B-ENT, 2016, **12**, 17-21

How does electronic cigarette smoking affect sinonasal symptoms and nasal mucociliary clearance?

T. L. Kumral, Z. Saltürk, G. Yıldırım, Y. Uyar, G. Berkiten, Y. Atar and M. İnan

Department of Otorhinolaryngology-Head and Neck Surgery, Okmeydanı Training and Research Hospital, Istanbul, Turkey

Key-words. Electronic cigarette; SNOT-22, mucociliary clearance; smoking cessation

Abstract. *How does electronic cigarette smoking affect sinonasal symptoms and nasal mucociliary clearance? Objective*: is to evaluate the sinonasal symptom scores and mucociliary clearance (MCC) after starting to use electronic cigarette
Methodolgy: This prospective randomized single-blind clinical trial was conducted between March 2013 and November 2013. Patients (n=98) admitted to smoking cessation clinic were divided into two groups; Electronic cigarette smokers (group 1) and non-electronic cigarette smokers (group 2). SNOT-22 and saccharin transit time for MCC were evaluated before starting electronic cigarettes and after the third months.
Results: SNOT-22 scores and MCC time were evaluated between groups and within groups after 3 months. SNOT 22 scores and MCC measurements showed no difference between groups before the cessation of cigarette smoking ($p>0.05$). SNOT 22 results of both groups revealed statistically significantly lower scores after the three months ($p<0.05$). However, SNOT-22 scores of group 2 was significantly better than group 1 ($p>0.05$).
Comparison of MCC results of group 2 revealed statistically significantly lower scores after the three months ($p<0.05$). However, group 1 did not show any significant difference after three months ($p>0.05$). There was a significant difference between the groups at the third month measurements ($p<0.05$).
Conclusions: Although EC is widely used as a method of quitting smoking, it has negative effects on the sinonasal symptoms and MCC.

Introduction

Smoking of tobacco is the leading cause of preventable deaths worldwide.[1] Smoking is a common and early-onset habit. Today, the onset age for smoking has decreased to childhood, and early onset is inversely related to the quitting rate. Nicotine replacement therapies, nicotine receptor agonists, and antidepressants, all of which are commonly applied therapies for smoking cessation, have low success rates.[2,3] In the absence of any assistance, only 6% of attempts to quit smoking are successful.[4] Therefore, new techniques that aim to decrease the adverse effects of tobacco and nicotine have been developed.

The electronic cigarette (EC) is a device that carries aerosolized nicotine to the respiratory tract. The EC has a battery that vaporizes a sweetened liquid that contains nicotine. As the user creates a vacuum, the battery begins to work and heats the liquid inside.[5] The EC does not involve the burning responsible for the production of chemicals that cause heart and lung problems.[6,7] The EC attempts to satisfy not only physical addiction but also psychological addiction. As a result, it enables quitting smoking.[8]

Quitting smoking interrupts the continuous exposure to several chemicals present in the cigarette smoke that cause carcinogenic, mutagenic, toxic and irritant effects and a sustained inflammatory response, which can lead in respiratory epithelium's damage. Although theoretically ECs appear less toxic, in recent years, articles have begun to emerge claiming that there may be an impact on health.[9-11] Mucociliary clearance (MCC) is an important defense mechanism. The association between MCC and smoking was documented before.[12] Some studies have reported that chronic smokers have decreased MCC of the respiratory system.[13,14] However, correlation of EC and MCC has not been documented.

The effects of smoking cessation on sinonasal outcomes and MCC have not been described in detail. We aimed to evaluate changes in sinonasal symptoms and MCC in cigarette smokers who started to use ECs.

Materials and methods

This prospective randomized single-blind clinical trial was conducted at the Department of Otorhinolaryngology-Head and Neck Surgery between March 2013 and November 2013 and was approved by the ethics committee of Okmeydanı Training and Research hospital.

