E-cigarettes and oral health - What do dental professionals need to know?

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Abstract

The use of electronic cigarettes (e-cigarettes) has been exponentially increasing worldwide. These electronic vaping devices are widely available and are being marketed as a smoking cessation tool and a safer alternative to conventional tobacco cigarettes. However, there is inadequate evidence to support these safety marketing claims. The oral cavity is the first encounter of the e-cigarettes smoke and aerosols, yet data regarding the effects of e-cigarettes on oral health are still limited and controversial. Dental professionals may have a major role in raising public awareness about the potential hazards of e-cigarettes on the oral mucosa, teeth, and their supporting structures. Moreover, dental records may serve as a leading repertoire for observations and follow-up data for future studies. The aim of this review is to provide dental professionals with an updated overview of the available data regarding the effects of e-cigarettes on oral health.

Keywords:
E-cigarettes, Oral health, Vaping

Introduction

Electronic cigarettes (e-cigarettes) or electronic vaping devices are nicotine delivery systems originally designed for individuals who wish to quit smoking. The components of e-cigarettes comprise a battery, a heating element (coil), an air flow sensor, a temperature controlling microchip, and a tank holding the e-liquid. When the e-liquid is subjected to heat, it vaporizes releasing an aerosol which is inhaled by the user. The levels of nicotine and other constituents in the inhaled aerosol are determined by the coil, where the used voltage and heating temperature make these levels highly variable.

E-cigarettes were introduced to the American and European markets in 2006 and 2007, respectively. Since then, the use of e-cigarettes has been rapidly increasing all over the world, especially among young adults. In 2014, vaping became the most common smoking method among young adults, which raised the public community concerns regarding their safety, long-term health effects, and the factors leading to its initiation at an early age. A recent study published in 2020 reported a relationship between adverse childhood experiences (ACEs) and the use of vaping devices among middle school children in the US. The study explained that the use of e-cigarettes at a young age may be a coping mechanism for troubled children. This result is consistent with the previous publication by Rothman et al. which suggested that ACEs may lead to various undesirable habits such as alcoholism. Troubled children may start such habits at an early age to cope with their problems rather than to seek pleasure or social acceptance.

On the other hand, another study interviewing high school students in the United Kingdom revealed a general agreement that vaping devices are more accessible than tobacco cigarettes. Students described vaping as being “casual” and socially motivated among their peers. Many of the participants reported that they have experimented with vaping devices for fun, but regular vaping was rarely reported. Furthermore, recent data published in the New England Journal of Medicine (NEJM) showed that vaping has almost doubled among high school students in the US between 2017 and 2019. One of the most disturbing findings in these studies is the increase in the proportions of youths who became nicotine addicts as a direct outcome of using e-cigarettes.

E-cigarettes are considered a cheaper, “healthier” alternative to traditional cigarettes. Social media plays a role in the marketing of vaping devices. This partly explains the ubiquitous use of these devices among the younger generations.

Marketing e-cigarettes as a safe alternative to conventional tobacco smoking is misleading unless both short- and long-term
health implications are thoroughly investigated and compared to those of conventional cigarette users and non-smokers. One of the major concerns of e-cigarettes is the lack of standardization of the manufactured e-liquids, which heightens the risk of presence of unforeseen carcinogenic constituents. Studies have shown that e-cigarettes exclusively contain certain chemicals that are not present in conventional cigarettes and have unknown health effects. Other chemicals that are listed as safe ingredients, such as glycerol, are normally safe when ingested, but no data are available for their inhalation effects. In 2020, the WHO described the potential health effects of e-cigarettes as “inconclusive” and highlighted a major concern regarding their long-term effects. A recently published review discussed the latest evidence of harmful effects of e-cigarettes on respiratory health. In 2019, The Centers for Disease Control and Prevention (CDC) reported the e-cigarettes or vaping product use associatedlung injury (EVALI). EVALI has led to the hospitalization of almost 2807 cases across the 50 states (as of February 2020), some cases needed intubation and mechanical ventilation. Most of the reported cases were e-cigarettes smokers who were otherwise healthy.[15] To further explain this effect, an in vivo experiment was performed with 30 mice being exposed to e-cigarettes aerosols containing Vitamin E acetate and propylene glycol and vegetable glycerin (PG–VG). After inhaling Vitamin E acetate, mice showed markers of lung epithelial injury.[16] These findings were consistent with the clinical observations in EVALI patients. It was also reported that e-cigarettes increase the severity of asthmatic attacks,[17] and the prolonged use of nicotine-containing e-cigarettes increases oxidative stress, which can subsequently increase the risk of strokes[18] and cardiovascular diseases.[19]

In addition, marketing e-cigarettes as a quitting aid for smokers is still debatable. Although some studies have shown that the use of e-cigarettes was strongly associated with quitting, others have shown that the use of e-cigarettes did not guarantee smoking cessation and that dual users became more nicotine dependent.[21] Moreover, e-cigarettes smoking is permitted indoors in places where conventional smoking is prohibited.[22] Accordingly, further studies are necessary to disclose the risks, potential health hazards, and possible carcinogenic effects of e-cigarettes.

