

**ORIGINAL
ARTICLE**

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Nasal Mucociliary Activity Changes In Smokers

ABSTRACT

Objective: Nasal mucociliary activity, which is a good indicator of nasal mucosal function, is one of the most important defense mechanisms of the body. The aim of the present study is to investigate the effect of smoking and cigarette consumption on nasal mucociliary activity per se by singling out other factors affecting nasal mucociliary activity.

Methods: One hundred ninety seven patients aged 18-55 years, one hundred twenty three smokers (case group) and seventy four non-smokers (control group), were included in the present study. Saccharin transfer time (STT) test, CO measurement, Fagerstrom Test for Nicotine Dependence, and a questionnaire including smoking characteristics were applied to all participants.

Results: No statistically significant difference was determined between the case and control group in terms of age and body mass index parameters affecting mucociliary activity. In the present study, a statistically significant difference was determined in the mucociliary transfer time between the case and the control group. Moreover, a positive correlation between saccharin transfer time (STT) and number of cigarettes smoked per day, STT and package-year, STT and total smoking years was also determined.

Conclusions: In conclusion, smoking has been in the present study determined to deteriorate nasal mucociliary system with a direct proportion to the amount and total duration of smoking.

Keywords: Smoking, Saccharin Transfer Time, Mucociliary Activity

Sigara İçenlerde Nazal Mukosilyer Aktivitedeki Değişimler

ÖZET

Amaç: Nazal mukosilyer aktivite nazal mukozal fonksiyonların iyi bir göstergesi olup vücut için önemli savunma mekanizmalarından birisidir. Bu çalışmanın amacı, nazal mukosilyer aktiviteyi etkileyen diğer faktörleri çalışma dışı bırakarak, sigara içiminin ve sigara miktarının nazal mukosilyer aktivite üzerindeki etkisini araştırmaktır.

Gereç ve Yöntem: Yüz yirmi üç sigara içen (vaka grubu) ve yetmiş dört sigara içmeyen (kontrol grubu) olmak üzere 18-55 yaş arasındaki toplam yüz doksan yedi hasta çalışmaya alındı. Tüm katılımcılara, sakarin transfer zamanı (STT) testi, CO ölçümü, Fagerstrom Testi ve sigara içme özelliklerini içeren bir anket uygulandı.

Bulgular: Vaka ve kontrol grubu arasında mukosilyer aktiviteyi etkileyen yaş ve beden kitle indeksi parametreleri açısından istatistiksel olarak anlamlı fark bulunmadı. Bu çalışmada, olgu ve kontrol grubu arasındaki mukosilyer transfer süresinde istatistiksel olarak anlamlı bir fark tespit edildi. Ayrıca, STT ile günde sigara içilen sigara sayısı, STT ve paket yılı, STT ve sigara içilen yıllar arasında pozitif bir korelasyon tespit edildi.

Sonuç: Sonuç olarak bu çalışmada sigaranın nazal mukosilyer sistemi bozduğu ve bu durumun içilen sigara miktarı ve süresiyle doğru orantılı olarak gerçekleştiği gösterilmiştir.

Anahtar Kelimeler: Sigara, Sakarin Transfer Süresi, Mukosilyer Aktivite

INTRODUCTION

Smoking is one of the most important health problems in the world, especially in developing countries like our country. According to the World Health Organization (WHO), around 1.3 billion people smoke in the world and more than five million people die annually from smoking (1,2).

Mucociliary system consists mainly of the ciliated epithelium, the mucus layer, and of glands that produce mucus (3). Ciliated epithelium is present in the nose tip, larynx, terminal bronchial branches, except the posterior oropharyngeal walls in all respiratory tract, paranasal sinuses, the eustachian tube, and in the major part of the middle ear (4).

The nasal mucociliary activity, a primary indicator of the nasal mucosal function, is an important defense mechanism of the body. Mucociliary clearance is the most important defense mechanisms of the nasal respiratory epithelium. Potentially toxic substances are isolated in this mucus layer and distanced from the nasal cavity through the mechatronic cilia movement (5). Mechanical and immunological cleaning of the air inhaled is realized by nasal mucociliary activity.

Various pharmacological agents affect this system besides pathological conditions such as acute or chronic rhinitis or nasal allergies (6, 7). Recurrent otitis media and frequent of upper and lower respiratory tract infection incidence increase due to the structural defects of the cilia such as Kartagener syndrome or immotile cilia, due to diseases leading to changes in mucus consistency such as cystic fibrosis, and due to viral diseases where ciliary activity is spoiled.