All patients (n=98) admitted to smoking cessation clinic for a month were enrolled in the study. These patients smoked one pack of cigarettes per day for at least 5 years. All patients were willing to quit smoking. Patients participating in the study were randomly divided into two groups; EC smokers (group 1) and non-EC smokers (group 2). EC-smokers (n=58) were the smokers who started EC to quit smoking. Non-EC smokers (n=40) were the smokers who quitted smoking without the aid of medical therapy and a device. Non-EC smokers had cognitive behavioral treatment during the course. However, sixteen patients in the group 1 and ten patients in the group 2 who cannot stop smoking were excluded from the study.

Patients underwent a complete ear, nose, and throat examination. A history of allergic rhinitis, chronic sinusitis, vasomotor rhinitis, asthma, malignancy, or surgery in the upper respiratory tract, age under 18 years, and usage of psychoactive drugs were criteria for exclusion. All subjects gave their written informed consent.

A wide range of EC devices are available for smokers to substitute smoking. In this study, the patients were allowed to select the brand of the device and flavor of the cartridge. Liquid in the cartridge contained alkaloids fluid with propylene glycol, ethanol, water, tobacco flowers, essential oil, consists of nicotine. Light Cigarettes in the markets has 0.7 mg nicotine per stick. Consuming all 20 cigarettes in a pack will give 14 mg nicotine. For this reason, we chose medium density (11-12 mg/ml) liquid for this study. It was also for those light cigarette users.

Patients underwent Sino-Nasal Outcome test (SNOT-22) to evaluate changes in subjective symptoms and saccharin transit test to evaluate the nasal MCC function. Researcher who collected the data did not know which method patients used to quit smoking. Data were collected by means of a self-administered questionnaire. Sinonasal outcome test 22 (SNOT-22), which was validated by Hopkins *et al.*,[15] was used to evaluate sinonasal symptoms. SNOT 22 is composed of 22 questions that are scored from 0-5. A lower score implies a better result.

Nasal MCC time was assessed for all individuals of by blinded researcher. Saccharin transit time test was used to measure the nasal MCC, as previously described.[16] Subjects were seated upright position. Granulated sodium saccharin (250 mg) was deposited under visual control. A saccharin granule was placed 2 cm inside the right nostril lateral to inferior turbinate by the tester. They were instructed to swallow every 30 s per minute with a chronometer. The time when the subjects first percepted the sweet taste of the saccharin were recorded in minutes. Individuals were instructed not to breathe deeply, talk, cough, sneeze or sniff during the test.

The SNOT-22 results and saccharin transit time for MCC were compared within and between the groups at the end of the third month.

Statistical analyses of the data were conducted using SPSS ver. 17.0. Descriptive statistical methods (mean and standard deviation, SD), as well as paired sample t-test and independent sample t-test were used to compare qualitative data. Results were evaluated using the 95% confidence intervals (CI), and the level of significance was set at $p<0.05$.

Results

Twenty-four patients were male and eighteen female in group 1 (n=42). The mean age was 33.9±7.9 years. The mean duration of smoking was 13.5±6.5 years. Sixteen patients were male and fourteen female in group 2 (n=30). The mean age was 38±8.2 years. The mean duration of smoking was 9.8±4.7 years (Table 1).

SNOT-22 scores were evaluated before and after cessation of cigarette smoking between groups and within groups. SNOT 22 scores were insignificant between groups before the cessation of cigarette smoking ($^{a}p=0.133$). SNOT-22 scores of group 1 and group 2 were evaluated after 3 months. There was a significant difference between the groups at the third month measurements ($^{a}p=0.001$) (Table 2). Comparison of SNOT 22 results of groups at the beginning of the study and after 3 months revealed statistically significantly lower scores after the three months ($^{b}p=0.001$; $^{b}p=001$) (Table 2).

