



INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

"Balancing Act: Unravelling The Health Effects Of E-Cigarettes - Debunking Myths And Discovering Truths"

1Berlyn Rebekah John, 2Dr. C Ganesh, 3Dr. Divya V.C, 4Dr. M Shanthi, 5Dr. Haripriya S

1Undergraduate , 2Associate Professor, 3Associate Professor, 4Associate Professor, 5Tutor

1SRM Kattankulathur Dental College & Hospital, Chennai,

2SRM Kattankulathur Dental College & Hospital, Chennai,

3SRM Kattankulathur Dental College & Hospital, Chennai,

4SRM Kattankulathur Dental College & Hospital, Chennai,

5SRM Kattankulathur Dental College & Hospital, Chennai

Abstract

Recent decades have seen a transformation in the tobacco industry thanks to the electronic cigarette, or "e-cigarette," which has been viewed as an effective replacement for standard cigarettes. Because e-liquid heats as opposed to burning tobacco in e-cigarettes, several manufacturers have claimed that smoking e-cigarettes have fewer adverse respiratory effects than utilizing tobacco. Many customers have been won over by additional revolutionary characteristics including the option to customize the nicotine dosage and the variety of delicious flavours. But since there is no proof to support either position, there is still controversy concerning the safety of e-cigarette use and its ability to serve as a way to quit smoking strategy. Furthermore, the heating process itself has been found to have the potential to produce distinct, potentially hazardous breakdown products. Multiple investigations have been conducted both in vivo and in vitro for better insight of the effects.

Keyword : Electronic Cigarettes, Cessation, Tobacco, Battery-powered, Nicotine-replacement.

INTRODUCTION

The world's greatest preventable cause of death is still tobacco usage. Despite the fact that many smokers wish to stop, very few are able to do so because they are addicted to the nicotine that tobacco delivers. Therefore, cutting back on cigarette use is a top priority for public health. Conventional approaches to decreasing smoking include public awareness campaigns, limitations on the promotion and availability of cigarettes, higher taxes, and enhanced cessation techniques. The introduction of a new class of devices called electronic cigarettes, or "e-cigs," is one of these strategies that is the most contentious [1]. Hon Lik, a Chinese pharmacist, created and received a patent for the first electronic cigarettes (e-cigs) in 2003. This innovation was released as a substitute nicotine delivery method in the ensuing years [2]. The makers of e-cigarettes advertised their product as a delivery method for quitting smoking[3]. Subsequently, the burgeoning sector opposed to being governed as a tobacco product following its victory in court [4]. They were unable to prove that e-cigarettes were more effective than alternative nicotine replacements [3]. As a result, there is dispute regarding whether switching to e-cigarettes from regular tobacco use can help people stop smoking or not [5].

E-CIGARETTES

E-cigarettes are electronic cigarettes that mimic the effects of smoking in many ways. They typically include a set level of nicotine and shield the user from the dangerous carbon monoxide gas and extremely carcinogenic tar found in traditional cigarettes.

Electronic cigarettes also known as e-cigs, are devices that powered by batteries made up of an atomizer, an atomizer cartridge, a battery, and a Stainless-steel shell enclosing a metal heating element. A variety of chemicals, including nicotine, as well as various additives and humectants, such as glycerol, propylene glycol, glycerine and thousands of flavouring ingredients, including candy, fruit, mint, cold flavours, are vaporized by the heating element [7]. When e-cigarette aerosols vaporize, different quantities of aldehydes and carbonyls are found in together with inhaled nicotine [8]. The heating element atomizes the liquid when the user activates it, producing an aerosolizing nicotine vapour and a visible plume. Nicotine is absorbed when this vapour is taken into the lungs, a process known as "vaping."

STYLES

There are several models and styles of e-cigarettes available. Many imitate the design of conventional cigarettes, which has a red or orange light tip and a white tubing "filter" at the bottom. The exterior of the cartomizer—a device that combines an atomizer and a cartridge—serves as the "filter," while the exterior of the battery serves as the "tobacco" component. Others don't imitate the appearance of cigarettes since some patrons wish to clearly show that they are not in fact smoking in a designated non-smoking area. Additionally, some businesses are launching modifiable gadgets that enable various looks through the use of interchangeable exteriors [10].

