Araştırma Makalesi (Research Article)

Dumansız Tütünün Ön Segment Parametreleri Üzerindeki Akut ve Kronik Etkisinin Değerlendirilmesi

Evaluation of the Acute and Chronic Effect of Smokeless Tobacco on Anterior Segment Parameters

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ÖZET

Amaç: Dumansız tütün (DT) kullanımının oküler ön segment üzerine akut etkisinin optik biyometri ile değerlendirilmesi.

Gereç ve Yöntemler: Dumansız tütün kullanan, herhangi bir sistemik ve oküler patolojisi olmayan 32 bireyin 32 sağ gözü çalışmaya dahil edildi. Bireylerin tam bir oftalmolojik muayenesinden sonra optik biyometri ile baseline ölçümü gerçekleştirildi. DT kullanımından sonra 5. Dk, 30. Dk ve 60. Dk da optik biometri ölçümleri tekrar edildi. Bu ölçümlerde, Santral kornea kalınlığı (SKK), ön kamara derinliği (ÖKD), lens kalınlığı (LK), pupiller çap (PÇ) ve aksiyal uzunluk (AU) da oluşan akut değişimler incelendi.

Bulgular: Dumansız tütün kullanımı öncesi ve kullanımdan sonraki ortalama SKK, AU, ÖKD ve LK açısından istatistiksel olarak anlamlı fark saptanmadı (sırası ile p=0.62, p=0.72, p=0.77, p=0.72). PÇ açısından ST kullanımı ile oluşan değişimler için istatistiksel olarak anlamlı fark saptanmıştır (p<0.01).

Bu farklılık DT kullanımı öncesi ile kullandıktan sonraki 5.dk ile 30.dk arasında anlamlı iken 60.dk da ki ölçüm arasında anlamlı görülmedi (sırası ile p<0.01, p<0.01, p=0.71). DT kullanımı sonrası 5.dk ile 30.dk ve 60.dk arasında anlamlı fark bulundu (sırası ile p<0.01, p<0.01). Benzer olarak 30.dk ile 60.dk arasında istatistiksel olarak anlamlı fark tespit edildi (p<0.01).

Sonuç: Dumansız tütün kullanımının akut olarak oküler ön segmentte SKK, AU, ÖKD ve LK üzerine etkisi görülememiştir. Fakat PÇüzerine belirgin etki göstermiştir. Bu etki nikotinin sempatik ve parasempatik sistemi etkilemiş olmasından dolayı kaynaklanmış olabilir. DT' nin bilinenin aksine daha zararlı olduğu görülmektedir. PÇ deki değişim günlük yaşamda zorluklar oluşturabilir.

Anahtar Kelimeler: Ön kamara, Optik biyometri, Pupiller çap, Dumansız tütün, Nikotin

Abstract

Objective: To evaluate the acute and chronic effects of smokeless tobacco (ST) on the anterior segment parameters using optical biometry.

Material and Methods:The comparativestudy included 53 right eyes of 53subjects (study group), who used ST and 54 right eyes of 54 healthy subjects without ST (control group). Following a full ophthalmological examination, baseline measurements were taken with optical biometryand these measurements were repeated at 5, 30 and 60 mins after using ST. Central corneal thickness (CCT), anterior chamber depth (ACD), lens thickness (LT), pupillary diameter (PD), and axial length (AL) were measured.

Results: No statistical difference between the control group and study group in terms of CCT, AL, ACL and LT (p=0.771, p=0.706, p=0.546, p=0.984, respectively) however, PD values were statistically significantlydifferent (p=0.040) in baseline measurements. In the study group, similary, no statistically significant difference was determined between the measurements taken before and after ST use in respect of CCT, AL, ACD, and LT (p=0.660, p=0.058, p=0.344, p=0.059, respectively). The changes in the PD value with the use of ST were determined to be statistically significant (p<0.01). Thus, the difference in PD value was found to be statistically significant between 5 and 30 mins, between 5 and 60 mins, and between 30 and 60 mins after ST use (p<0.01, p<0.01, p<0.01 respectively).

Conclusion: ST use did not show any acute and chronic effect on CCT, AL, ACD and LT. However, there was seen to be a significant effect on PD.