MCC measurements were evaluated before and after cessation of cigarette smoking between groups

Table 1

The distribution of the patients' age, gender and duration of smoking

	Group 1 (EC) (n=42)	Group 2 (Non EC) (n=30)
Age (years)	33.9±7.9	38.0±8.2
Gender	24 F, 18 M	14F, 16 M
Duration of smoking (years)	9.79±4.41	9.77±5.07

F: Female; M; Male; EC: Electronic cigarette.

and within groups. MCC measurements were insignificant between groups before the cessation of cigarette smoking ($^{a}p=0.811$). Group 1 scores were compared with group 2 after 3 months. There was a significant difference between the groups at the third month measurements ($^{a}p=0.003$) (Table 3). Comparison of MCC results of group 2 at the beginning of the study and after 3 months revealed statistically significantly lower scores after the three months ($^{b}p=0.001$). However, group 1 did not show any significant difference after three months ($^{b}p=0.194$) (Table 3).

Discussion

Smoking is the leading cause of preventable death today, and the risk decreases rapidly after cessation of smoking.[17] Therefore, various smoking cessation strategies are used. ECs are a promising method. The majority of toxic agents in cigarette smoking occur with burning, but there is no burning process with ECs.[6,7] Therefore, EC use is considered to be safer than smoking.

Propylene glycol is the primary ingredient in the majority of e-liquids and EC cartridges on the marketplace today. Most e-liquid contains 80-92% propylene glycol. This is the ingredient that produces the smoke like vapor when the EC is exhaled. Products with propylene glycol can be found in various common items such as pharmaceuticals, beauty products and pet food. Because of its low chronic oral toxicity, propylene glycol was generally recognized as safe.[18]

Although theoretically ECs appear less toxic, in recent years, articles have begun to emerge claiming that there may be an impact on health.[9,10,11] This issue should be researched. Short-term studies investigating possible side effects revealed that ECs were safer than cigarettes but had more side effects than nicotine replacement therapy.

Williams *et al*.[9] found that metal and silicate particles, including nanoparticles, were present in EC cartomizer fluid and aerosol. Farsalinos *et al*.[11] studied 20 different EC solutions and found that some EC samples have cytotoxic properties on cultured cardiomyoblasts, associated with the production process and materials used in flavorings. However, McAuley *et al*.[19] showed that ECs spread minimal fragments in the room environment and have shown no apparent risk to human health from EC emissions in this respect. Goniewicz *et al*.[20] showed that the levels of toxicants were 9-450-fold lower than in cigarette smoke, and so substituting ECs for tobacco cigarettes may reduce substantially exposure to selected tobacco-specific toxicants.

The purpose of this study was to evaluate the effect of ECs on sinonasal symptoms and to assess the impact on MCC. No prior studies have examined the effects of ECs on the upper respiratory tract; this study is the first of its kind. Our findings revealed that sinonasal symptoms were better after 3 months cessation of cigarette smoking (Table 2). Although SNOT-22 scores showed improvement in both groups ($p^{b}<0.05$), the sinonasal symptoms of EC users were worse than those of non-EC smokers ($p^{a}<0.05$) (Table 2). The decline in symptoms was

Table 2

Comparison of the SNOT-22 measurements before and after cessation of cigarette smoking between groups and within groups

SNOT-22	Smoking	3.Month	*First-Last Change*
	Mean±SD	Mean±SD	*^{b}p*
Group 1 (EC) (n=42)	33.29±5.97	24.19±4.49	*0.0001**
Group 2 (Non EC) (n=30)	31.23±5.16	17.37±2.75	*0.0001**
^{a}p	*0.133*	*0.0001**	

^{a}p: Independent Samples T test; *p<0.05; EC: Electronic cigarette; ^{b}p: Paired Samples T test.

Table 3

Comparison of the MCC measurements before and after cessation of cigarette smoking between groups and within groups

MCC	Smoking	3.Month	*First-Last Change*
	Mean ± SD	Mean ± SD	[b]*p*
Group 1 (EC) (n = 42)	12.15 ± 2.06	11.93 ± 1.81	*0.194*
Group 2 (Non EC) (n = 30)	12.04 ± 1.64	10.36 ± 1.61	*0.0001**
[a]*p*	*0.811*	*0.0003**	

[a]p: Independent Samples T test;*p < 0.05; EC: Electronic cigarette; [b]p: Paired Samples T test.

thought to be due to the small amount of toxic substances and particles contained in ECs, as shown by Goniewicz *et al*.[20]

Mucociliary clearance plays a crucial role in defense of the respiratory system from the nose to the lower respiratory tract.[21] Several factors such as acute infection and long-term smoking may interfere with MCC.[22] Some studies have shown that the exposure of the ciliated epithelium to cigarette smoke results in a significant decrease in ciliary beat frequency (CBF), therefore MCC has been shown to be increased in active smokers.[14] Habesoglu *et al*.[23] reported that both active and passive smoking increases nasal MCC time when compared with healthy controls. However, as far as we know, no previous study has focused on the effects of electronic cigarette on nasal mucociliary clearance.

