer's I test. Perubahan dalam purata parameter penyakit mata kering dibandingkan antara pengguna rokok elektronik dengan bukan perokok, dan korelasi antara parameter penyakit mata kering dan output kuasa rokok elektronik telah dikaji.

Keputusan

Semua peserta yang terlibat dalam kajian ini adalah lelaki. Purata umur dalam kumpulan pengguna rokok elektronik adalah 29.28±8.1 tahun, manakala kumpulan kawalan adalah 28.64±6.7 tahun. Keputusan median(Interquartile range (IQR)) skor OSDI adalah 0.00(0.00-6.25) dalam kumpulan pengguna rokok elektronik dan 0.00(0.00-2.08) dalam kumpulan bukan perokok (p=0.101). 32.94% pengguna rokok elektronik didapati mempunyai ketinggian meniskus air mata yang lebih rendah (<0.2mm) dibandingkan dengan hanya 5.88% bukan perokok (p<0.001). Perubahan ketara dalam purata TBUT didapati di kalangan pengguna rokok elektronik 10.41±2.65 saat berbanding dengan bukan perokok, 12.66±3.14 saat (p<0.001). Purata Schirmer's I test telah didapati lebih rendah dalam kalangan pengguna rokok elektronik 12.75±7.24mm, berbanding dengan bukan perokok, 20.02±7.98mm (p<0.001). Namun, perbezaan median skor OSDI dan pewarnaan fluorescein kornea di antara pengguna rokok elektronik dengan bukan perokok adalah tidak ketara (p=0.061). Korelasi positif (r=0.315, p=0.003) didapati antara skor OSDI dengan output kuasa rokok elektronik. Korelasi yang ketara telah diperolehi antara tanda mata kering dengan output kuasa rokok elektronik, di mana ketinggian meniskus air mata yang lebih rendah(r=-0.216, p=0.047), TBUT yang lebih singkat (r=-0.330, p=0.002), Schirmer's I test yang lebih rendah (r=-0.488, p<0.001) dan peningkatan dalam pewarnaan fluorescein kornea (r=0.378, p<0.001) telah dilaporkan apabila output kuasa rokok elektronik bertambah.

Kesimpulan

Perubahan ketara dalam purata ketinggian meniskus air mata, TBUT dan Schirmer's I test telah didapati dalam kalangan pengguna rokok elektronik berbanding dengan bukan perokok. Kenaikan output kuasa rokok elektronik menghasilkan lebih banyak gejala penyakit mata kering dengan skor OSDI yang lebih tinggi. Kenaikan output kuasa rokok elektronik jugak menghasilkan lebih banyak tanda penyakit mata kering, termasuk ketinggian meniskus air mata yang lebih rendah, TBUT yang lebih singkat, peningkatan dalam pewarnaan fluorescein kornea skor dan Schirmer's I test yang lebih rendah. Justeru, kesedaran berkenaan kesan buruk penggunaan rokok elektronik harus dibangkitkan dan penguatkuasaan mengenai larangan rokok eletronik harus dikaji semula.

Abstract

Introduction

The emergence of electronic cigarettes as the "healthier" version of smoking has been popular these days, especially among young adults. However, the knowledge about the potential effects of e-cigarettes on ocular structures is scarce. This study investigates on the effects of electronic cigarette smoking on dry eye parameters.

Objective

To compare the mean change in dry eye parameters between electronic cigarette smokers and non-smokers, and to correlate between dry eye parameters with device power output.

Methodology

This is a cross-sectional, single-visit study conducted between January 2021 to June 2022 in ophthalmology clinics of Hospital Tengku Ampuan Afzan (HTAA) and Hospital Universiti Sains Malaysia (HUSM). 85 electronic cigarettes smokers who aged between 18 to 45 years, attending quit smoking clinics of HTAA and HUSM, or electronic cigarette retail shops around Kuantan, Pahang and Kubang Kerian, Kelantan, and fulfilled the inclusion and exclusion criteria were recruited. Another group of 85 non-smokers were recruited as control. Electronic cigarettes smokers were being interviewed on electronic cigarette smoking duration, number of puffs taken per day and device power output used. Subsequently, all participants were evaluated on dry eye parameters, including Ocular Surface Disease Index (OSDI) questionnaire, tear meniscus height (TMH), tear break-up time (TBUT), cornea fluorescein staining and Schirmer's I test. Mean change in dry eye parameters was compared between

electronic cigarette smokers and non-smokers. Correlation between dry eye parameters with device power output was analysed.