Smoking poses a significant risk for respiratory tract diseases such as lung cancer, chronic obstructive pulmonary disease, and upper respiratory tract infection (8).

Inhaled cigarette smoke disrupts the mucociliary clearance, the basic defense mechanism of the upper and lower respiratory tract. Smoke of cigarettes lead to decrease in number and activity of the cilia in the mucociliary clearance (9, 10).

The adverse effect of cigarettes on nasal mucociliary activity has been suggested in various studies. The aim of the present study is to determine the effect of smoking and the amount of cigarettes smoked per on nasal mucociliary activity.

MATERIAL AND METHODS

The protocol of this study was reviewed and approved by the Ethics Committee of Selcuk University (2016-009). The study was carried out in Selcuk University Family Medicine and Konya Training and Research Hospital Family Medicine polyclinics. One hundred twenty three patients who smoked to work were included in the case group and seventy four non-smokers (participant who has never smoked before) were included in the control group. Upon informing the patients about the study,

informed consent forms compatible with the Helsinki Declaration of World Medical Association were received from each. Age, BMI (Body Mass Index), and housing location of the participants in both groups were compatible. Exclusion criteria were alcohol abuse history, < 18 and 55 > years, Diabetes Mellitus, Rheumatoid Arthritis, Systemic Lupus Erythematosus, nasal and paranasal operation history, and the use of flunisolide, phenylephrine, epinephrine, lidocaine, atropine and antihistamines with an impact on ciliary activity and mucus structure. Furthermore, presence of chronic obstructive pulmonary disease, asthma, bronchiectasis, chronic bronchitis, upper and lower respiratory tract infections within the last two months, pregnancy, nursing mothers, concha bullosa, cystic fibrosis, Kartagener Syndrome, primary ciliary dyskinesia patients, septum deviation, turbinate hypertrophy, allergic rhinitis, atrophic rhinitis, chronic sinusitis, chronic otitis media, nasal discharge, and nasal polyps were the other exclusion criteria (11, 12).

CO (Carbon monoxide) measurement: CO measurements were performed in the expiration air by piCO Smokerlyzer Breath CO Monitor Bedfront Scientific England UK device. PiCO Smokerlyzer Breath device measures the level of CO in the expiration air between 0 and 100 ppm. CO level of $5 \leq$ ppm was non-smoking indicator (13).

Smoking characteristics: Whereas the Turkish version of the questionnaire proposed by Prochaska et al. (14) and used in the US for the evaluation, ranking, and classification of the stages of change in cessation of smoking and its characteristics was employed for all, Fagerstrom Test for Nicotine Dependence (FTND) (15) was used for the scoring and classification of smoking dependence.

Saccharin Transit Time test: Participants of the study were first examined by an Ear Nose Throat (ENT) specialist. Those who were considered eligible underwent saccharin test made by the same ENT specialist. Hereby, they were first asked to clean the secretions in their noses. Tests were made at room temperature (21-24 degrees Celsius) while the patient was sitting straight in the chair. A quarter saccharin tablets ($\frac{1}{4}$ of 12.5 mg hermesetas) was placed right behind the front end portion of the inferior turbinate in the left nasal cavity with the help of port cotton. A stopwatch was started and the participant was asked to sit still and not to sneeze or sniff, do any eating and drinking actions, and tilt forward until he could feel the taste. Every 30 seconds, the participant was asked whether he/she could feel the taste. The first time when the patient could feel the taste was recorded as mucociliary clearance time.

Statistical Analyses: SPSS (Statistical Package for the Social Sciences) 21.0 statistics package program was used to analyze the data

obtained using percentages, means, and standard deviations. Chi-square test, ANOVA test, Student-t test, Pearson correlations were conducted between the groups by handing out the frequency distribution of categorical data. A p-value of <0.05 was considered level for significance.

RESULTS

The present study has been conducted with 123 smokers in the case group with currently smoking individuals and 74 control group members who have never smoked. The mean age of the 197 participants was 39,75±9,22 years (min:20, max:55, median:40,0), mean BMI 27,84±4,78 kg/m² (min:18,94, max:40,27, median:27,63). Out of the participants 47,2% (n=93) were primary school, 12,7% (n=25) middle school, 18,3% (n=36) high school, 21,8% (n=43) college or university graduates. 5,1% (n=10) of the participants were living in rural areas and the remaining 94,9% (n=187) in the city.