OPERATION

The automated or manual battery type has a significant impact on the e-cigarette's operation. When the battery is automatically charged, using the electronic gadget is as simple as dragging on a regular cigarette. But you must click a button to turn on and start heating with a manual battery. Traditional cigarettes behave differently from the mechanized variety.

A voltage potentiometer is a feature found in many e-cigarette models that lets the user adjust how much aerosol is produced and, consequently, how much nicotine is inhaled. There are single-use disposable variants available. Others are meant to be used repeatedly and need to be cleaned on a regular basis and manually refilled or using prefilled cartridges (Fig 2.C) [10].

CATRIDGE STYLE E-CIGARETTE

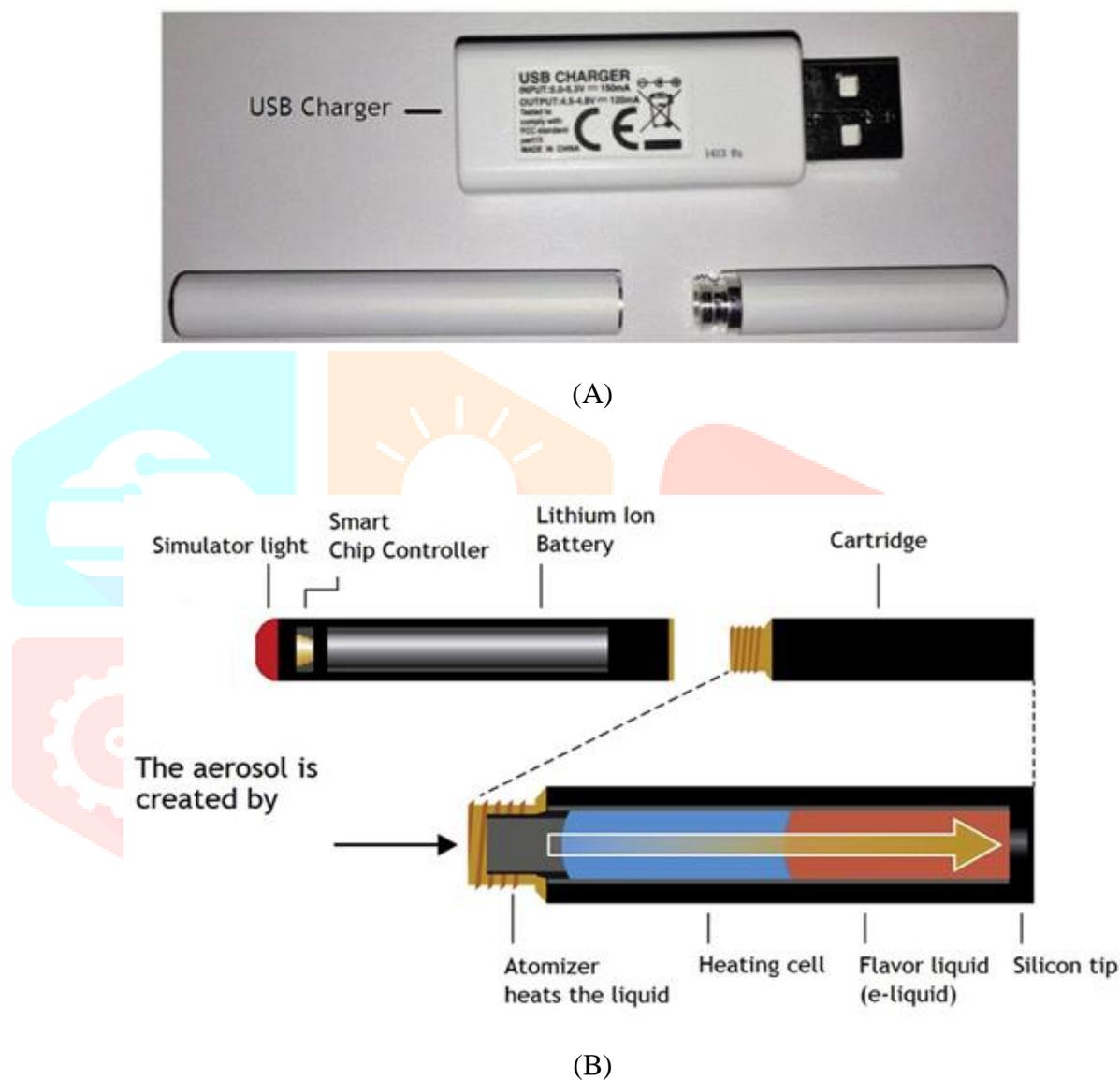


Figure:1. The structure of Vaping Device.

