

## Review Article

### Effects of Vaping on Periodontium - A Review

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#### ABSTRACT:

The electronic-cigarettes (e-cigs) represent a remarkable and increasing proportion of the tobacco product consumption, which can pose an oral health concern. Due to the protein carboxylation, oxidative/carbonyl stress is an important factor in causing the inflammation and the DNA damage. This will lead to the stress-induced premature senescence i.e, a state of irreversible growth arrest which re-enforces chronic inflammation in the gingival epithelium, which as a result may contribute to the pathogenesis of several oral diseases. This article describes the effects of e-cigs with the flavorings and its effects leading to an increased oxidative/carbonyl stress as well as the inflammatory cytokine release in the human periodontal ligament fibroblasts. It also leads to increased levels of cyclooxygenase-2 and prostaglandin-E2 which are analogous with the up regulation of the receptor for advanced glycation end products (RAGE) by the e-cig exposure-mediated carbonyl stress in the gingival epithelium/tissue. Furthermore, the e-cigs cause an increased oxidative/carbonyl as well as inflammatory responses and the DNA damage. The present data highlights the pathologic role of the e-cig aerosol and its flavoring to the cells and tissues of oral cavity.

**Key words:** E-cigarettes, ENDS, oral health, periodontal diseases.

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#### INTRODUCTION:

The e-cigarettes are the battery operated devices which contains a metal heating element in a stainless steel shell, an atomizer, a cartridge and a battery. The heating element vaporizes a solution that contains a mixture of the chemicals including nicotine and other additives or

humectants, such as base/carrying agents propylene glycol or glycerin/glycerol and the flavoring agents including candy and fruit flavors. Apart from the inhaled nicotine, variable levels of the carbonyls and aldehydes have been detected in the e-cig aerosols during the vaporizations. <sup>1</sup>Aldehyde causes the

carbonyl/oxidative stress, DNA damage and stress-induced cellular senescence leading to the oral health problems. The periodontal disease is characterized by the chronic inflammation of supporting tissues of the teeth. The gingival fibroblasts, periodontal ligament as well as the epithelial cells are most abundant structural cells in the periodontal tissue. In stress, these cells are able to incite as well as maintain the inflammatory responses<sup>1, 2</sup> There is an association between smoking and periodontal attachment level, tooth loss, deeper periodontal pockets, as well as more extensive alveolar bone loss along with destruction of the connective tissue and matrix which leads to an increased risk of the periodontitis. Many clinical studies have also shown that the habitual tobacco smokers manifest a greater number of sites with the clinical attachment loss, plaque accumulation and probing depth  $\geq 4$  mm as compared to those individuals who had never used tobacco in any of the form. It is crucial to mention that the bleeding upon probing which is a classical marker of the periodontal disease activity is masked in the tobacco smokers than the non-smokers.<sup>2</sup> This occurs most likely as a result of vasoconstrictive effect of the nicotine which is the main component in e-cigs on the gingival blood vessels. Hence, the tobacco smokers may remain unaware of the continuously progressing periodontal destruction until the inflammatory process reaches a stage where the tooth mobility becomes evident. The tobacco smoking contributes to the progression of the periodontal disease.<sup>3</sup> Periodontal and gingival cells in the oral cavity are the first targets by the aerosols of e-cigs. In the present article, the mechanism of gingival epithelial inflammation and the pro-senescence by the e-cig aerosols with the flavorings in human oral epithelial cells and periodontal ligament fibroblasts have been concise.<sup>3</sup>

**Electronic nicotine delivery system (ENDS) and inhaled nicotine-** The nicotine is a main bioactive component of the tobacco-derived products, including the conventional cigarettes, e-cigarettes, cigars and water pipes ranging from 0 mg–100 mg/ml. Nicotine is well known for its addictive properties.<sup>3, 4</sup> Electronic nicotine-delivery system [ENDS] is the recently emerged nicotine delivery systems. ENDS are proposed to reduce the craving for conventional cigarettes. In recent times, a rapid growth has been taken place in both the marketing and consumption of these e-cigs. Each “puff,” results in heating element vaporization of a small amount of liquid. In this way, the ENDS user is not really inhaling the smoke but an aerosol/vapor of nicotine up to 24–100 mg as mist/vapor. Thereby, ENDS will deliver a significant amount of the nicotine compared to the tobacco cessation devices which are available commercially.<sup>4</sup>

**E-cigarette aerosol, inhaled nicotine, and the periodontal complications-** Periodontal disease is characterized by the chronic inflammation of the supporting tissues of the teeth. The gingival fibroblasts and periodontal ligament cells as well as the epithelial cells are the most abundant structural cells in the periodontal tissues that play a crucial and fundamental role in the periodontal regeneration.<sup>4</sup> The oxidants/reactive oxygen species reactivity from the e-cig aerosols is comparable to the conventional cigarette smoke. Moreover, the direct exposure to e-liquids has also been shown to produce harmful effects in the periodontal ligament cells as well as in the gingival fibroblasts in culture. The reactive aldehydes and carbonyls which have been derived from the e-cig aerosol can cause the protein carbonylation and DNA damage. The protein carbonylation results in the autoantibody production which in turn may lead to the destruction of matrix as well as bone loss during periodontitis.<sup>4, 5</sup> Thereby, it is possible that the carbonyls or aldehydes play an important role in the e-cig aerosol-induced oral toxicity. The nicotine has also shown to have the anti-proliferative properties and affects the fibroblasts in vitro. This implies that the E-cig containing nicotine affects the oral myofibroblast differentiation in the users of e-cig; and thus it may affect their ability to heal the wounds by decreasing the wound contraction by the myofibroblasts. This can be due to release of matrix metalloproteases (MMP-9, MMP-12) and prostaglandins (PGE2) as well as their effects on the mesenchymal stem cells (MSCs). The e-cigarette devices or ENDS deliver the nicotine at various concentrations.<sup>5</sup> The nicotine has been associated with the impaired leukocyte activity as well as the healing by inhibiting the neovascularization and also the osteoblastic differentiation. Likewise, the tobacco smoking including the nicotine is associated with an increased risk of the impaired healing, implant failure, poor papilla regeneration as well as increased bone loss. Thereby, it is possible that the nicotine derived from the e-cig may impair the healing potential at the bone and implant interface. This may also be due to the impairment in the functions of resident stem cells or MSCs by nicotine.<sup>7</sup> It has been reported by Berley et al. in 2010 that the decreased bone to implant contact after 4 weeks of the implant placement in rats’ femur receiving the subcutaneous nicotine. Similar results have been reported in the same year by Yamano et al. that indicated a down-regulation in expression of the bone matrix-related genes around the implants in rats that received the nicotine for 8 weeks. Although, the effects of nicotine delivery by e-cig on peri-implant hard and soft tissues as well as the other periodontal complications have not studied vigorously.<sup>6, 7</sup>

