North Clin Istanb
doi: 10.14744/nci.2018.50024

Original Article PUBLIC HEALTH

UNCORRECTED PROOF

Otorhinolaryngolojical symtoms among smokeless tobacco (Maras powder) users

Saime Sagiroglu,[1] Aysegul Erdogan,[2] Adem Doganer,[3] Ramazan Azim Okyay[2]

[1]Department of Otorhinolaringology, Kahramanmaras Sutcu Imam University Faculty of Medicine, Kahramanmaras, Turkey

[2]Department of Public Health, Kahramanmaras Sutcu Imam University Faculty of Medicine, Kahramanmaras, Turkey

[3]Department of Biostatistics and Medical Informatics, Kahramanmaras Sutcu Imam University Faculty of Medicine, Kahramanmaras, Turkey

ABSTRACT

OBJECTIVE: This study aims to investigate the relationship between smokeless tobacco (Maras Powder) consumption and otorhinolaryngological symptoms.

METHODS: This descriptive study was carried on a total of 599 participants. The participatns were divided into two groups. Of these, 299 (49.9%) patients aged over 18 years were the first group who have used smokeless tobacco for at least 5 years and the rest were the second group which included 300 (50.1%) healthy volunteers who did not use tobacoo or its products and demonstrated similarities to first group. For data collection a questionnaire consisting of 45 questions was applied to the participants.

RESULTS: Cough, sputum, shortness of breath, dysphagia, snore and apnea-hypopnea were found to be significantly increased in smokeless tobacco users. The highest odds ratio was found for sputum as 2.615. Similarly oral cavity symptoms, such as mouth tickling, dryness of throat, mouth sores, halitosis, taste disorders and toothache were found to be significantly increased in smokeless tobacco users. It is noteworthy that halitosis was 9.4 times more among smokeless tobacco users than the non tobacco user group. Sinonasal symptoms such as sneeze, headache, facial fullness and anorexia were found to be significantly increased in smokeless tobacco users. However there were no differences between groups in terms of ear symptoms.

CONCLUSION: This study demonstrated that the negative effect of smokeless tobacco consumption was greater particularly in the oral cavity and in addition gave a rise to a number of serious upper respiratory tract complaints.

Keywords: Maras powder; otorhinolaryngology; smokeless tobacco; symptoms.

Cite this article as: *Sagiroglu S., Erdogan A., Doganer A., Okyay R. A. Otorhinolaryngolojical symtoms among smokeless tobacco (Maras powder) users. North Clin Istanb*

Recently, tobacco consumption has soared particularly in developing countries. According to the World Health Organization (WHO) the tobacco epidemic is one of the biggest public health threats the world has ever faced, killing more than 7 million people a year. More than 6 million of those deaths are the result of direct tobacco use while around 890 000 are the result of passive exposure to tobacco smoke [1].

Although tobacco consumption is occuring mainly as cigarette smoking, there are also other forms of tobacco usage called as smokeless tobacco. Smokeless tobacco is used by numerous cultures in many parts of the world, including The United States, Sweden, India, as well as the Middle East [2–5]. Some of commonly used smokeless tobacco products may be counted as chewing tobacco, snuff, snus, and topical tobacco paste [4]. In

Received: January 25, 2018 *Accepted:* May 04, 2018 *Online:* August 08, 2018

Correspondence: Dr. Saime SAGIROGLU. Kahramanmaras Sutcu Imam Universitesi Tip Fakültesi, Kulak Burun Bogaz Bas ve Boyun Cerrahisi Anabilim Dali, Kahramanmaras, Turkey.
Tel: +90 505 240 05 44 e-mail: ssguzelsoy@hotmail.com

© Copyright 2018 by Istanbul Provincial Directorate of Health - Available online at www.northclinist.com

Turkey, the most common smokeless tobacco product is called Maras Powder, a snus like product that is used by compressing the powder filled mini bag to the buccal mucosa between the teeth and lips [6]. Maras Powder is obtained from a plant called Nicotina Rustica Linn. The nicotine content of this plant is 6–10 times higher than that of Nicotina Tobacum which the cigarette is produced from [7].