RE-FILLABLE TANK STYLE E-CIGARETTE



Figure:2. (C)

E-CIGARETTES AND SMOKING CESSATION

Concerns have been raised concerning the amounts of cytotoxic metals in the vapour produced by heating flavours in e-cigarettes, like diacetyl, which is linked to lung disorders. Supporters of ENDS counter that many of them are present at low concentrations, but they fail to mention that some users may be breathing these deeply into their lungs for decades. Additionally, just because something is approved for use as a food additive does not imply that it is safe to breathe in over an extended period of time.

ENDS proponents have a plethora of tales to support their claims, however a single randomised controlled experiment concluded that ENDS was not statistically superior to traditional nicotine replacement therapy (NRT) [11].

Furthermore, some tobacco cigarette consumers have started using e-cigarettes as an aid to stop smoking. It's unknown, yet, how much ECIGs can aid in quitting [12].

SAFETY OF E- CIGARETTES

This begs the question of why there are people working in the field of public health who are so vocally against them. Safety is one issue that is concerning. This implies that we have to base our decisions on the vapor's toxicity. Studies on the toxicology of vapor reveal that, contrary to alarmist remarks, the concentrations of some toxins are actually relatively low and propylene glycol is an irritant. Despite the fact that e-cigarette vapor does not have nearly the same concentration of toxins and carcinogens as cigarette smoke, some reviews have oddly concluded that we cannot say for sure if e-cigarettes are safer than smoking. Indeed, the majority of toxic concentrations are far lower than one twentieth of cigarette smoke [6].

ELECTRONIC NICOTINE DELIVERY SYSTEM AND INHALED NICOTINE

Water pipes, e-cigarettes, cigars, cigarillos, and traditional cigarettes all include nicotine, which is a major bioactive ingredient and ranges from 1mg to 100 mg/ml. The addictive qualities of nicotine are recognized globally. Electronic nicotine delivery systems or (ENDS), are a relatively new development in the field of nicotine delivery. It is suggested that these ENDS lessen the desire for traditional cigarettes. Instead of breathing in smoke, ENDS users inhale an aerosol or vapor that contains up to 24–100 mg of nicotine. Therefore, in comparison to commercially available tobacco cessation devices, ENDS will provide a substantial amount of nicotine [7].

HEALTH EFFECTS OF ELECTRONIC CIGARETTES

In general, three factors—liquid components, user puffing behaviour & device features —can change the acute effects of e-cigarettes. For instance, higher wattage e-cigarettes provide users with nicotine more efficiently than lower wattage models. Increasing the concentration of nicotine in e-cigarette liquid can also improve product satisfaction and suppress symptoms of nicotine withdrawal while also changing the subjective effect profiles. Finally, compared to shorter and less intense puffs typical of beginner individuals, the lengthy and bigger puffs commonly found in professional users of e-cigarettes result in elevated nicotine consumption and inhibition of symptoms associated with withdrawal [13]. The biological consequences of

e-cigarette aerosol are covered in this section, along with how nicotine affects the central nervous system, respiratory, cardiovascular, and immune systems [1].

E-CIG AEROSOLS AND RESPIRATORY SYSTEM

Approaches to assess how e-cigarette aerosols affect the respiratory system are being developed [1]. It's critical to ascertain how using e-cigarettes affects lung function in addition to the possible carcinogenic risk linked to the vapor of the device [9]. According to several research, those cells that were exposed to aerosols of e-cigarettes had higher oxidative stress and decreased viability of epithelial cells [1].

Although propylene glycol, the main ingredient in e-liquids, is usually regarded by the FDA as safe, prolonged exposure to it can irritate the mucosa of the upper and lower respiratory tracts [10].

Like acetyl choline (ACh), nicotine binds a family of nicotinic acetyl choline receptors (nAChRs). Lung epithelial cells and fibroblasts both exhibit high levels of nAChR expression. Additionally, these receptors cause the formation of mucin, the expression of proteases, and contractions of smooth muscles, all of which contribute to airway blockage in chronic obstructive pulmonary disease (COPD) [7]. Nonetheless, in multiple human trials, smokers who entirely switch from tobacco to electronic cigarettes report experiencing fewer subjectively harmful health effects related to their respiratory system, particularly when compared to the effects of conventional smoking. This suggests that e-cigarettes may be beneficial in lowering the risks associated with respiratory health. This implies that e-cigarettes might help reduce the negative health effects associated with breathing. E-cigarettes may carry comparable hazards as tobacco cigarettes with regard to inflammatory reactions in the airways. However, those who fully switch to e-cigarettes typically report fewer side effects than those who smoke cigarettes detrimental consequences on respiratory health that are subjective. It is typical to smoke both tobacco and electronic cigarettes, which is obviously bad for respiratory health.