One of the major health hazards of e-cigarettes that investigators usually underestimate is the potential effect on oral health. According to the World Health Organization (WHO), oral health is defined as “a key indicator of overall health, well-being, and quality of life as it encompasses a range of diseases and conditions that include dental caries, periodontal disease, tooth loss, oral cancer, oral manifestations of HIV infection, orodental trauma, and birth defects such as cleft lip and palate.” The impact of oral diseases ranges from pain and suffering to social withdrawal or adverse psychological effects. Dental practitioners need to be aware of all the possible effects of e-cigarettes on the oral cavity to raise awareness among their patients and help the monitoring and reporting of any unidentified adverse effects. In this review, we present an overview of the reported effects of e-cigarettes in the oral cavity. Our main goal is to raise awareness among dentists, dental hygienists, and their patients regarding the possible adverse effects of e-cigarettes on oral health.

Tobacco and Oral Health

Over the years, the health consequences of smoking (active and passive) have been extensively studied and well documented. In 2004, the US Surgeon General presented startling damaging effects of tobacco smoking on almost all body organs.[23] According to the report, smoking was identified as a direct cause of several diseases including malignancies, cardiovascular diseases, and respiratory disorders. Head-and-neck cancers were among the list of diseases associated with tobacco smoking. The mechanism of carcinogenesis of tobacco is a combination of gene mutation, enhancement of cell growth, migration, and invasion. These effects are facilitated by nicotine and the diverse array of tobacco-containing carcinogens, such as nitrosamines.[24] Thus, smoking has ascertained serious adverse effects on oral health.[25] In 2014, another Surgeon General’s report discussed the efficiency of tobacco control efforts in the United States.[26] The report emphasized the need for expanded efforts to monitor all forms of smoking, including e-cigarettes, across diverse segments of society. This adjustment is especially important with the widespread consumption of conventional and non-conventional tobacco products among youth.

Moreover, a study by Wu et al.[27] has drawn remarkable data regarding the effect of tobacco-smoking on oral microbiome. The oral microbiome changes were related to the oral oxygen availability which affects the rate of microbial degradation. They concluded that this effect may lead to progressive loss of beneficial oral species of bacteria allowing pathogen colonization which may cause various oral diseases including periodontitis. This was further supported by another study that reported a difference in the buccal mucosa microbiota in smokers versus non-smokers.[28] In fact, tobacco smoking is considered a chief modifiable risk factor for periodontal disease[29] and oral cancers.[30] In 2018, a study by AlHarthi et al.[31] analyzed a combined data set from two national US health surveys, directed by the CDC, between 2009 and 2012. Based on this study, smoking status was strongly associated with periodontal status where periodontitis was more common among smokers than non-smokers or former smokers. Surprisingly, smoking cessation had a significant positive impact on periodontal health recommending that tobacco cessation should be an integral part of the treatment of periodontitis. A possible explanation for these adverse effects may be the cytotoxic effect of nicotine on human periodontal ligament fibers. Nicotine also inhibited DNA synthesis and hence fibers proliferation.[32] Nonetheless, an in vitro study published in 2007 showed that nicotine dose-dependently enhanced collagen I degradation in human gingival fibroblasts.[33] To date, there are obvious implications of tobacco smoking on oral health. To support the assumption that vaping is a safe alternative to tobacco smoking, there should be tangible evidence regarding the lack of adverse effects of e-cigarettes on oral health.
Effects of E-cigarettes on Oral Mucosa

A systematic review by Ralho et al.\(^\text{[36]}\) compared the biological alterations affecting oral mucosa of conventional smokers, e-cigarette smokers, ex-smokers and non-smokers. The review included eight studies, but none of them included dual smokers (tobacco and e-cigarettes). The results showed that the oral mucosa in e-cigarette smokers had fewer biological alterations as compared to conventional tobacco smokers. However, there were more alterations happening in e-cigarette smokers than non-smokers and ex-smokers. Nicotine stomatitis, hairy tongue, and angular cheilitis were the most common lesions among e-cigarette smokers. Moreover, recurring hyperplastic candidiasis was also common among e-cigarette smokers.\(^\text{[35]}\)