The participants of the study were divided into two cohorts as the case (123 smoker) and control (74 non-smoker). Whereas the average age of the participants in the case group was 40.33 ± 8.94 years, of the control 38.79 ± 9.66 years. There is no statistically significant difference between the smokers and non-smokers regarding the variable of age (p = 0.259). Average BMI of the smokers was 27.34 ± 4.30 kg/m² and of the non-smokers 28.68 ± 5.41 kg/m² without a statistically significant difference between both groups. (p = 0.073). Regarding the variable of residence, 94.3% of the cases (n = 116) are living in the city center and 5.7% (n = 7) in rural areas. Out of the control group 95.9% (n = 71) are residing in the city center and 4% 1 (n = 3) out of the city again without a statistically significant difference between the smokers and non-smokers (p = 0.612) (Table 1).

Table 1. Demographic characteristics of the studied population

	Non-smoker (n=74)		Smoker (n=123)		t	p
	Mean±SS	Mean±SS				
Age (years)	38.79±9.66	40.33±8.94			1.132	0.259
BMI	28.68±5.41	27.34±4.30			-1.911	0.073
Residence						
City	71 95.9	116 94.3			0.257	0.612
Out of city	3 4.1	7 5.7				
Sex						
Female	58 78.4	23 18.7			67.968	<0.001
Male	16 21.6	100 81.3				
Total	74 100.0	123 100.0				

Out of the 123 smoking cases 46.3% (n = 57) had been graduated from primary schools, 13.8% (n = 17) from secondary schools, 23.6% (n = 29) from high schools, and 16.3% (n = 20) from higher education institutes. Out of the 74 participants in the control group, 48.6% (n = 36)

had been graduated from primary schools, 10.8% (n = 8) middle schools, 9.5% (n = 7) high schools, and 31.1% (n = 23) from higher education institutes. The outcomes of the statistical analyses made about graduation revealed a statistically significant difference between smokers and non-smokers (p = 0.018).

Out of the 123 people in the case group 12.2% (n = 15) were housewives, 47.2% (n = 58) workers, 13.0% (n = 16) civil servants, 19.56% (n = 24), private sector employees, 8.1% (n = 10) retired. Out of 74 people in the control group 50.0% (n = 37) were housewives, 8.1% (n = 6) workers, 36.5% (n = 27) civil servants, 1.4% (n = 1) private sector employees, 4.1% (n = 3) retired. In terms of profession there a statistically significant difference between the smoker and non-smokers (p<0.001).

Characteristics of the smokers related to their smoking habits are presented in Table 2. The mean beginning age of smoking is 15.57 ± 5.08 years, the amount of cigarettes per day is 18.45 ± 8.78. Smokers are smoking throughout a period of 24.31 ± 9.66 years. The average amount of packs consumed per year is 28.49 ± 15.68. Mean FTND scoring of the smokers is 6.82 ± 2.30.

Table 2. Characteristics of the Smokers

(n=123)	Mean ±SD	Med.	Min.	Max.
Onset of smoking (years)	15.57±5.08	15	7	30
Cigarettes/day	18.45±8.78	20	5	30
Years of smoking	24.31±9.66	24	3	48
Pack/years	28.49±15.68	27	10	110
FTND	6.82±2.30	7	1	10

Whereas the mean CO level of the smoking group was 5,82±3,30 ppm, of the nonsmoker group, it was 1,56±1,12 ppm revealing a statistically significant difference between the two groups regarding their CO levels (p<0.001) (Table 3).

Table 3. Comparison of saccharin clearance test time and CO levels between non-smokers and smokers

	Non-smoker (n=74) (Mean ± SS)	Smoker (n=123) (Mean ± SS)	t	P
CO levels	1.56±1.12	5.82±3.30	13.103	<0.001
Saccharin clearance test (min)	5.34± 3.08	8.93± 4.24	6.345	<0.001
Gender				
Female	5.14± 3.16 (n=58)	8.47± 3.75(n=23)	-3.754	0.001
Male	6.03± 2.73 (n=16)	9.04±4.36(n=100)	-3.708	0.001

The mean saccharin test measurement period of the case group participants in our study was 536.19 ± 254.81 seconds and of the control group 320.43 ± 184,98 seconds with a statistically significant difference between smokers and non-smokers (p<0.001). In terms of gender in both male

and female smokers, the saccharin test measurement time was prolonged revealing a statistically significant difference compared to non-smokers of the same sex ($p=0.001$) (Table 3).

Evaluation of Saccharin Test Results According to the Yearly Pack Consumption of Smokers Compared with Non-Smokers was seen in

Table 4. Evaluation of Saccharin Test Results According to the Consumption Years of Smokers Compared to Non-Smokers was seen in Table 5. Evaluation of Saccharin Test Results According to the Consumption Years of Smokers Compared to Non-Smokers was seen in Table 6.