While there is not enough data from biomarker studies to assess the processes of causality, it is evident that e-cigarette users are less exposed to lung carcinogen biomarkers than smokers. In clinical settings, encouraging the total replacement of tobacco cigarettes with

e-cigarettes and disseminating this message via a variety of public health channels may have significant benefits for respiratory health in general at population-level [14].

CARDIOVASCULAR SYSTEM

Those who have or are at risk of developing cardiac disease may experience cardiac events and arrhythmias as a result of using e-cigarettes, which can also raise blood pressure and heart rate. Nevertheless, research employing echocardiography to evaluate heart function did not find any consequences from using e-cigarettes. The majority of the alleged cardiac effects are believed to be incidental to the nicotine that e-cigarettes deliver [10]. Preclinical research on the cardiovascular system generally shows that using ECIGs may have some molecular and developmental impacts, but it does not seem that ECIG usage has greater acute effects on the cardiovascular system than smoking does. Nevertheless, more research is required to thoroughly investigate the ECIG parameter and its impact on cardiovascular function [1].

IMMUNOLOGICAL SYSTEM

Concerns regarding ECIG liquid's immunological consequences have also been voiced, and research on animals indicates that both nicotine and ECIG liquid aerosol can harm the immune system. Research has demonstrated that nicotine can modify macrophage activation and weaken antibacterial defences.

Exposure to ECIG aerosol was linked to airway inflammation and a compromised immune response to germs and viruses. The components of ECIG aerosol that are linked to lung inflammation include nicotine, acrolein, propylene glycol, and glycerol. Following the usage of combustible tobacco, similar consequences arise. Nevertheless, some research indicates that ECIGs have a less noticeable acute effect on pulmonary function when compared to combustible tobacco smoke [1].

CENTRAL NERVOUS SYSTEM

Both rats and humans can self-administer the psychomotor stimulant nicotine, which can become dependable. In different parts of the brain, nicotine binds to nicotine acetyl choline receptors after crossing the blood brain barrier. The reward pathway, which includes the ventral tegmental area of the midbrain, is made up of the primary brain regions linked to reliance. among others, the prefrontal cortex and the nucleus accumbens.

One of the ICD-10 criteria is the occurrence of withdrawal symptoms during drug abstinence. In addition to other signs and symptoms, abstinence symptoms in tobacco users are frequently marked by anxiety, difficulties concentrating, depression, slowed heart rate, increased hunger or weight gain, sleeplessness, irritability, difficulty concentrating, and restlessness. There is evidence that some of these abstinence symptoms could be experienced by ECIG users.

Overall, it seems that some ECIG consumers do experience certain attributes of dependence; however, it is unclear to what degree ECIGs actually cause dependence, as opposed to sustaining dependence in former smokers who transition to ECIG [1].

EFFECTS OF NICOTINE ON FETAL AND ADOLESCENT DEVELOPMENT

ECIG-delivered nicotine may have additional CNS consequences in addition to maintaining and developing dependence in ECIG users. These effects may include effects on the development of the adolescent ECIG user's brain and on the fetal development of pregnant women who use them. Because nicotine enters the placenta, exposure to it during pregnancy is likely to be the cause of behavioural issues in children whose mothers smoked, including but not limited to hyperactivity, anxiety, cognitive impairment, and sensitivity to nicotine and other stimulants. These effects pose a serious threat to public health, especially for moms who smoke cigarettes and may think about switching to electronic cigarettes since they think there is no longer any harm to the foetus [1].

ORAL HEALTH EFFECTS

The mouth cavity is the part of the human body that is directly exposed to the effects of tobacco smoke, even though it is widely recognized that smoking cigarettes increases the chance of developing cancer, lung illnesses, cardiovascular disorders, and other systemic pathologies [3].