Apart from the possible adverse effects of e-cigarettes on the oral mucosa, dentists may receive inquiries regarding the safety of vaping after oral surgeries. One of the major factors that govern post-operative healing is tissue vascular perfusion. A study aimed at finding a safe alternative to conventional smoking during the post-operative healing phase, used laser Doppler to test the effect of vaping on blood flow in the buccal mucosa. This study compared the effect of plain e-liquids (nicotine free) versus nicotine-containing e-cigarettes in 10 volunteers. The outcome showed that higher blood perfusion occurred with the nicotine-containing e-cigarettes as compared to the nicotine-free ones. This study concluded that e-cigarettes, especially those with nicotine-containing liquids, may be a safe short-term alternative for post-operative smoking, as it maintains adequate blood perfusion to the oral mucosa.\(^\text{[47]}\)

However, the number of subjects (10 volunteers) included in the study was not enough for a definitive conclusion. Moreover, they studied the effect of e-cigarettes on oral mucosa with no surgical wound which provides limited data about the actual effect of post-surgical vaping.

Another risk of e-cigarettes smoking is the chance of explosion leading to serious injuries including burns.\(^\text{[58]}\) According to the 2014 published U.S. Fire Administration’s document, 25 e-cigarettes related fire and explosions cases have been reported since 2009.\(^\text{[39]}\) Two of these cases had severe mouth injuries following the incident, with one man losing his teeth and part of his tongue. Another case report of a 28-year-old male showed avulsed teeth and trauma to the maxillary alveolar bone alongside burns to the dorsal surface of the tongue, maxillary anterior gingiva, and mucosa.\(^\text{[40]}\)

In addition to the previous hazards, the role of e-cigarettes in the incidence of oral cancer is still debatable. A 2017 paper outlined two case reports of long-term e-cigarettes smokers (for over a decade) showing oral tumors.\(^\text{[41]}\) Traces of heavy metal, such as aluminum, arsenic, zinc, lead, copper, and nickel have been previously detected in e-cigarettes-released aerosols.\(^\text{[42]}\) These metals are well-known carcinogens and hence may play a role in inducing cellular damage with the prolonged use of e-cigarettes.\(^\text{[43]}\) Moreover, the tobacco-specific carcinogen, N-nitrosomorpholine (NNN) that is associated with the incidence of oral and esophageal cancers, has been found to be endogenously produced in the oral cavity of e-cigarettes users.\(^\text{[44]}\) Another study conducted by Franco et al. studied the role of e-cigarettes on the primary prevention of mouth cancer. This group divided 65 subjects into three groups; Group A (conventional smokers), Group B (e-cigarette smokers), and Group C (non-smokers acting as a control group). Mucosal swabs were collected from the anterior and middle portions of the buccal mucosa and tested for micronuclei where the CMN (micronucleated cells/1000 cells) and TMN (total micronuclei/1000 cells) were calculated. Both the CMN and TMN were lower in Group B than A; however, they were higher than Group C, which means that e-cigarettes smoking could be a safer option than conventional smoking, but it still poses some cytotoxic effects on the oral mucosa when compared to non-smokers. In this study, 30% of the e-smokers quit smoking altogether 6 months after the sampling was done, helping the argument that e-cigarettes can be used as a useful quitting tool.\(^\text{[45]}\) On the contrary, an in vitro study comparing the effects of conventional and electronic cigarette extracts on antigen-presenting cells showed similar or even increased toxicity of the e-cigarette extracts. This can cause an increased susceptibility to tobacco-induced diseases, as chronic obstructive pulmonary disease.\(^\text{[46]}\) In 2018, a consensus report was published by the National Academy of Sciences on the public health consequences of e-cigarettes.\(^\text{[47]}\) This report included in vitro studies that detected cytotoxic effects of e-cigarettes smoke and liquids on cell cultures. However, they argued that although some of the chemicals (like formaldehyde) are mutagenic, there is limited evidence that the levels of exposure are high enough to lead to carcinogenesis. The studies cited within this report examined a variety of human cell types, including tracheobronchial cells, head-and-neck squamous cell carcinoma, embryonic stem cells, immortal keratinocytes (Hacat), gingival fibroblasts, and periodontal ligament fibroblasts. Yu et al. have shown that the vapors from e-cigarettes were cytotoxic to normal and cancerous epithelial cell lines, causing DNA breaks and apoptosis.\(^\text{[48]}\) Despite the available data, no further clinical evidence is found to prove an increased risk of cancer with long-term use of e-cigarettes. Hence, there is persistent demand for studying the effect of the various brands and flavors of the marketed e-liquids on oral mucosa.