The prevalence of smoking in Turkey is well-known. According to WHO data, age-standardized estimated prevalence of being have ever smoked tobacco among those aged 15 years or more is 41.6% for men and 13.2% for women. However there are no studies demonstrating the nation-wide prevalence of smokeless tobacco consumption [8].

The health effects of cigarette smoking [9], its role in carcinogenesis [10] and symptomatology [11] have been examined in detail in the literature. However, to the best of our knowledge, there is no study focusing on symptomatology of smokeless tobacco use in Turkey.

In the light of this basis we aimed to investigate relationship between the use of smokeless tobacco use and otorhinolaryngological symptoms in Kahramanmaras, which is the city giving the smokeless tobacco product Maras Powder its name, and where the usage is very common.

MATERIALS AND METHODS

Study Design

This descriptive study aiming to determine the relationship between the use of smokeless tobacco (Maras powder) and otorhinolaryngological symptoms was carried out in Kahramanmaras, in 2016.

In the study a questionnaire consisting of 45 questions was used. The first 9 questions were querying the socio-demographic characteristics and the rest of the questions were related to otorhinolaryngological symptoms and smokeless tobacco consumption.

Data collection

299 (49.9%) patients aged over 18 years who applied to Department of Otorhinolaryngology polyclinic between April-September 2016 and who consumed smokeless tobacco three times or more per day for at least five years were included in the study as the smokeless tobacco user group. 300 (50.1%) healthy volunteers, who did not use tobacoo or its products and demonstrated similarities to smokeless tobacco user group in terms of age, gender and certain socio-demographic characteristics, formed the non tobacco user group.

The following were excluded from the study: those with upper respiratory tract infection and chronic respiratory system diseases such as chronic obstructive pulmonary disease and asthma. The smokeless tobacco user group was enrolled among those who were not with an obvious pathology that explained the symptoms. The non tobacco user group was recruited among healthy patient companions who had no health problems.

Each member of both groups filled in and signed the detailed questionnaire form that queries socio-demographic characteristics and otorhinolaryngological symptoms.

Statistical analysis

Data were analyzed using SPSS statistical software version 22. Symptoms and Socio-demographic variables were presented as frequencies and percentages in tables. Pearson chi-square test and Student's t test were applied to assess the results. The level of statistical significance was accepted as $p<0.05$ and the estimated Odds Ratios (OR) were presented with 95% confidence interval.

Ethical considerations

The study was approved by Local Scientific Researchs Ethics Committee. Written informed consent was obtained from all participants and participation in the study was purely voluntary.

RESULTS

A total of 599 participants were included in the research. Of these, 299 have used smokeless tobacco for at least 5 years and the rest 300 people were the non-tobacco user group. Distribution of some of socio-demographic factors such as age, gender, marital status, education, economic status and settlement place of the groups are shown in Table 1. There were no differences between groups in terms of age, gender, marital status, education, economic status and settlement place ($p>0.05$).

Comparison of smokeless tobacco users and non-tobacco users according to upper respiratory tract

Table 1. Comparison of smokeless tobacco users and non-tobacco usersaccording tosocio-demographic characteristics

Socio-demographic characteristics	Smokeless tobacco users		Non-tobacco users		p
	n	%*	n	%*	
Age	36.80±15.42		38.92±14.44		**0.123**
Gender					
Female	24	38.7	38	61.3	**0.062**
Male	275	51.2	262	48.8	
Marital status					
Married	198	47.3	221	52.7	
Single	91	58.3	65	41.7	**0.055**
Divorced	8	44.4	10	55.6	
Education					
Illiterate	6	35.3	11	64.7	
Literate	22	61.1	14	38.9	
Elementary school	82	54.7	68	45.3	**0.091**
Middle school	38	44.7	47	55.3	
High school	101	53.4	88	46.6	
University	49	41.9	68	58.1	
Economic status					
Low	49	41.5	69	58.5	
Moderate	220	52.9	196	47.1	**0.080**
High	26	46.4	30	53.6	
Settlement place					
Village	36	61.0	23	39.0	
District	50	43.9	64	56.1	**0.100**
City	210	50.4	207	49.6	

