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ORIGINAL ARTICLE

Oral mucosal lesions in electronic cigarettes consumers versus former smokers

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ABSTRACT

Objectives: Electronic cigarettes (ECs) have become very popular in recent years. However, many uncertainties remain about their side effects. This study aims to evaluate the prevalence and characteristics of oral mucosal lesions (OMLs) in former smokers compared to ECs consumers.

Methods: A prospective case-control study was carried out. Outpatients for dental consultation were consecutively enrolled into two groups based on their habits, i.e. former smokers and ECs consumers. Each patient was examined to detect possible oral lesions and, if needed, a swab or biopsy of the lesion was taken for diagnosis. Data was entered into a spreadsheet and analyzed.

Results: A total of 90 patients were examined, 45 were former smokers (group A) and 45 were ECs consumers (group B). OMLs were detected in 55 cases, of which 19/55 (34.6%) belonged to group A and 36/55 (65.4%) to group B. Nicotine stomatitis, a hairy tongue and angular cheilitis resulted to be significantly more common among EC consumers.

Conclusions: We found no statistically significant differences in terms of total prevalence of OMLs between former smokers and ECs consumers. An increased prevalence of three specific types of OMLs was detected among ECs consumers.

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Smoking; oral lesion; electronic cigarette

Introduction

Electronic cigarettes (ECs) are battery-powered, nicotine-delivery devices marketed as safe substitutes for traditional cigarettes [1]. In recent years, ECs have rapidly gained popularity. Although ECs were developed as a safer alternative to smoking tobacco products, there is a growing body of evidence to substantiate that their produced aerosols contain low levels of toxicants and carcinogens, though generally lower than the quantities found in conventional tobacco cigarettes [2,3].

The few existing toxicological studies investigating the cellular effects of exposure to ECs' aerosol in human bronchial cells have produced conflicting results. Some studies seem to indicate either no or very little toxicity from ECs *in vitro* [4], while others suggest potential oxidative stress and inflammatory response [5,6].

Relatively little is known about the clinical effects of the ECs on the oral mucosa, especially on a long-term basis. This study aims to investigate the oral mucosal lesions (OMLs) in ECs consumers.

Materials and methods

Study population

This case-control study was performed at the Dental Clinic of the University of Brescia, within a 2-year period, from January 2015 to December 2016 on consecutively enrolled patients.

The study was undertaken on former cigarettes smokers and current EC users. Former smokers were defined as daily or almost daily smokers, who had smoked at least 100 cigarettes in their lifetime and who had quit smoking from at least 6 months to a maximum of 2 years prior to their involvement in the study. EC consumers considered were those who had been smoking ECs for at least 6 months. Inclusion criteria were: age older than 18 years, no dental procedures in the last six months, no chronic alcoholism, no occupational exposure to carcinogens, no history of malignancy.

OMLs were classified following the WHO criteria [7]. Patients were examined by two calibrated clinicians (EB, FA) under standardized conditions, with artificial lighting and with a mouth mirror. If needed, the clinical diagnosis was confirmed by a swab or biopsy of the lesion. Carious lesions, endodontic lesions and periodontal lesions were excluded from the oral lesions studied.

The following data was recorded from each patient: age, gender, systemic chronic diseases, clinical aspects of the OMLs and eventual histological diagnosis.

Data analysis

The data was put on a spreadsheet. A 5% level of significance was used and the data was analyzed using R® software for Mac. Descriptive analysis, bivariate analysis and Fisher's test were used.

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Ethical considerations

The research was conducted in accordance with the principles of the Declaration of Helsinki. All subjects gave a written informed consent indicating their voluntary and anonymous participation in the study. They completed a questionnaire that collected demographic data and information on the consumption of cigarettes/e-cigarettes, use of alcohol, exposure to occupational carcinogens and the presence of concomitant or previous systemic diseases.

Results

During the 2-year period, we consecutively enrolled former smokers and EC consumers in order to have two numerically similar groups. Ninety patients met the inclusion criteria, 45 were former smokers (group A) and 45 were EC consumers (group B). Group A was composed of 23 females and 22 males (mean age 47 ± 11) while group B contained four females and 41 males (mean age 47 ± 10). About 43.3% of the patients ($n = 39$) had some form of the systemic disease, which included diabetes ($n = 8$), hypertension ($n = 16$), heart disease ($n = 8$) or HCV ($n = 5$). The sociodemographic data is shown in Table 1.

OMLs were detected in 55 cases, of which 34.6% ($n = 19/55$) belonged to group A and 65.4% ($n = 36/55$) to group B. Nine different types of OMLs were detected. The type and distribution of the lesions are shown in Table 2.

Discussion

E-cigarettes are currently used to stop smoking or at least reduce the consumption of traditional cigarettes. However, the Food and Drug Administration has yet to fully regulate the composition or given approval of the e-liquid contained by ECs, although it has provided information about the known side effects of such usage (e.g. congestive heart failure, cough, hypotension, and mental confusion) and defined the common components found in these liquids [8].

There have been few studies that address the direct health effect of EC smoking, especially regarding the oral mucosa. A recent study [9] based on cytological examination of scrapings from the oral mucosa in three groups of patients (smokers, ECs smokers, and non-smokers) demonstrated that there were no statistically significant differences in the micronuclei distribution, suggesting that the use of ECs seems to be safe for oral cells. On the other hand, Reuther et al. [10] found that ECs may have an effect on the blood flow (measured using a laser Doppler) of the oral mucosa. The laser Doppler measurements were expressed as arbitrary perfusion units: a significant difference in the arbitrary perfusion units was found with respect to the baseline capillary blood flow after vaping with both nicotine and nicotine-free ECs. However, the Doppler measurements were not performed in smokers.