Keywords: Anterior chamber,optical biometry, pupillar diameter, smokeless tobacco, nicotine.

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INTRODUCTION

Tobacco products are used by approximately 1.5 billion people worldwide (1). The use of tobacco is in the form of cigarettes or smokeless tobacco (ST), and it has been reported that more than 300 million people use ST (2). Tobacco use is the most important cause of preventable deaths throughout the world. Approximately 5 million people per year die because of tobacco use (1).

ST use is applied from oral or nasal mucosa (3). Although it is well known in under-developed countries, such as in southeast Asia in particular, it is also used in several countries such as the USA under different names (gutka, bibi, snuff, snus, naswar, gul, maras weed, etc.) (1,3).

There is increasing worldwide use of ST as it is cheap, easily available and most importantly, oral use is believed to be less harmful than cigarettes. While 3% of adults in the USA use ST, this rate is 30% in Scandinavian countries (1). In Turkey, the most concentrated use of ST (Maras Powder) is in the East Mediterranean region with reported rates of use between 4% and 16.8% (2,3).

ST is obtained by drying the leaves of the wild tobacco plant (Nicotiana rustica linn) and mixing these with oak and walnut ash. The nicotine concentration in this tobacco plant is approximately 6-10 fold higher than that of the tobacco used in cigarette production. By wetting the mixture, the wetness ratio is increased to increase absorption from the oral mucosa (4-6). The mixture is used by placing a small amount (up to 1 gr) inside the mouth between the gums and the lower or upper labial mucosa, or sometimes below the tongue (6,7).

Nicotine is the primary active component responsible for the acute pharmacological effect of tobacco products (1,8). It is known to increase heart rate by stimulating the sympathetic system in the body, increase blood pressure and increase psychomotor activities (8,9). It may also create a parasympathetic activity with a nicotinergic cholinergic effect (8).

There are studies in the literature which have investigated the effect on ocular vascular structures of cigarettes, which are known to be the most widely used tobacco products (9,10).However, few studies have examined the effect of nicotine on ocular anterior segment parameters (11-13). To the best of our knowledge, there have been no previous studies on the effect of ST on ocular anterior segment findings. Therefore, this study aimed to evaluate the acute and chronic effect of ST, which has a higher ratio of nicotine, on the anterior segment parameters.

MATERIAL and METHODS

Study Design and Participants

Approval for this observational, comparative, cross-sectional study was granted by the Local Ethics Committee (decision no: 285, dated:24-2018/12) and was conductedin accordance with the Declaration of Helsinki. Registered at Clinical Trial Registry (ClinicalTrials.gov Identifier: NCT04776863). The study subjects were enrolled from those who presented at the tertiary clinic with no ocular pathology (Between March and July 2020, Department of Ophthalmology, Kahramanmaras Sutcu Imam University Medical Faculty). Informed consent was obtained from all the study participants.Fifty-three right eye of 53 individuals using at least 5 years/packes ST between the ages of 28-48 were included in the study group. For the control group, 54 right eyes of 54 individuals who were not using ST between the ages of 26-49 were included.Subjects were excluded if they had spherical error higher than ±3 diopters and/or cylindrical defect error than ±2 diopters. Other exclusion criteria were any systemic disease (diabetes, hypertension, neurological, etc.) that can affect the ocular anterior segment, the use of topical or systemic medication, ocular trauma, a history of ocular surgery, the presence of glaucoma or optic disc abnormalities orany congenital oracquired eye disorder, or alcohol, cigarette, or substance dependence.

All the study subjects underwent a full ophthalmological examination. Best visual acuity was measured with the snellen chart and those with full vision level were included in the study. Biomicroscopic examination, intraocular pressure measurement with non-contact tonometryand fundus evaluation were performed. The anterior segment parameter measurements were taken with optical biometry.

Each subject was questioned in respect of for how many years and how many times a day they used ST. Before taking the optical biometry measurements, the subjects were questioned as to whether they had used ST, drunk anything containing caffeine or smoked cigarettes in the previous 12hours, and those who had were excluded from the study.