*Row percentage.

symptoms are shown in Table 2. Cough, sputum, shortness of breath, dysphagia, snore and apnea-hypopnea were found to be significantly increased in smokeless tobacco users ($p<0.05$). On the other hand there were no significant differences between groups in terms of hoarseness, reflux, neck pain, swelling in the neck and pruritus ($p=0.031$, $p=0.938$, $p=0.785$, $p=0.879$, $p=0.287$). The highest odds ratio was found for sputum as 2.615.

Comparison of groups in regard to oral cavity symptoms are shown in Table 3. Mouth tickling, dryness of throat, mouth sores, halitosis, taste disorders andtoothache were found to be significantly increased in smokeless tobacco users ($p<0.05$). It is noteworthy that halitosis was 9.4 times more among smokeless tobacco users than the non tobacco user group. However there were no differences between groups in terms of sore throat, throat stinging and gingival bleeding ($p=0.187$, $p=0.790$, $p=0.424$).

Comparison of smokeless tobacco users and non-tobacco users according to sinonasal symptoms are shown in Table 4. Sneeze, headache, facial fullness and anorexia were found to be significantly increased in smokeless tobacco users ($p<0.05$). On the other hand there were no significant differences between groups in terms of runny nose,nasal bleeding, postnasal drainage and nausea ($p=0.134$, $p=0.345$, $p=0.475$, $p=0.084$).

Comparison of groups in regard to ear symptoms are shown in Table 5. There were no differences between groups in terms of hearing loss, dizziness, ear disorders, ear fullness and tinnitus ($p=0.310$, $p=0.185$, $p=0.248$, $p=0.330$, $p=0.586$).

Table 2. Comparison of smokeless tobacco users and non-tobacco users according to upper respiratory tract symptoms

Upper respiratory tract symptoms	Smokeless tobacco users		Non-tobacco users		x^2	p	OR
	n	%	n	%			
Cough							
Yes	111	60.7	72	39.3	12.17	**<0.001**	**1.871** (1.313–2.667)
No	187	45.2	227	54.8			
Sputum							
Yes	127	65.8	66	34.2	28.55	**<0.001**	**2.615** (1.829–3.738)
No	170	42.4	231	57.6			
Hoarseness							
Yes	62	53.4	54	46.6	0.62	0.031	–
No	237	49.4	243	50.6			
Shortness of breath							
Yes	99	59.3	68	40.7	7.99	**<0.005**	**1.683** (1.171–2.418)
No	199	46.4	230	53.6			
Reflux							
Yes	85	50.0	85	50.0	0.00	0.938	–
No	213	50.4	210	49.6			
Dysphagia							
Yes	65	60.7	42	39.3	6.43	**0.011**	**1.733** (1.130–2.657)
No	226	47.2	253	52.8			
Snore							
Yes	155	55.6	124	44.4	6.87	**0.009**	**1.540** (1.115–2.129)
No	142	42.8	175	52.2			
Apnea hypopnea							
Yes	68	63.0	40	37.0	8.75	**0.003**	**1.900** (1.237–2.918)
No	230	47.2	257	52.8			
Neck pain							
Yes	82	49.1	85	50.9	0.07	0.785	–
No	217	50.3	214	49.7			
Swelling in theneck							
Yes	24	51.1	23	48.1	0.02	0.879	–
No	275	49.9	276	50.1			
Pruritus							
Yes	46	55.4	37	44.6	1.13	0.287	–
No	253	49.1	262	50.9			

Pearson Chi-Square Test; α: 0.05.