Effects of E-cigarettes on the Periodontium

Periodontal disease is the inflammation of the teeth supporting tissues (cementum, bone, periodontal ligaments, and gingiva) and is one of the significant causes of bone resorption and tooth loss. Susceptibility to periodontal disease is usually provoked by environmental factors such as cigarette smoking, poor oral hygiene, and underlying systemic diseases.\(^\text{[49]}\) Despite the evident association between tobacco smoking and poor oral health, especially periodontitis, the mechanism of tissue damage linked to smoking is not yet clearly explained. With the increased popularity of using e-cigarettes, it is absolutely necessary to assess their influence on periodontal health. Only a few recent studies have investigated such effects. In addition, most of these
studies included a limited number of participants. Despite these limitations, similar to tobacco smoking, the available studies showed various adverse effects of e-cigarettes use on the PDL.

A recent study analyzed data from the Population Assessment of Tobacco and Health (PATH) as a national representative sample to investigate the association between the use of nicotine-containing e-cigarettes and periodontal disease. This study indicated that the use of nicotine-containing e-cigarettes is significantly associated with the risk of developing periodontal disease.\(^{[50]}\) Various in vitro studies have also studied the effect of e-cigarette aerosols and flavorings on the periodontium. A study by Kouabhi et al. showed that exposure to e-cigarette vapors resulted in morphological changes, enhanced cell apoptosis and necrosis to primary gingival epithelial cells.\(^{[51]}\) Another study showed that these vapors increased oxidative stress, inflammatory cytokine release and DNA damage in human periodontal ligament fibroblasts, human gingival epithelium, and EpiGingival 3D epithelium. This study tested the effect of classic tobacco flavor and menthol flavor; as well as nicotine and non-nicotine-containing e-liquids.\(^{[52]}\) This study showed that the detrimental effects of aerosols on cells were independent of the nicotine content, indicating that the flavors themselves may have a deleterious effect on the periodontium. This suggests that the long-term use of nicotine-free liquids is still problematic. Another study by Willerheusen et al.\(^{[53]}\) tested the effect of different flavors on human periodontal ligament fibroblasts. This study used three different market available flavors; lime, hazelnut, and menthol. The results showed that the menthol flavor had a significant negative impact on the cell viability and migration of the fibroblasts. Such studies are key determinants of the safety of the different components of e-cigarettes and may be considered to prohibit or limit the use of certain additives or flavors.

It has also been shown in a 2014 study, that a nicotine dose above 1.5 mM demonstrated a cytotoxic effect on cementoblasts, and increased the release of inflammatory cytokines, such as IL-6 and TNF-α. Moreover, the results proved that nicotine inhibited cementoblast migration and cell growth in a dose-dependent manner, which can directly provoke the progression of periodontal disease, and impair the repair and regeneration capacity of the periodontium.\(^{[54]}\) Another study also showed that nicotine dose dependently exerted a cytotoxic effect on periodontal and alveolar bone stem cells. High doses of nicotine were significantly cytotoxic to gingival, periodontal ligament and alveolar bone stem cells. Conversely, the effect of low (0.155 μM–0.311 μM) to intermediate nicotine doses (0.622 μM–1.556 μM) was different depending on the cell type. Alveolar bone stem cells were the most sensitive to the low and intermediate doses of nicotine after 24 h. This study concluded that nicotine has both dose-dependent and time-dependent cytotoxic effects on periodontium stem cells, and that the different types of stem cells exhibited variable responses.\(^{[55]}\) This further highlights the importance of studying the long-term side effects of nicotine-containing e-cigarettes on periodontal health, as well as its effect on the repair and regenerative capacity of different cell types. Although nicotine seems to be a major factor of periodontal disease, it is still necessary to assess the effect of nicotine-free e-cigarettes on the periodontium.