Following baseline optical biometry measurements, each subject was given 1mg ST and the optical biometry measurements were repeated after 5, 30 and 60 mins. Until the measurements were completed, the study participants were instructed not to have any food, drinks containing caffeine, cigarettes or to take any medicine and exercise was also restricted in this period. Single measurementwas performed with optical biometry in the control group. To avoid diurnal variations, the measurements were taken in the morning between 09.00 and 12.00 hours.

Optical Biometry Measurement Techniques

Following the full ophthalmological examination, the measurements were taken in the same room under the same lighting conditions, without dilatation. A Lenstar LS900 (Haag-Streit Inc, Koeniz, Switzerland) non-contact optical biometer was used.These measurements can be repeated easily. The head was positioned correctly and the subject was instructed to look at the fixed blue light. All the measurements were taken by the same specialist (AÇ), and the mean of 5 consecutive measurements was calculated for use in the evaluations. The CCT, AL, ACD, LT, and PD values were calculated automatically by the device. Measurements were taken a total of 4 times for study group; before ST then at 5, 30 and 60 mins after ST. In addition, the control group was measured.

Statistical Analysis

Data obtained in the study were analysed statistically using SPSS for Windows vn. 22.0 software (Statistical Package for the Social Sciences). The conformity of the data to normal distribution was assessed with the Shapiro-Wilk test. Categorical data were analysed using the Chi-square test. In the group comparisons, it was seen that the data had a normal distribution. Independent T test was used to compare two independent groups. In the analysis of repeated dependent data, ANOVA with repeated measures test was applied. Post hoc analysis was performed of the difference between meaningful data. Bonferroni confidence intervals were used. Continuous data were stated as mean ± standard deviation (SD) values, and categorical data as number (n) and percentage (%). A value of p<0.05 was accepted as statistically significant.

RESULTS

Fifty-three right eyes of 53 healthy subjects, comprising 44 (83%) males and 9 (17%) females with a mean age of 38.15±5.75 years (range; 28-48 years) were included in the study group. The mean period of ST use was 5±0.6 years/packets (range; 4-6). Fifty-four right eyes of 54 healthy subjects, comprising 44 (81.5%) males and 10 (18.5%) females with a mean age of 38.76±5.66 years (range; 26-49 years) were included in the control group. There was no significant difference between the groups in age and gender (p=0.583, p=0.836, respectively).Control and working groups were compared in terms of CCT, AL, ACD, LT and PD. No difference in CCT, AL, ACD and LT (p=0.771, p=0.706, p=0.546, p=0.984, respectively). There was significant difference in terms of PD (p=0.040) **(Table 1).** The mean CCT, AL, ACD, LT and PD were compared, respectively, in measurements taken before and 5, 30 and 60 minutes after ST. No statistically significant difference was determined between the time points in respect of CCT, AL, ACD and LT (p=0.660, p=0.058, p=0.344, p=0.059, respectively). The changes in PD as a result of ST use were determined to be statistically significant(p<0.01) **(Table 2).**The significance in PD between the measurements is shown in **Table 3.** The mean PD value was determined as 4.52±0.60 mm before ST, 4.23±0.51 mm at 5 mins after ST, 4.69±0.57 mm at 30 mins, and 4.56±0.55 mm at 60 mins. The changes in the PD value with the use of ST were determined to be statistically significant (p<0.01). The difference from baseline to 5 and 30 mins after the use of ST were seen to be statistically significant (p=0.003, p<0.01) but the difference from baseline to 60 mins was not significant

Table 1. Comparison of anterior segment parameters study and control group.

	Study Group (n1:53) (mean±SD)	Control Group (n2:54) (mean±SD)	*p*- value*
CCT(µm)	541.68±39.01	543.83±37.41	0.771*
AL(mm)	23.68±0.73	23.73±0.72	0.706*
ACD(mm)	2.77±0.36	2.81±0.36	0.546*
LT(mm)	4.05±0.21	4.05±0.21	0.984*
PD(mm)	4.52±0.60	4.29±0.53	**0.040***

n1: Number of people using ST
n2: Number of people non-using ST
CCT; Central corneal thickness, AL; Axial lentis, ACD; Anterior chamber deep, LT; Lens thickness, PD; Pupillar diameter, SD; Standart deviation.
**Independent T test.*
P value of <0.05 was considered as significant

Table 2. Comparison of anterior segment parameters before and after ST use.