Results

All participants recruited are males. The mean age of electronic cigarette smokers was 29.3±8.1 years, whereas the mean age for the non-smokers was 28.64±6.7 years. For dry eye symptoms (OSDI score), median (IQR) of 0.00(0.00-6.25) among the electronic cigarette smokers and 0.00(0.00-2.08) among the non-smokers were obtained (p=0.101). 32.94% of e-cigarette smokers were found to have a TMH<0.2mm, compared to only 5.88% of non-smokers with TMH<0.2mm (p<0.001). Significant change in mean TBUT was found between the e-cigarette smokers, 10.41±2.65 sec, and non-smokers, 12.66±3.14 sec (p-value<0.001). No significant change in the median corneal fluorescein staining score (p=0.061). Lower mean Schirmer's I test was found among electronic cigarette smokers, 12.75±7.24mm, compared to non-smokers, 20.02±7.98mm (p<0.001). OSDI score and device power output were found to have significant positive correlation (r=0.315, p=0.003). There was significant association between dry eye signs and device power output, in which reduced TMH (r=-0.216, p=0.047), TBUT (r=-0.330, p=0.002), and Schirmer's I test readings (r=-0.488, p<0.001), as well as increased corneal fluorescein staining (r=0.378, p<0.001) were reported with the increase in device power output.

Conclusions

There is significant mean change in TMH, TBUT and Schirmer's I test reading among electronic cigarette smokers compared to non-smokers. Higher electronic cigarette device power output results in more dry eye symptom with higher OSDI score. Higher electronic

cigarette device output also results in more dry eye signs, including reduced TMH, TBUT and Schirmer's I test readings, as well as increased corneal fluorescein staining. Therefore, concern should be raised on the risk of electronic cigarette use on ocular health and regulation on e-cigarettes ban should be revisited.

CHAPTER 1

INTRODUCTION

1.1 BACKGROUND OF STUDY

Ocular surface is the interface between the functioning eye and environment. It is the most environmentally exposed mucosal surface of the body. (Altinors et al., 2006) Tear film, which is the first refractive surface of the eye overlying the ocular surface, is important in providing optimum vision by maintaining its stability and protecting the corneal and conjunctival tissues. (Cheng et al., 2000) Dry eye disease (DED), also known as dry eye syndrome, is defined by Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop II as a multifactorial disorder of the ocular surface, characterised by eye discomfort and visual disturbance secondary to the loss of homeostasis and instability of the tear film, hyperosmolarity and inflammation of the ocular surface. (Craig et al., 2017)

Beaver Dam Eye study in 2000 showed that the prevalence of DED was 14.4% among the population aged between 48 to 91 years and a two-fold increase in the incidence of DED was found among smokers. (Moss et al., 2000) According to National Health & Morbidity Survey 2015 that report on smoking status among Malaysian adults aged 15 years and above, 22.8% of Malaysians are smokers, including both daily smoker and occasional smoker. Smoking has been known to be associated with a wide range of health-related problems, especially cardiovascular and respiratory diseases. The complex chemical composition of cigarette smoke, including free radical species, aldehydes, peroxides, epoxides, nitrogen oxides, peroxyl radical and other pro-oxidants may contribute to the pathogenesis of smoking-related health diseases.(E. R. Miller et al., 1997) Ocular-related adverse effects such as Graves' ophthalmopathy, age-related macular degeneration, glaucoma, and cataract were reported to be associated with tobacco smoking behaviour. (Cheng et al., 2000)

Electronic cigarettes (E-cigarette) usage has been on the rise in recent years. It has gained popularity among smokers as it has been presumed as a "healthier" version of tobacco cigarettes smoking with lesser side effects. (Md Isa et al., 2019) Conventional cigarette smokers are switching to e-cigarette as a substitute for combustible tobacco cigarette. However, little is known about the potential side effects of electronic cigarette usage. A rise in the numbers of e-cigarette users from 1.5% in year 2011 to 20.8% in year 2018 was previously reported among high school students in the United States.(Cullen et al., 2018) In 2019, a further increase in e-cigarette usage was seen with an estimation of 27.5% of high school students in the United States were found to have e-cigarette use. (Cullen et al., 2019) Similar pattern of e-cigarette usage rise was observed among Malaysian.

The emergence and rising trend of school aged adolescents who have been engaged with electronic cigarette smoking habit could be a potential health and environmental hazards. The exposure to e-cigarette among youths and young adults may results in nicotine addiction, impaired development of brain affecting cognition, attention and mood, illicit drug use and effects on psychosocial health. (United States. Department of Health and Human Services, 2016) Systemic side effects of electronic cigarette involve respiratory system, resulting in increased airway resistance, bronchiolitis, and lung carcinoma; cardiovascular system, resulting in increased diastolic blood pressure and acute myocardial infarction; and neurological system such as reversible cerebral vasoconstriction syndrome. (Hua and Talbot, 2016)

However, studies about effect of electronic cigarettes on ocular surface has been very limited. Md Isa et al. in her study found that e-cigarette users shared comparable adverse effects of

electronic cigarette use on dry eye symptoms and tear film integrity to that of conventional tobacco cigarette smokers. (Md Isa et al., 2019) Moderate to severe dry eye, reduced tear break up time (TBUT) level and lowered tear meniscus height (TMH) were discovered, suggesting poorer tear film quality among e-cigarette smokers. (Md Isa et al., 2019) This may suggest that electronic cigarette may risk for DED similar as conventional cigarette smoke despite it is believed to have less harmful constituents with absence of combustion by-products compared to tobacco cigarette.