DISCUSSION

Maras Powder is obtained from a plant which has higher nicotine content than those which are used in usual cigarette production. It is mostly consumed in Kahramanmaras and Gaziantep, which are cities located in the Southeastern Region of Turkey. There is a wrong opinion among the public such asto use Maras Powder to get rid of known health effects of cigarette smoking. On the contrary, studies show that Maras Powder can cause many systemic diseases in humans [12–14] Maras Powder consumption causes genotoxic, mutagenic and car-

TABLE 3. Comparison of smokeless tobacco users and non-tobacco users according to oral cavity symptoms

Oral cavity symtoms	Smokeless tobacco users		Non-tobacco users		x^2	p	OR
	n	%	n	%			
Mouth tickling							
Yes	114	69.1	51	30.9	33.94	**<0.001**	**3.038** (2.074–4.451)
No	181	42.4	246	57.2			
Dryness of throat							
Yes	168	66.4	85	33.6	48.84	**<0.001**	**3.304** (2.351–4.645)
No	128	37.4	214	62.6			
Sore throat							
Yes	87	54.4	73	45.6	1.73	0.187	–
No	211	48.3	226	51.7			
Throat stinging							
Yes	61	50.8	59	49.2	0.07	0.790	–
No	236	49.5	241	50.5			
Mouth sores							
Yes	56	62.2	34	37.8	6.50	**0.011**	**1.810** (1.143–2.869)
No	242	47.6	266	52.4			
Halitosis							
Yes	226	75.1	75	24.9	154.56	**<0.001**	**9.417** (6.489–13.665)
No	72	24.2	225	75.8			
Taste disorders							
Yes	75	63.3	43	36.4	11.08	**<0.001**	**2.010** (1.327–3.046)
No	223	46.5	257	53.5			
Toothache							
Yes	111	56.6	85	43.4	5.26	**0.022**	**1.494** (1.060–2.108)
No	187	46.6	214	53.4			
Gingival bleeding							
Yes	111	52.1	102	47.9	0.63	0.424	–
No	187	48.7	197	51.3			

Pearson Chi-Square Test; α: 0,05.

cinogenic effects particularly due to the N-nitrosamines in its content.

There are many evidence that nicotine is a major immunosuppressive. Nicotine induces ACTH secretion which releases chatecholamines with suppressive effects on the immune system [15]. This leads to the emergence of clinical symptoms, which are indicators of a number of diseases. Smoking also causes changes in the mucus production mechanism. Chronic exposure to smoke increases the number and size of goblet cells, resulting in metaplastic changes in the respiratory mucosa and a consequent increase in upper respiratory secretion [16, 17] Although there are many studies in the literature about the effect of cigarette on upper respiratory tract, a limited number of studies on the use of smokeless tobacco has been reached. In a study which the effect of local herbal tobacco use on pulmonary function was assessed, pulmonary dysfunction was determined in chronic consumption and symptoms such as coughing were reported to be at high rates [18]. Yet, in another study [19] it was found that people who use smokeless tobacco had a higher risk of chronic bronchitis. Even though Maras Powder has systemic effects through oral route which is different than the direct effect of cigarette smoke; we

Table 4. Comparison of smokeless tobacco users and non-tobacco users according to sinonasal symptoms

Sinonasal symtoms	Smokeless tobacco users		Non-tobacco users		x^2	p	OR
	n	%	n	%			
Runny nose							
Yes	89	54.9	73	45.3	2.24	0.134	–
No	210	48.1	227	50.9			
Nasal bleeding							
Yes	36	45.0	44	55.0	0.89	0.345	–
No	263	50.7	256	49.3			
Sneeze							
Yes	157	54.9	129	45.1	5.25	**0.022**	**1.457** (1.056–2.011)
No	142	45.5	170	54.5			
Post nasal drainage							
Yes	69	52.7	62	47.3	0.51	0.475	–
No	229	49.1	237	50.9			
Smell disorders							
Yes	56	57.1	42	42.9	2.33	0.126	–
No	243	48.7	256	51.3			
Headache							
Yes	150	54.5	125	45.5	4.35	**0.037**	**1.409** (1.021–1.946)
No	149	46.0	175	54.0			
Facial fullness							
Yes	58	59.2	40	40.8	4.02	**0.045**	**1.564** (1.008–2.427)
No	241	48.1	260	51.9			
Nausea							
Yes	71	56.8	54	43.2	2.99	0.084	–
No	228	48.1	246	51.9			
Anorexia							
Yes	97	61.8	60	38.2	12.00	**0.001**	**1.922** (1.324–2.790)
No	201	45.7	239	54.3			