Earlier studies have demonstrated that tobacco smoking damages the respiratory epithelium and impairs host respiratory defenses, thereby contributing to increased susceptibility to infections.[24] Mucociliary clearance is impaired in smokers compared with non-smokers. Ramos *et al*.[13] showed that STT values decreased to within the normal range on day 15 after smoking cessation, and remained in the normal range until the end of the study period. The short term smoking abstinence decreased systemic inflammation and improved nasal mucociliary clearance.

Saccharin test and rhinoscintigraphy are commonly used techniques for the measurement of nasal MCC.[25] We used saccharin transit test to measure the MCC time. The present study showed that MCC time of non-EC smokers (group 2) were significantly better after the three months ([b]p = 0.001). However, EC smokers did not show improvement after the three months and MCC measurements were significantly worse compared to non-EC smokers (group 2) (Table 3). These results revealed that mucociliary clearance was impaired by oxidative stress induced by nicotine exposure. When chronic exposure to aggressive agents present in cigarette smoke is ceased, MCC function can be recovered. However, this improvement was not observed in the EC smokers.

One of the limitations of our study is that saccharin test depends on the sensation of taste. Saccharin test could not supply an objective and detailed information for quantitative analyses like rhinoscintigraphy. But saccharin test is seemed a safer and easier method to evaluate nasal MCC.

Conclusion

Although EC is widely used as a method of quitting smoking, it has negative effects on the sinonasal symptoms and MCC. Poor sinonasal symptoms for the EC revealed the disturbing effects to the sinonasal function. Mucociliary clearance was impaired by oxidative stress induced by ECs.

References

1. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Med*. 2006; 3(11):e442.
2. Casella G, Caponnetto P, Polosa R. Therapeutic advances in the treatment of nicotine addiction: present and future. *Ther Adv Chronic Dis*. 2010;1(3):95-106.
3. Etter JF, Burri M, Stapleton J. The impact of pharmaceutical company funding on results of randomized trials of nicotine replacement therapy for smoking cessation: a meta-analysis. *Addiction*. 2007;102(5):815-822.
4. Zhu S, Melcer T, Sun J, Rosbrook B, Pierce JP. Smoking cessation with and without assistance: a population-based analysis. *Am J Prev Med*. 2000;18(4):305-311.
5. Flouris AD, Oikonomou DN. Electronic cigarettes: miracle or menace? *BMJ*. 2010;340:c311.
6. Lee S, Kimm H, Yun JE, Jee SH. Public Health Challenges of Electronic Cigarettes in South Korea. *J Prev Med Public Health*. 2011;44(6):235-241.