1.2 DRY EYE DISEASE

The preocular tear film is made up of three layers.(Golden et al., 2022) The most superficial layer is the lipid layer, which is secreted by the meibomian glands, and functions to reduce aqueous layer evaporation. The middle aqueous layer is produced by both the main lacrimal gland and accessory lacrimal glands. The innermost mucin layer is produced by conjunctival goblet cells. Disturbance to the tear film may contribute to DED. DED can be divided into aqueous-deficient dry eye and evaporative dry eye, however the divisions of these two categories are not mutually exclusive.(Messmer, 2015) Aqueous-deficient dry eye can be divided into Sjogren syndrome or non-Sjogren syndrome dry eye.(Holland et al., 2013) Evaporative dry eye occurs due to excessive tear loss from the ocular surface in the presence of normal lacrimal secretory function.

1.3 PATHOGENESIS OF DED

In aqueous-deficient DED, reduction in tearing either basal or reflex tearing, due to dysfunction of lacrimal gland and accessory lacrimal glands, predisposes to ocular surface desiccation. The pathological causes include Sjogren syndrome, inflammation of lacrimal

glands, blockage of lacrimal secretion and medications such as decongestants, anti-histamines, and beta-blockers.(Golden et al., 2022) Evaporative DED can be divided into intrinsic or extrinsic causes. The examples of intrinsic causes are meibomian oil deficiency, increased exposure time of ocular surface due to disorder of lid aperture or low blink rate secondary to loss of corneal sensitivity, or drug action. (Holland et al., 2013)In evaporative form of dry eye with tear lipid deficiency, there is deficiency of the two polar lipids, phosphoethanolamine and sphingomyelin, which results in pathological change in composition of lipid layer of tear film in various form of meibomian gland dysfunction, and thus results in tear film instability. (Sangwan and Tseng, 2001) Extrinsic causes of evaporative dry eye comprises of contact lens wear, vitamin A deficiency, drug preservatives, or allergies. (Holland et al., 2013)

1.4 ASSESSMENT OF DED

A variety of clinical assessments are available to aid the diagnosis of DED. Symptoms of DED can be elicited with the use of Ocular Surface Disease Index (OSDI) questionnaire to evaluate dry eye symptoms and the effects on patient's vision-related function. Other questionnaires available are Dry Eye Questionnaire (DEQ-5), and Symptoms Analysis in Dry Eye (SANDE). (Golden et al., 2022) Tear film stability can be assessed with TBUT measurement. TMH, Schirmer's test and phenol red test are designed to measure tear volume and are easily accessible to general ophthalmologists. Other ocular surface assessments include meibomian gland evaluation with meibography, fluorescein staining and Lissamine green staining.(Golden et al., 2022) Various diagnostic tear film imaging can be offered such as optical coherence tomography (OCT) for evaluation of tear meniscus and functional tear analysis light scatter, corneal topography, impression cytology and serologic testing of autoantibody biomarkers for diagnosing a systemic condition. (Holland et al., 2013; Milner et

al., 2017) It lies in the fact that some of the diagnostic tests have low specificity and sensitivity with low reproducibility. Emergence of new diagnostic tools such as tear osmolarity, matrix metalloproteinase-9 analysis, comprehensive analysis of the tear film thickness and lipid, and confocal microscopy to evaluate ocular surface at the cellular level have added value in the diagnostic accuracy, however these are not widely available. (Wu et al., 2022)

1.5 TREATMENT OF DED

DED can be very distressing to patient. Thus, management of DED follows a step-wise approach according to the severity of disease. Thorough patient education and counselling on environmental modification such as reduce screen time, avoid direct airflow area, are helpful to reduce symptoms and prevent recurrences. Besides, topical eyedrops with preservatives can be the source of ocular irritation. Minimize the usage of eyedrops with preservative and use of preservative free eyedrops would be beneficial in treatment of DED.

1.5.1 Medical Treatment

The use of ocular lubricants are usually the first line treatment to provide support and replenish the tear film, as well as promote epithelium regeneration. Different lubricant product may contain one or more of the following ingredients such as hyaluronate, carboxymethylcellulose, dextran, glycerin, hypromellose, propylene glycol, polyvinyl alcohol, and paraffin. (Jones et al., 2017) Traditional treatment of meibomian gland dysfunction include lid hygiene with lid scrubs or lid wipes, warm compression and frequent expression of the glands. (Jones et al., 2017; Messmer, 2015) Next step for treatment of DED includes night-time ointment, moisture goggles, anti-inflammatory medications, oral antibiotics such as tetracycline and doxycycline, and intense pulsed light therapy. (Golden et al., 2022; Lee et al., 2020) Weak steroid can also