Pearson Chi-Square Test; α: 0,05.

also found that cough, sputum and shortness of breath symptoms were significantly higher among the smokeless tobacco users than the non tobacco user group. We thought that these symptoms paved the way for pulmonary disorders.

In chronic voice disorders, the negative effect of usual cigarette on vocal cords is a known fact. Despite that, we found that smokeless tobacco does not have any effect on voice morbidity which is already an expected situation. Smoking affects the gastroesophageal reflex and pharyngeal swallowing reflex negatively [20, 21]. These may cause dysphagia and respiratory complications due to gastroesophageal reflux among smokers. Aro et al. [22] found that smokless tobacco significantly changes the histology of the distal esophagus, but does not lead to gastrointestinal symptoms or peptic ulcer. As a matter of fact, in our study, we found the reflux symptoms at the same rates in both groups. However, dysphagia was found to be higher among smokeless tobacco users.

Due to its high nicotine content, sleepiness tends to increase during the day in people using smokeless tobacco. Current studies have shown that, there is a synergistic effect between smoking and snoring and smoking increases the risk of cardiovascular disease with both

TABLE 5. Comparison of smokeless tobacco users and non-tobacco users according to ear symptoms

Ear symtoms	Smokeless tobacco users		Non-tobacco users		x^2	p	OR
	n	%	n	%			
Hearingloss							
Yes	53	54.6	44	45.4	1.03	0.310	–
No	246	49.0	256	51.0			
Dizziness							
Yes	91	54.2	77	45.8	1.75	0.185	–
No	207	48.1	223	51.9			
Ear disorders							
Yes	46	44.7	57	55.3	1.33	0.248	–
No	252	50.9	243	49.1			
Earfullness							
Yes	33	55.9	26	44.1	0.94	0.330	–
No	266	49.3	274	50.7			
Tinnitus							
Yes	88	51.8	82	48.2	0.29	0.586	–
No	211	49.3	217	50.7			

Pearson Chi-Square Test; α: 0,05.

oxidative stress and endothelial dysfunction through abnormal inflammatory response [12, 13, 23]. In our study, snore and apnea-hypopnea rates were higher in smokeless tobacco users.

There are more than 700 species of bacteria identified in the human oral cavity [24, 25] These bacteria play a role in both oral and systemic health. One of the causes of halitosis is the deterioration of the bacterial flora. These bacteria in the oral flora produce oral malodor by producing various substances such as sulfur compounds, diamines and short chain fatty acids [26, 27]. Keene and Johnson [28] found that the *Streptococcus mutans* (*S. Mutans*) flora increases in the oral mucosa due to increased nicotine. Increased levels of nicotine in saliva have been thought to stimulate colonization of S.Mutans and increase the risk of possible carriage. In our study, the most notable symptom among oral symptoms in smokeless tobacco users was halitosis. In an in vitro study, it was found that the number of fibroblasts and the amount of gingiva type 1 collagen increased with nicotine use [29]. Hence, nicotine use may cause fibrosis in the oral mucosa. As a matter of fact, we found that mouth tickling, dryness of throat, throat stinging, taste disorders and toothache were higher among smokeless tobacco users. These findings suggest that smokeless tobacco consumption may lead to a deterioration of the oral flora and a rise in infection risk.