### Electronic Cigarettes and Dental Caries

Dental caries is a dynamic complex process that involves interactions between the tooth structure, bacteria, sugars, saliva, and genetic factors. The occurrence of dental caries is mediated by the formation of a bacterial biofilm (dental plaque).\(^{[56]}\) This biofilm first starts off as a layer called the acquired enamel pellicle, which is formed by salivary proteins, and is essential for bacterial adhesion. Saliva contains various protective proteins, such as immunoglobulins A (IgA), lactoferrin, lysozymes, and salivary amylase, and hence acts as the first line of defense of the oral cavity.\(^{[57]}\) Modern dentistry considers dental caries a disease affected by behavioral, psychological, social, and biological factors.

Several studies have demonstrated that behavioral factors such as smoking and vaping can contribute to caries incidence. A study conducted on traditional cigarette smokers, e-cigarette smokers, and non-smokers showed several altered antibacterial properties of saliva among e-cigarette users. Their saliva showed a reduced level of IgA; the only antibody that is actively secreted in saliva and is important for the innate and acquired immune response of the oral cavity. The level of IgA was significantly lower in non-smokers, but not significantly different from traditional cigarette smokers. Moreover, the level of lysozyme, the enzyme responsible for lysis of the bacterial cell wall, was significantly lower in the saliva of e-cigarette smokers as compared to non-smokers. Lactoferrin, another salivary constituent that plays an immunomodulatory and anti-inflammatory role in the oral microenvironment, was surprisingly higher in the saliva of e-cigarette smokers than that of traditional smokers. These results indicate changes in the oral ecosystem that may lead to a higher caries incidence in e-cigarette smokers.\(^{[58]}\)

In addition to the aforementioned effects of e-cigarettes smoking on the overall defense mechanisms of the oral microenvironment, vaping seems to affect the cariogenic bacterial strains and formation of biofilm. Another study showed that the e-cigarettes vapors promoted *Streptococcus mutans* growth and promoted the expression of some virulence genes that regulate adhesion and viability. A possible explanation is that the bacteria may have sensed the aerosols as a stressor leading to activation of specific genes. Activation of these virulence genes may increase the bacterial cariogenic potential. Interestingly, this effect was achieved using both nicotine-free and nicotine-rich e-liquids. E-cigarette vapors increased the biofilm mass and promoted the adhesion/growth of *S. mutans* on the surface of extracted teeth.\(^{[59]}\)

E-liquids are viscous solutions that have a wide variety of sweet flavors. This sweetness is obtained by adding sucrose or sorbitol, and the sugary fragrance is achieved by the addition of sugar alcohol. Some e-liquids also contain glycerin to increase the viscosity and hence their capability to adhere to hard and soft surfaces. A study was designed to examine the adherence,
biofilm formation, and demineralization of enamel discs exposed to aerosols. The study has shown that certain constituents of e-liquids such as esters allow S. mutans to flourish in the oral environment. The study further confirmed the previous results indicating improved adhesion of S. mutans to the surfaces exposed to e-cigarettes aerosols.[60]

Discussion

The oral tissues are the primary encounter of e-cigarette aerosols, vapors, flavors, and various additives. The aim of this review is to explore the current available data on the effects of vaping, as a new smoking trend, on oral health. Although the available studies have serious limitations, most of the reviewed studies revealed that e-cigarette are not as harmless as they are marketed. Studies have reported recurring incidence of hyperplastic candidiasis among E-cigarettes smokers. Hairy tongue, angular cheilitis, and nicotine stomatitis were also common lesions. In addition to the clinical studies, in vitro data have shown that e-cigarettes have some cytotoxic effects on cells such as periodontal ligament fibroblasts, gingival epithelial cells, and embryonic stem cells. These effects included apoptosis, DNA breaks, increased oxidative stress, and the release of inflammatory cytokines. Furthermore, an imbalance of the immunomodulatory and anti-inflammatory factors was also detected in the saliva of e-cigarette smokers suggesting predisposition to caries incidence.

Conclusion

Long-term clinical findings regarding the effects of e-cigarettes on oral health are necessary to validate the safety of their long-term use as an alternative to tobacco smoking. Most of the available e-cigarette-related studies have various limitations. One of the major limitations of the current studies is the history difference between conventional cigarette smokers and e-cigarettes smokers. The history of vaping for most smokers is relatively shorter than with tobacco smokers. To overcome this limitation, future studies should have longer follow-up periods, larger populations, a variety of age groups, and a wider range of products (e-liquids) with different nicotine concentrations. It is also necessary to include dual smokers who consume both e-cigarettes and tobacco. Vaping may have unidentified adverse consequences on the oral mucosa, periodontium, teeth, and oral microbiome that still need further investigations. Dental professionals can play a major role in monitoring, reporting, as well as raising awareness of these potential adverse effects among their patients.

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