**DISCUSSION:** The e-cigarette was introduced as a product that aids with the smoking cessation. One of the most important risk factors for the oral cancer, periodontal diseases and implant failure is smoking.<sup>7</sup> The e-cigarette companies claim that it can improve the oral health by providing alternatives to smoking. Although it is still unclear that e-cigarettes play a role in smoking cessation or not. E-cigarettes are tobacco-free and also they do not generate toxic combustion products.<sup>7, 8</sup> However, e-cigarette vapor aerosols contain variable levels of carbonyls and aldehyde which can cause the carbonyl or oxidative stress, DNA damage as well as stress-induced cellular senescence i.e., irreversible growth arrest that induces the chronic inflammation. Till now there is not full understanding of the effect of e-cigarette on oral health and it is still debated among many clinicians and scientists. The various periodontal parameters were compared between the smokers, e-cigarette users who never smoked the conventional cigarette before and no smokers. It was observed that the periodontal probing, plaque index and clinical attachment loss were significantly higher in the smokers compared to other groups and there was no difference between the e-cigarette users and no smokers. Moreover, there was no significant difference in the self-perceived gingival pain as well as swelling between the e-cigarette users and non smokers.<sup>9</sup> However; it is still a topic to be argued that e-cigarette use is not as hazardous to the periodontal health compared to that of conventional cigarette smoking. But the bleeding on probing which is a classical marker for the periodontal disease severity was masked in both the smokers as well as the e-cigarette users compared to the non smokers; which is likely to be the result of vasoconstriction effect of the nicotine on gingival blood vessels.<sup>8, 9</sup> The micronucleus assay test is a cytologic method which samples the cells from oral cavity in order to screen for the drug toxicity on cells. Presence of the micronuclei within a cell is accepted as a predictive factor for the risk of cancer.<sup>8, 9</sup> A study that conducted the micronucleus assay test on the three groups namely smokers, e-cigarette users and non smokers found that the number of micronuclei was significantly higher in the smoker group compared to the e-cigarette group, although the number of micronuclei was similar between the e-cigarette and no smoker control groups. With this the authors concluded that the e-cigarettes cause no harm in oral cavity and is a reliable smoking cessation method. However, the study followed the patients only for 6 months which may not be long enough to see the true effect of e-cigarette on oral cancer risk. Although the carcinogens appear to be reduced in e-cigarettes, there are several health concerns regarding the nicotine.<sup>9</sup> In vitro, the nicotine has an anti proliferative property. Thereby, the nicotine exposure through the e-cigarette may potentially impair

the wound healing. Nicotine is associated with impairment of the leukocyte activity and thereby delaying the healing by inhibiting the neurovascularization and osteoblastic differentiation.<sup>9, 10</sup> Hence, it is hypothesized that the e-cigarette may also impair the healing of the bone and implant interface. Sundar et al in 2016 reported in an *in vitro* study that the amount of reactive oxygen species (ROS) reactivity is similar between the conventional smoking and e-cigarette smoking. Since the gingival and periodontal cells are the first targets by the e-cigarette aerosols, there is a concern that e-cigarette may have an adverse effect on the gingival and periodontal health. With the introduction of e-cigarettes, there have been reports of the fires and explosions that have been caused by e-cigarettes.<sup>10</sup> The explosions of e-cigarette inside the mouth of user result in the oral ulcerations, abdominal burns, teeth fractures and also avulsions. The explosion may be due to the various factors like the design of e-cigarette device, battery quality and the compatibility between the charger and device. It is necessary that during the history taking, the dentists should identify all the forms of nicotine and tobacco use including the e-cigarettes, conventional cigarettes, cigars, chewing tobacco and all other forms. The dentists should always advise patients about the unknown danger of the e-cigarette use.<sup>10</sup> Based upon the evidence-based tobacco-cessation strategies, there is still insufficient evidence for the clinicians in order to promote the e-cigarettes as a tobacco cessation method.

**CONCLUSION:** The e-cigarettes are relatively new devices and hence no long-term evidence study regarding their effect on oral health is available. Although, the e-cigarettes may be less harmful than the traditional or conventional smoking, but the e-cigarettes can still contribute to the pathogenesis of the periodontal diseases by the cell injury, inflammation and impaired repair ability. The chemicals in the e-cigarette vapor are known to cause the DNA damage and also cellular senescence. Still, there is insufficient evidence for the clinicians in order to promote the e-cigarettes as a smoking cessation aid. However, further research is needed in order to establish the risk of using the e-cigarette.

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