Smokeless tobacco may cause hyperkeratotic lesions, periodontal diseases and intra-oral premalign lesions in oral mucosa. It also chronically stimulates the lymphoid tissue in the oral mucosa and consequently rises the risk of gingivitis, erythroplakia, leukoplakia, submucous fibrosis and lichen planus. Epidemiological and experimental studies have shown a strong association between oral and pharyngeal cancers and smokeless tobacco [30, 31]. Dodani et al. [32] found pathological findings in mucosa as a result of direct exposure of gingiva to various toxic chemicals. In previous studies, epithelial anomalies and precancerous lesions were determined from biopsies of gingival tissues of Maras Powder users [6, 33]. With increased nicotine-induced vasoconstriction, gingival keratinization increases and as a result, smokers have less gingival bleeding. Although we found mouth sores higher in smokeless tobacco users, gingival bleeding and sore throat was not different from the non tobacco user group.

Epidemiological studies suggest a correlation between exposure to tobacco smoke and rhinosinusitis. Goldstein-Daruech et al. [34] found that exposure to tobacco led the formation of synonasal biofilms and contributed to the conversion of a transient and medically treatable infection to a tenacious and therapeutic persistent state. Mahakit P et al [35] have shown that cigarette smoking affects mucociliary function negatively. Sanli et al [36] found that, while nasal obstruction, malodor and snoring were significantly higher in smokers; symptoms such as nasal discharge, sneezing, nasal discharge, and headache were similar to the control group. In our study, while sneeze, headache, facial fullness and anorexia were higher in smokeless tobacco users, the rates of runny nose, nasal bleeding, post nasal drainage and smell disorders were similar in both groups. These results suggest that the negative effects of cigarette smoke on nasal function is more than smokeless tobacco.

Gaur et al. [37] found that smokers had more otological diseases. Sanlı et al. [36] found that ear discharge, hearing loss, dizziness and tinnitus were more common in smokers. While there are many studies in the literature demonstrating that cigarette disrupts cochlear function, not many studies on the effect of smokeless tobacco on the ear have been reached [37–39]. In our study, we found ear symptoms at equal rates in both groups. However, it is thought that there is a need for more extensive research in this regard.

Strengths and limitations

A strength of the present study is that it was conducted in a city where smokeless tobacco consumption is prevalent. Another strength is the study population is relatively large.

Several limitations should be addressed however. First, the study was carried out on the applicants of a hospital which hinders the results to be extrapolated to general population. Second, the duration of smokeless tobacco presence in the oral cavity was not questioned, therefore the dose-response relationship between the usage habit and symptoms can not be assessed. Lastly, as it is a survey study, memory factors that affect the responses to the questionnaire may exist.

Conclusion

As a result, our study revealed that the effect of smokeless tobacco on the oral cavity was excessive and that there were no difference between groups in terms of any ear symptoms. We found that smokeless tobacco users have significant potential clinical symptoms compared to non-tobacco users. Clinical symptoms are premonitors of a number of diseases. By the elimination of the etiology that causes the symptoms and performing screening for emerged symptoms, the disease may be prevented and thus preventive medicine may be brought to the forefront.