OTHER HEALTH EFFECTS

Recurrent ulcerative colitis, reversible cerebral vasoconstriction syndrome, subacute bronchial toxicity, acute eosinophilic pneumonitis, lipid pneumonia and reversal of chronic idiopathic neutrophilia are among the health issues linked to ECIG that have been suggested by a number of case studies [1].

E-CIGARETTE AEROSOL AND PERIODONTAL COMPLICATIONS

Additionally, oral leukoplakia, palatal leukokeratosis, and melanosis, as well as changes to the oral microenvironment that can result in a number of opportunistic diseases such oral candidiasis and hairy tongue, are all known to be significantly influenced by cigarette smoking. Moreover, smoking tobacco poses a significant risk for periodontal disorders [3]. Chronic inflammation of the tissues that support the teeth is a hallmark of periodontal disease. There is a correlation between smoking and the following: a greater loss of alveolar bone, larger periodontal pockets, a higher degree of periodontal attachment, and the breakdown of connective tissue and matrix. Aldehyde dehydrogenase (ALDH) cleaves carbonyls, which are reactive aldehydes or carbonyls formed from e-cigarette aerosol that can cause DNA adducts or damage as well as protein carbonylation. When a person has periodontitis, protein carbonylation causes the development of autoantibodies, which can cause the matrix to be destroyed and bone loss [7].

It is abundantly evident from epidemiological studies that tobacco users maintain poorer dental hygiene than non-smokers. There is evidence to suggest that smoking improves saliva's mineralizing potential. Furthermore, recent research has shown that the amount of plaque, the architecture of the plaque, and the bacteria that make up it are similar in smokers and non-smokers; rather, Smokers' gingival tissue exhibits vasoconstriction linked to nicotine, which results in a little reduction in the flow of crevicular fluid. The immune response to bacterial growth on tooth tissues may be hampered by such flow reduction, and gingival vasoconstriction may prevent the onset of gingivitis [3].

However, research has demonstrated that nicotine impacts fibroblasts' capacity to adhere, the formation of integrins, and the synthesis of collagen, all of which contribute to periodontal deterioration. Furthermore, in cultured gingival keratinocytes and fibroblasts, nicotine raises the quantity of pro-inflammatory cytokines [3]. Through apoptotic processes, nicotine-containing e-cigarette products may have an impact on by blocking human periodontal ligament fibroblasts from proliferating and developing [15].

E-CIG AEROSOLS AND ORAL SUBMUCOUS FIBROSIS

Progressive submucosal fibrosis of the oral tissue and oropharynx is the hallmark of oral submucous fibrosis (OSF), a chronic, potentially malignant condition. Oral squamous cell carcinoma (OSF) develops in 7% to 13% of persons with OSF. There is evidence linking tobacco use to increased risks of OSF. Moreover, the increase is higher among smokers who chew tobacco. It has been proposed that arecoline and nicotine may cause oral keratinocytes to overexpress human telomerase reverse transcriptase (hTERT) mRNA, which could result in OSF malignancy.

Furthermore, it has been demonstrated that arecoline promotes the growth of fibroblasts through endothelial necrosis and growth factor expression upregulation. It is hypothesised that through cellular senescence, e-cigarettes and end products may contribute to the development and aggressiveness of OSF. On the other hand, nothing is known about how e-cigarettes affect OSF [7].

E-CIGARETTES AND PRO- SENESENCE RESPONSES

Damage to DNA and decrease of histone deacetylase 2 (HDAC2) in gingival epithelium through RAGE-dependent pathways, with flavored e-cigarettes producing a stronger response. Through elevated oxidative stress, pro-inflammatory and pro-senescence responses (DNA damage and HDAC2 reduction), pro-inflammatory and pro-senescence reactions in periodontal cells might result in dysregulated healing. Because of their heightened inflammatory and DNA damage responses, e-cigarettes have an impact on the regeneration ability of human progenitor cells. Numerous clinical studies demonstrated that flavor-infused e-cigarettes elicited a stronger reaction to e-cigarette aerosol, which in turn caused inflammatory responses, cellular senescence and higher oxidative/carbonyl stress linked to permanent DNA damage in gingival epithelium through RAGE-HDAC2-dependent mechanisms [8].

E-CIGS AND GLASS FIBER PARTICLES

It has been documented that ECs releases metal/silica particles as well as nanoparticles. It has been found that some glass particles produce harmful oxygen and superoxide dismutase, which irritate the bronchi. Therefore, it is anticipated that if glass particles in EC smoke are continuously present for smokers, the incidence of respiratory diseases will rise. The more puffs there were, the more glass particles there were. The more EC was used, the more glass particles were released. Subsequent investigations ought to be conducted to enable the measurement of glass particles produced by EC ingestion [16].