7. Watelet JB, El Shazly A, Collet S, Doyen A. Chronic inflammation of upper airways in children: basic principles. *B-ENT*. 2012;8(19):29-40.
8. Odum LE, O'Dell KA, Schepers JS. Electronic Cigarettes: Do They Have a Role in Smoking Cessation? *J Pharm Pract*. 2012;25(6):611-614.
9. Williams M, Villareal A, Bozhilov K, Lin S, Talbot P. Metal And Silicate particles Are Present In Electronic Cigarette Cartomizer Fluid and Aerosol. *PloS One*. 2013; 8(3):e57987.
10. Manzoli L, La Vecchio C, Flacco ME, Capasso L, Simonetti V, Boccia S, Di Baldassarre A, Villari P, Mezzetti A, Cicolini G. Multicentric Cohort Study On The Long Term Efficacy and Safety Of Electronic Cigarettes: Study Design And Methodology. *BMC Public Health*. 2013;13:883-889.
11. Farsalinos KE, Romagna G, Allifranchini E, Ripamonti E, Bocchietto E, Todeschi S, Tsiapras D, Kyrzopoulos S, Voudris V. Comparison of the cytotoxic potential of cigarette smoke and electronic cigarette vapour extract on cultured myocardial cells. *Int J Environ Res Public Health*. 2013;10(10):5146-5162.
12. Proenca M, Fagundes Xavier R, Ramos D, Cavalheri V, Pitta F, Cipulo Ramos EM. Immediate and short term effects of smoking on nasal mucociliary clearance in smokers. *Rev Port Pneumol*. 2011;17(4):172-176.
13. Ramos EM, De Toledo AC, Xavier RF, Fosco LC, Vieira RP, Ramos D, Jardim JR. Reversibility of impaired nasal mucociliary clearance in smokers following a smoking cessation programme. *Respirology*. 2011;16(5): 849-855.
14. Stanley PJ, Wilson R, Greenstone MA, MacWilliam L, Cole PJ. Effect of cigarette smoking on nasal mucociliary clearance and ciliary beat frequency. *Thorax*. 1986;41(7): 519-523.
15. Hopkins C, Gillett S, Slack R, Lund VJ, Browne JP. Psychometric validity of the 22-item Sinonasal Outcome Test. *Clin Otolaryngol*. 2009;34(5):447-454.
16. Salah B, Dinh Xuan AT, Fouilladieu JL, Lockhart A, Regnard J. Nasal mucociliary clearance in healthy subjects is slower when breathing dry air. *Eur Respir J*. 1988;1(9): 852-855.
17. World Health Organization. *Report on the global tobacco epidemic*. Available at: www.who.int/tobacco/mpower/ 2008/en/index.html. 2008. Accessed May 5, 2015
18. Fowles JR, Banton MI, Pottenger LH. A toxicological review of the propylene glycols. *Crit Rev Toxicol*. 2013; 43(4):363-390.
19. McAuley TR, Hopke PK, Zhao J, Babaian S. Comparison of the effects of e-cigarette vapor and cigarette smoke on indoor air quality. *Inhal Toxicol*. 2012;24(12):850-857.
20. Goniewicz ML, Knysak J, Gawron M, Kosmider L, Sobczak A, Kurek J, Prokopowicz A, Jablonska-Czapla M, Rosik-Dulewska C, Havel C, Jacob P 3rd, Benowitz N. Levels of selected carcinogens and toxicants in vapour from electronic cigarettes. *Tob Control*. 2014;23(2):133-139.
21. Sleigh MA, Blake JR, Liron N. The propulsion of mucus by cilia. *Am Rev Respir Dis*. 1988;137(3):726-741.
22. Verra F, Escudier E, Lebargy F, Bernaudin JF, De Crémoux H, Bignon J. Ciliary abnormalities in bronchial epithelium of smokers, ex-smokers, and nonsmokers. *Am J Respir Crit Care Med*. 1995;151 (3 Pt 1):630-634.
23. Habesoglu M, Demir K, Yumusakhuylu AC, Yilmaz AS, Oysu C. Does passive smoking have an effect on nasal mucociliary clearance? *Otolaryngol Head Neck Surg*. 2012;147(1):152-156.
24. Almirall J, González CA, Balanzó X, Bolíbar I. Proportion of community acquired pneumonia cases attributable to tobacco smoking. *Chest*. 1999;116(2): 375-379.
25. Di Giuda D, Galli J, Calcagni ML, Corina L, Paludetti G, Ottaviani F, De Rossi G. Rhinoscintigraphy: a simple radioisotope technique to study the mucociliary system. *Clin Nucl Med*. 2000;25(2):127-130.

Tolgar Lütfi Kumral
Darülaceze Cad. No: 25
34400 Okmeydanı - Şişli, Istanbul
Tel.: +90 212 314 55 55
Fax: +90 212 221 78 00
E-mail: tolgins@hotmail.com