The pathologic effects on the oral mucosa in terms of clinical OMLs have yet to be thoroughly evaluated and therefore, to our knowledge; this is the first report describing OMLs in ECs consumers. Before discussing the results of this study, it should be emphasized that the study was carried out on a small sample of patients, so the findings must be considered preliminary.

From our results, the prevalence of total OMLs was higher among ECs consumers, but the difference between the two groups was not statistically significant. One of the most common lesions in both groups was smoker's melanosis and this was consistent with the observations made by Saraswathi et al. [11] and Hedin et al. [12]. Polycyclic amines such as nicotine and benzopyrenes, present in tobacco, can activate the production of melanin by melanocytes, perhaps as a protective mechanism of the oral mucosa against tobacco agents. Tobacco-associated melanin pigmentation has been reported in about 22% of smokers and is dose-dependent. In our study, the prevalence of such pigmentation was we found no difference between the former tobacco smokers and the EC consumers, confirming that former smokers have a lower incidence of melanosis [13], as the cessation of tobacco usage can be sufficient in reducing or eliminating the pigmentation.

Table 1. Demographic characteristics of the group A (former smokers) and of the group B (EC consumers).

	Group A ($n = 45$)	Group B ($n = 45$)
Gender		
Male	22	41
Female	23	4
Mean age	47 + 11	47 + 10
Systemic diseases	16	23
Diabetes	3	5
Hypertension	9	7
Heart disease	2	6
HCV	2	5

Table 2. Distribution of OMLs in the group A (former smokers) and in the group B (EC consumers).

Oral mucosal lesions	Group A (45) *n* (%)	Group B (45) *n* (%)	OR (95% CI)	*p* Value
Melanosis	5 (11.1)	6 (13.3)	1.23	.74
Nicotine stomatitis	1 (2.2)	6 (13.3)	6.77	.04*
Hairy tongue	1 (2.2)	7 (15.5)	8.11	.02*
Hyperplastic candidiasis	2 (4.4)	8 (17.7)	4.65	.04*
Median rhomboid glossitis	3 (6.6)	4 (8.8)	1.37	.69
Lichen planus	2 (4.4)	0	0	.15
Erythematous candidiasis	2 (4.4)	4 (8.8)	2.1	.39
Leukoplakia	2 (4.4)	1 (2.2)	2.05	.55
Hyperkeratosis	2	1		
Dysplasia	0	0		
Squamous cell carcinoma	1 (2.2)	0 (0)	0	.31
Total	19	36	0.42	.28

*Significant, *p* value < .05.

Regarding other OMLs, nicotine stomatitis occurred more frequently in 6/45 EC consumers and only in 1/45 former smokers ($p = .04$). The many irritants, toxins and carcinogens, found naturally in tobacco, cause the typical opacification or keratinization of the palate seen as red dots surrounded by white keratotic rings [14]. Although ECs do not contain as many ingredients as conventional tobacco, they are vaporized by heat starting from a liquid solution (a mixture of propylene glycol, glycerine, nicotine and flavouring) [15]. The nicotine content in ECs varies widely among brands, typically ranging from 0 to 34 mg/ml [16]. Emissions from ECs may also contain fine particles of flavours, aroma transporters, glycerol, propylene glycol, nicotine, trace amounts of carcinogens, heavy metals and other chemicals [1].

We can speculate that nicotine stomatitis in ECs consumers may depend not only on the exposure of the palatal mucosa to nicotine but also to some of these chemical compounds. For instance, a recent study found that the product characteristics of electronic nicotine delivery systems, including flavouring, might induce inhalation toxicity, with a strawberry-flavoured product being the most cytotoxic [17].

Likewise, we can also interpret the high percentage of hyperplastic candidiasis in the retrocommissural area (17.8%) found in the group of ECs consumers ($p = .04$). Many cross-sectional studies show a higher prevalence of hyperplastic candidasis among smokers while there are no data about ECs consumers. Candidal ability to invade superficial layers of the epithelium, aided by their hyphal appendages with tips containing concentrated amounts of candidal proteinases (secreted aspartyl proteinases [SAP]) and lipases – is optimal at acidic pH. Several studies have shown that many protective salivary proteins such as lactoferrin, lactoperoxidase, and immunoglobulins, especially IgA1 and IgA2, are susceptible to degradation by candidal SAPs. We can presume that hyperplastic candidiasis in ECs consumers could be favoured by a pH alteration induced by the aforementioned chemical compounds [18].

Hairy tongue resulted in a statistically greater prevalence among EC consumers than in former smokers. There are numerous initiating or predisposing factors for the abnormal coating on the dorsal surface of the tongue, particularly with smoking-associated pH changes [14]. We can speculate that the mucosal changes may also arise from other factors, i.e. the mucosal drying effects, the high intraoral temperatures, intraoral pH changes, local alteration of membrane barriers and immune responses, or altered resistance to fungal and viral infections.

No differences in terms of precancerous OMLs (lichen planus, leukoplakia) were found between the two groups. Only one case of squamous cell carcinoma was found on the lateral surface of the tongue in a 52-year-old former smoker.

Our results show that e-cigarettes are linked to three types of inflammatory lesions in the oral cavity. Future case-control or cohort studies for individual lesions with larger sample sizes are necessary to evaluate the risk for OMLs resulting from EC habits.

Disclosure statement

No potential conflict of interest was reported by the authors.

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