Table 4. Evaluation of Saccharin Test Results According to the Yearly Pack Consumption of Smokers Compared with Non-Smokers

	Non smoker (n=74) (Mean ± SS)	0-20 Pack/years (n=35) (Mean ± SS)	20-40 Pack/years (n=65) (Mean ± SS)	40 Pack/years and ↑ (n=23) (Mean ± SS)	F	p
Saccharin clearance test time (min)	5.35± 3.10 ^a	7.66± 1.99 ^b	9.50± 3.89 ^c	9.26± 6.79 ^d	15.167	<0.001

a vs b= p value=0,020, a vs c= p value=0,000

Evaluation of Saccharin Test Results According to the Daily Cigarette Consumption of Smokers Compared to Non-Smokers was seen in Table 6. Correlation of Saccharine Test Results with Daily Consumption, Package a Year, Fagerstrom Test for Nicotine Dependence Scores,

and Total Consumption Period was seen in table 7. Comparison of saccharin test results time according to (a) smokers – nonsmokers, (b) package/year consumption, (c) total years of consumption, (d) daily consumption was seen in Figure 1.

Table 5. Evaluation of Saccharin Test Results According to the Consumption Years of Smokers Compared to Non-Smokers

	Non smoker (n=74) (Mean ± SS)	0-20 years (n=57) (Mean ± SS)	20-40 years (n=64) (Mean ± SS)	40 years and ↑ (n=8) (Mean ± SS)	F	p
Saccharin clearance test time (min)	5.34± 3.08 ^a	7.84± 2.16 ^b	9.78± 5.46 ^c	10.04± 3.13 ^d	16.579	<0.001

a vs b= p value=0,002, a vs c= p value=0,000, a vs d= p value=0,006

Table 6. Evaluation of Saccharin Test Results According to the Daily Cigarette Consumption of Smokers Compared to Non-Smokers

	Non smoker (n=74) (Mean ± SS)	0-20 cigarettes /day (n=65) (Mean ± SS)	20-40 cigarettes /day (n=54) (Mean ± SS)	40 cigarettes /day and ↑ (n=4) (Mean ± SS)	F	p
Saccharin clearance test time (min)	5.34± 3.08 ^a	8.71± 2,77 ^b	8.28± 3.63 ^c	11.02± 7.82 ^d	16.120	<0.001

a vs b= p value=0,000, a vs c= p value=0,001, a vs d= p value=0,000

Table 7. Correlation of Saccharine Test Results with Daily Consumption, Package a Year, Fagerstrom Test for Nicotine Dependence Scores, and Total Consumption Period

	Cigarettes/day		Pack/year		FTND		Years of smoking	
	r	p	r	p	r	p	r	p
Saccharin clearance test time	0.225	0.012	0.296	0.001	0.088	0.332	0.200	0.027