Conflict of Interest: The authors declare no conflict of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. WHO. (accessed May 28, 2017) Tobacco fact sheet. World Health Organization, Geneva; 2016.
2. Cullen D, Keithly L, Kane K, Land T, Paskowsky M, Chen L, Hayes R, Li W. Smokeless tobacco products sold in Massachusetts from 2003 to 2012: trends and variations in brand availability, nicotine contents and design features. Tob Control, 2015; 24: 256-62.
3. Leon ME, Lugo A, Boffetta P, Gilmore A, Ross H, Schüz J, La Vecchia C, Gallus S. Smokeless tobacco use in Sweden and other 17 European countries. Eur J Public Health. 2016; 26: 817-21.
4. Shaik SS, Doshi D, Bandari SR, Madupu PR, Kulkarni S. Tobacco Use Cessation and Prevention - A Review. J Clin Diagn Res. 2016; 10: 13-7.
5. Alsanosy RM. Smokeless tobacco (shammah) in Saudi Arabia: a review of its pattern of use, prevalence, and potential role in oral cancer. Asian Pac J Cancer Prev. 2014; 15: 6477-83.
6. Erenmemisoglu A, Ustun H, Kartal M. Carcinoma of buccal mucosa in smokeless tobacco users: a preliminary study of the use of cytology for early detection. Cytopathology. 1995; 6: 403-8.
7. Saitoh F, Noma M, Kawashima N. The alkaloid contents of sixty nicotine species. Phytochemistry. 1985; 24: 477-80.
8. WHO. (accessed May 28, 2017) WHO report on the global tobacco epidemic, 2015: Raising taxes on tobacco—Appendix VII: Country profiles.
9. Duaso M, Duncan D. Health impact of smoking and smoking cessation strategies: current evidence. Br J Community Nurs. 2012; 17: 356-63.
10. Beral V, Gaitskell K, Hermon C, Moser K, Reeves G, Peto R. Collaborative Group on Epidemiological Studies of Ovarian Cancer. Ovarian cancer and smoking: individual participant meta-analysis including 28,114 women with ovarian cancer from 51 epidemiological studies. Lancet Oncol. 2012; 13: 946-56.
11. Lawless MH, Harrison KA, Grandits GA, Eberly LE, Allen SS. Perceived stress and smoking-related behaviors and symptomatology in male and female smokers. Addict Behav. 2015; 51: 80-3.
12. Bolinder G, Alfredsson L, Englund A, de Faire U. Smokeless tobacco use and increased cardiovascular mortality among Swedish construction workers. Am J Public Health. 1994; 84: 399-404.
13. Guven A, Tolun F. Effects of Smokeless Tobacco "Maras Powder" Use on Nitric Oxide and Cardiovascular Risk Parameters. Int J Med Sci. 2012; 9: 786-92.
14. Cok I, Oztürk R. Urinary cotinine levels of smokeless tobacco (Maraş powder) users. Hum Exp Toxicol. 2000; 19: 650-5.
15. Sopori ML, Kozak W. Immunomodulatory effects of cigarette smoke. J Neuroimmunol. 1998; 83: 148–56.