	Before ST (mean±SD)	After ST 5.mn (mean±SD)	After ST 30.mn (mean±SD)	After ST 60.mn (mean±SD)	*p*- value*
CCT(µm)	541.68±39.01	538.68±37.43	541.85±38.79	541.21±37.05	0.660*
AL(mm)	23.68±0.73	23.56±0.84	23.69±0.73	23.70±0.72	0.058*
ACD(mm)	2.77±0.36	2.76±0.35	2.78±0.37	2.77±0.36	0.344*
LT(mm)	4.05±0.21	4.09±0.22	4.03±0.23	4.05±0.21	0.059*
PD(mm)	4.52±0.60	4.23±0.51	4.69±0.57	4.56±0.55	**<0.01***

CCT; Central corneal thickness, AL; Axial lentis, ACD; Anterior chamber deep, LT; Lens thickness, PD; Pupillar diameter, ST; Smokless tobacco, SD; Standart deviation.
**Repeated measurement* ANOVA test.
P value of <0.05 was considered as significant

Table 3. PD changes before and after ST use and showing differences between changes.

	n	Mean	SD	Minimum	Maximum	
$PD_{Before\ ST}$	53	4.52	0.60	3.49	5.71	
$PD_{After\ ST\ 5.mn}$	53	4.23	0.51	3.21	5.55	
$PD_{After\ ST\ 30.mn}$	53	4.69	0.57	3.67	5.76	
$PD_{After\ ST\ 60.mn}$	53	4.56	0.55	3.51	5.73	
	$PD_{Before\ ST}$-$PD_{After\ ST\ 5.mn}$	$PD_{Before\ ST}$-$PD_{After\ ST\ 30.mn}$	$PD_{Before\ ST}$-$PD_{After\ ST\ 60.mn}$	$PD_{After\ ST\ 5.mn}$-$PD_{After\ ST\ 30.mn}$	$PD_{After\ ST\ 5.mn}$-$PD_{After\ ST\ 60.mn}$	$PD_{After\ ST\ 30.mn}$-$PD_{After\ ST\ 60.mn}$
P value	**0.003***	**0.000***	1.000*	**0.000***	**0.000***	**0.002***

n: Number of people using ST
PD; Pupillar diameter, ST; Smokless tobacco, SD; Standart deviation.
*Post hoc, Pairwise Comparisons
Bonferoni confidence interval applied
P value of <0.05 was considered as significant

(p=1.000). The difference in PD value was found to be statistically significant between 5 and 30 mins, between 5 and 60 mins, and between 30 and 60 mins after ST use (p<0.01, p<0.01, p=0.002 respectively).

DISCUSSION

Nicotine, which is one of the basic pharmacological components of tobacco products, affects the central and peripheral nervous systems (1). It is known to increase heart rate, elevate blood pressure and make changes in the psychomotor activities of the body (9). Also, various ocular disorders such as thyroid ophthalmopathy, retinal vascular occlusion, and glaucoma, are associated with nicotine (13). Although few, there are also studies in literature related to the effect of nicotine and cigarette smokingon the corneal endothelium, pupil diameter and the lens (8,10-18).

The general public believes ST to be less harmful than cigarettes, and so to meet the need for nicotine when they are stopping smoking, many people may start to use ST in the belief that it is less harmful (6,7). In previous scientific studies to evaluate the effect of nicotine, cigarette-derived products containing mean 1mg nicotine have been given to subjects (8,12). However, the amount of nicotine in ST is 6-10 fold more than in cigarettes (2,7). There are studies in the literature that have investigated the effects of ST on the nervous system, the vascular system and the psychomotor system (1-3,7,19). Although there are studies showing the effects of cigarettes on the anterior segment parameters (8,11-18), there are no studies showing the effects of ST. Therefore, to the best of our knowledge, this is the first study to have reported the acute and chronic effect of ST on ocular anterior segment parameters.