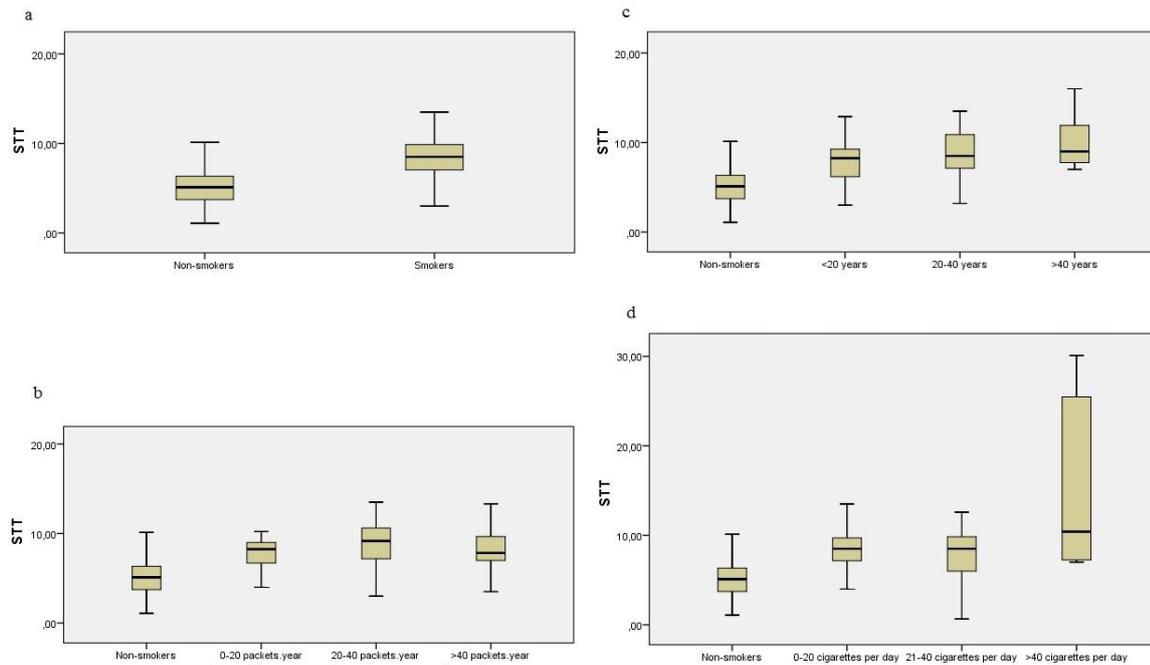


Figure 1. Comparison of saccharin test results time according to (a) smokers – nonsmokers, (b) package/year consumption, (c) total years of consumption, (d) daily consumption

DISCUSSION

Nasal mucociliary clearance is affected by various factors such as age, gender, tobacco, posture, sleep, exercise, environmental factors, and diseases (16). Tobacco consumption, as shown in previous studies, may lead to epithelial damage in the respiratory tract and to deteriorations in the immune system. Tobacco consumption contributes thus to increased susceptibility to infections (17-19). The aim of the present study was to show the negative impact of smoking on mucociliary clearance in smokers compared to non-smokers using more criteria for exclusion.

Studies on the effect of age on mucociliary clearance have reported different results different outcomes. Ho et al. (20) evaluated changes in nasal mucociliary clearance with saccharin test. They compared two groups, <40 and 40 > years, and determined prolonged mucociliary clearance time with increasing age. Kao et al. (21) reported that there were no statistically significant differences in nasal mucociliary clearance rate in people aged under and above 60 years old. In our study there was no statistical difference between the mean ages of the case and control groups indicating that there were no age related effects on saccharin transition time (STT).

Tamilselvan K. et al. have reported that patients with a high BMI had longer mucociliary clearance durations (22). In the present study no statistical difference between case and control group was determined with regard to BMI. Thus, in our study the impact of BMI on STT measured was excluded for the members of both groups participating.

Kao et al. have reported in their study that there were no statistically significant differences of mucociliary clearance rate measured in STT between the sexes (21). Likewise, the study of Tamilselvan K. et al. could not determine differences in nasal mucociliary clearance measurements between both sexes (23).

Baby et al. have reported statistically significant increase in STT of smokers compared to non-smokers in their study made in 2014 with 60 participants. They reported a statistically significant increase in STT parallel to prolonged total smoking period (24). Ramos E. M et al. also reported a significant increase in STT in their 2011 study made with a total of 66 patients in Brazil (25). Yadav J. et al. have investigated nasal mucociliary transportation time in 2014 in 150 people in India and determined that compared to nonsmokers, smokers had highly statistically significant prolonged times and in the group, compared to passive smokers, active ones had statistically significant prolonged mucociliary transportation times (11).

Cikojević D et al reported in their 2014 study conducted in Croatia with 176 smokers comparing mucociliary transportation time with old age and extended smoking history to younger age and shorter smoking histories that mucociliary transportation time was significantly slower in the former group (26).

Xavier RF. et al. have reported in their 2013 study conducted 75 participants in Brazil; medium (11-20 cigarettes / day) and heavy smokers (21 cigarettes / day) have longer STT compared with

light smokers (1-10 cigarettes / day) The same study also reported that there is a positive correlation between STT and the number of cigarettes smoked per day (27).

There are also other studies showing that the amount of cigarettes smoked per day, extends the duration of mucociliary transportation (11, 26).

In the present study, in line with the current literature, there are statistically significant differences between smokers and nonsmokers in terms of STT. A positive correlation was established between STT and the daily consumption of cigarettes, packs a year, smoking years.

Conditions affecting nasal mucociliary clearance such as diseases (inflammatory, infectious and allergic diseases) history of nasal surgery, and use of medications (antihistamines, epinephrine, lidocaine) were the exclusion criteria. As the variables of age, BMI were similar between both groups, the impact of smoking is seen more clearly in the present study investigating the effects of smoking on nasal mucociliary clearance.

In conclusion, the present study has revealed smoking to disrupt nasal mucociliary system showing a direct proportion between total duration of smoking and the amount of cigarettes smoked.

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