16. Tamashiro E, Cohen NA, Palmer JN, Lima WT. Effects of cigarette smoking on the respiratory epithelium and its role in the pathogenesis of chronic rhinosinusitis. Braz J Otorhinolaryngol. 2009; 75: 903-7.
17. Mullen JB, Wright JL, Wiggs BR, Pare PD, Hogg JC. Structure of central airways in current smokers and ex-smokers with and without mucus hypersecretion: relationship to lung function. Thorax. 1987; 42: 843-8.
18. Maduka SO, Osim EE, Nneli RO, Anyabolu AE. Effect of occupational exposure to local powdered tobacco (snuff) on pulmonary function in south eastern Nigerians. Niger J Physiol Sci. 2009; 24: 195-202.
19. Ayo-Yusuf OA, Reddy PS, van den Borne BW. Association of snuff use with chronic bronchitis among South African women: implications for tobacco harm reduction. Tob Control. 2008; 17: 99-104.
20. Dua K, Bardan E, Ren J, Sui Z, Shaker R. Effect of chronic and acute cigarette smoking on the pharyngoglottal closure reflex. Gut. 2002; 51: 771-5.
21. Dua K, Bardan E, Ren J, Sui Z, Shaker R. Effect of chronic and acute cigarette smoking on the pharyngo-upper oesophageal sphincter contractile reflex and reflexive pharyngeal swallow. Gut. 1998; 43: 537-41.
22. Aro P, Ronkainen J, Storskrubb T, Vieth M, Engstrand L, Johansson SE, Bolling-Sternevald E, Bolinder G, Alving K, Talley NJ, Agréus L. Use of tobacco products and gastrointestinal morbidity: an endoscopic population-based study (the Kalixanda study). Eur J Epidemiol. 2010; 25: 741-50.
23. Kilinc M, Okur E, Kurutas EB, Guler FI, Yildirim I. The effects of Maras powder (smokeless tobacco) on oxidative stress in users. Cell Biochem Funct. 2004; 22: 233-6.
24. Paster BJ, Olsen I, Aas JA, Dewhirst FE. The breadth of bacterial diversity in the human periodontal pocket and other oral sites. Periodontol. 2000; 42: 80-7.
25. Kirst ME, Li EC, Alfant B, Chi YY, Walker C, Magnusson I, Wang GP. Dysbiosis and alterations in predicted functions of the subgingival microbiome in chronic periodontitis, Appl Environ Microbiol. 2015; 81: 783-93.
26. Motta LJ, Bachiega JC, Guedes CC, Laranja LT, Bussadori SK. Association between halitosis and mouth breathing in children. Clinics (Sao Paulo). 2011; 66: 939–42.
27. Madhushankari GS, Yamunadevi A, Selvamani M, Mohan Kumar KP, Basandi PS. Halitosis – An overview: Part-I – Classification, etiology, and pathophysiology of halitosis. J Pharm Bioallied Sci. 2015; 7: 339–43.
28. Keene K, Johnson RB. The effect of nicotine on growth of Streptococcus mutans, Miss Dent Assoc J. 1999; 55: 38e39.
29. Takeuchi H, Kubota S, Murakashi E, Zhou Y, Endo K, Ng PS, Takigawa M, Numabe Y. Nicotine-induced CCN2: from smoking to periodontal fibrosis. J Dent Res. 2010; 89: 34–9.
30. Goud SN, Zhang L, Kaplan AM. Immunostimulatory potential of smokeless tobacco extract in in vitro cultures of murine lymphoid tissues. Immunopharmacology. 1993; 25: 95–105.
31. Erenmemisoglu A, Tekol Y, Kartal M, Kurucu S. The use of a smokeless tobacco in our country "Maras powder". In: Proceedings of the 2nd International Symposium of Pharmaceutical Sciences; June 1991; Ankara, Turkey.
32. Dodani K, Anumala N, Avula H, Reddy K, Varre S, Kalakonda BB, Arora N, Suri C, Avula JK. Periodontal findings in patients with oral submucous fibrosis and comet assay of affected gingival epithelial cells. J Periodontol. 2012; 83: 1038-47.
33. Okur E, Yildirim I, Kilic MA, Sasmaz S. Clinical changes in the oral cavity resulting from smokeless tobacco (Maraş powder). Kulak Burun Bogaz Ihtis Derg. 2004; 13:72-6.
34. Goldstein-Daruech N, Cope EK, Zhao KQ, Vukovic K, Kofonow JM, Doghramji L, González B, Chiu AG, Kennedy DW, Palmer JN, Leid JG, Kreindler JL, Cohen NA. Tobacco smoke mediated induction of sinonasal microbial biofilms. PLoS One. 2011; 6: e15700.
35. Mahakit P, Pumhirun P. A preliminary study of nasal mucociliary clearance in smokers, sinusitis and allergic rhinitis patients. Asian Pac J Allergy Immunol. 1995; 13: 119-21.
36. Şanlı A, Bekmez E, Yıldız G, Erdoğan BA, Yılmaz HB, Altın G. Relationship between smoking and otorhinolaryngological symptoms. Kulak Burun Bogaz Ihtis Derg. 2016; 26: 28-33.
37. Gaur K, Kasliwal N, Gupta R. Association of smoking or tobacco use with ear diseases among men: a retrospective study. Tob Induc Dis. 2012; 10: 1-4.
38. Chung DY, Gannon RP, Mason K. Factors affecting the prevalence of tinnitus. Audiology. 1984; 23: 441-52.
39. Paschoal CP, Azevedo MF. Cigarette smoking as a risk factor for auditory problems. Braz J Otorhinolaryngol. 2009; 75: 893-902.