In this study, the examination of the ocular anterior segment parameters was made with optical biometry. The acute effect of ST was evaluated on CCT, ACD, AL, LT and PD, and no significant difference was determined between the measurements taken before and after ST use in respect of CCT, ACD, AL and LT. In addition, there was no statical difference between control group and study group in terms of CCT, ACD, AL and LT.In studies that have compared smokers with a control group of non-smokers, generally no difference has been determined in respect of CCT (13,16).However, Wang et al. (20),reported that the CCT was thinner in chronic cigarette smokers, and suggested that this could be the result of cigarettes having impaired collagen synthesis. In the current study, a significant difference was determined between the PD measurements taken before and after ST use. Similarly, a statistical difference was found between working group and control group in terms of PD.As these were the first data evaluating PD in respect of ST, to be able to obtain some idea, they were compared with the results of studies conducted with cigarette smokers. Nevertheless, even if the smoke and toxic effects of cigarettes are discounted, the nicotine content of ST is approximately 6-10 fold higher than that of cigarettes (2-7).

The results of this study showed a significant decrease in PD at 5 mins after ST use compared to the measurements taken before ST use (4.23±0.51mm vs. 4.52±0.60mm).This was consistent with the findings of Erdem et al. (8), who suggested that the iris sphincter muscle was activated more by the parasympathetic system than by the sympathetic system. It has also been suggested that as a result of nicotine binding to nicotinic cholinergic receptors, the induced cholinergic activity causes myosis, resulting in parasympathetic activity in the iris sphincter muscle (12,14). It was similarly thought in the current study that the parasympathetic effect of the nicotinic receptors in the iris sphincter muscle was more predominant than the sympathetic effect in the early stage.In a study conducted by Bardak et al. (12), it was reported that no effect of cigarette smoking was determined on PD in the acute stage. In contrast, Sobaci et al. (14),reported that increased photopic PD was observed in chronic smokers compared to non-smokers. Similar to this study, we found PD larger in ST users compared to the control group. This was attributed to the fact that with the psychological relaxation experienced by chronic smokers after smoking, in a period of abstinence there could be inhibition of sympathetic activation (8,12).

An interesting finding of the current study was that the PD value at 30 mins after ST use (4.69±0.57mm) was greater than the measurement taken before ST use and at 5 mins after ST use. This could be attributed to a reduced effect of parasympathetic activity on the iris sphincter muscle as a result of the rebound effect and/or the reduced parasympathetic effect of the sympathetic effect resulting in an effect on the dilatator muscle. Sobaci et al. (14),found that PD was significantly high in the 8th minute in a group of smokers. It was assumed that this difference could be caused by autonomic neuropathy due to nicotine and increased PD below the photopic condition.

The PD measurement taken at 60 mins after ST use (4.56±0.55mm) was seen to be close to the measurement before use (4.52±0.60mm). It was thought that despite the 2-hour half-life of nicotine, this could have occurred because of a reduced effect on receptors in chronic ST users (21).

When all these effects were examined, as there was no other ocular anterior segment study in theliteratüre related to ST use, the data were compared with those of smokers. As the nicotine content of ST is approximately 6-10-fold greater than that of cigarettes (2-7), the differences may have been due to the higher ratio of nicotine.

There were some limitations to this study, primarily the low number of subjects and that measurements were not repeated after 60 mins until all the nicotine and metabolites had left the body. These metabolites were not evaluated in the blood or urine. However, this is the first study to have evaluated the ocular anterior segment about ST use and there were seen to be significant changes in PD. In particular, this change in PD could cause alterations in accommodation and aberrationin daily life. It would be useful to keep this in mind to avoid surprising changes associated with changes in PD size following surgery in patients planned to undergo refractive surgery and premium lens implantation. This study can be considered to contribute to the literature on this subject.

As a conclusion; The results of this study demonstrated that ST use showed a significant effect on PD. This effect may have shown a difference because the nicotine ratio of ST is much greater than that of cigarettes. It seems that ST effects on anterior segment parameters appear to be more harmful than what is publicly accepted. However, there is a need for further studies to make longer-term measurements in the determination of ocular effects until nicotine and metabolites are completely removed from the body.

Conflict of Interest and Financial Status

Our study has not been financed by an institution and institution. In this study, there is no conflict of interest among the authors on any subject

Research Contribution Rate Statement Summary

AB: Contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work.YK: Drafting the work or revising it critically for important intellectual content.AC: Literature review, data analysis.AM: Final approval of the version.

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