ADVERSE EFFECT OF E- CIG AEROSOLS

Reduced cell viability, higher apoptotic rates, increased DNA strand breaks, altered cell shape, and increased production of inflammatory mediators are some of the effects of e-cigarette aerosols on different cell types. Alveolar macrophages' ability to phagocytose microorganisms is impeded by flavors, which may intensify some of these adverse consequences [12].

Xerostomia, a condition brought on by the use of EC, reduces the dentin's ability to resist crack formation and can also be linked to teeth that are chipped or fractured. Generally speaking, xerostomia can be associated with a decrease in salivary flow rate brought on by aging, certain drugs, or other ailments. Tongue sores or a dry mouth /inflammatory reaction, and mucous membrane dryness are among the common health risks associated with EC use [17].

Oral ingestion, skin, respiratory, and ocular exposures were the most common modes of exposure that were documented. the use of ECIG solutions in suicide attempts, some of which resulted in serious injuries such burns to the face from device explosions and pneumonia or congestive heart failure [1].

FUTURE TRENDS OF ELECTRONIC CIGARETTES

However, there is currently little evidence to support the theory that e-cigarettes could serve as a "gateway" for traditional cigarette use and addiction. An alternate argument that warrants investigation is the possibility that these young tendencies point to an e-cigarette's potential function in primary tobacco use prevention [18]. Patches had the best compliance with prescribed NRT use, gums had the lowest compliance, and sprays and inhalers had the lowest compliance [19]. While there is evidence from a few studies that e-cigarettes can be a useful harm reduction tool for those who are not interested in quitting smoking, they don't seem to work any better than traditional nicotine replacement treatments.

CONCLUSION

The electronic cigarette holds promise as a smoking cessation tool. There aren't enough studies, though, to make a firm judgment. For those who wish to quit smoking, it is therefore preferable to adopt tried-and-true cessation techniques like nicotine replacement therapy, varenicline, or bupropion in conjunction with behavioral assistance.

There are some positive aspects of electronic cigarettes as well as some potentially alarming ones. We should advocate for additional high-quality, long-term clinical trials as well as urgently needed investigations into the interactions with dental health.

REFERENCES:

1. Breland A, Soule E, Lopez A, Ramôa C, El-Hellani A, Eissenberg T. Electronic cigarettes: what are they and what do they do? *Ann N Y Acad Sci.* 2017 Apr;1394(1):5-30. doi: 10.1111/nyas.12977. <https://doi.org/10.1111/nyas.12977>
2. Besaratinia A, Tommasi S. Electronic cigarettes: the road ahead. *Prev Med.* 2014. Sep;66:65-7 <https://doi.org/10.1016/j.ypmed.2014.06.014>
3. Tatullo M, Gentile S, Paduano F, Santacroce L, Marrelli M. Crosstalk between oral and general health status in e-smokers. *Medicine (Baltimore).* 2016 Dec;95(49):e5589. <https://doi.org/10.1097/md.0000000000005589>
4. Sharfstein JM. Electronic cigarettes: gateway to understanding the FDA? *Milbank Q.* 2015 Jun;93(2):251-4. <https://doi.org/10.1111/1468-0009.12119>
5. Rogér JM, Abayon M, Elad S, Kolokythas A. Oral Trauma and Tooth Avulsion Following Explosion of E-Cigarette. *J Oral Maxillofac Surg.* 2016 Jun;74(6):1181-5. <https://doi.org/10.1016/j.joms.2015.12.017>
6. West R, Brown J. Electronic cigarettes: fact and faction. *Br J Gen Pract.* 2014 Sep;64(626):442-3. <https://doi.org/10.3399/bjgp14x681253>
7. Javed F, Kellesarian SV, Sundar IK, Romanos GE, Rahman I. Recent updates on electronic cigarette aerosol and inhaled nicotine effects on periodontal and pulmonary tissues. *Oral Dis.* 2017 Nov;23(8):1052-1057. <https://doi.org/10.1111/odi.12652>
8. Sundar IK, Javed F, Romanos GE, Rahman I. E-cigarettes and flavorings induce inflammatory and pro-senescence responses in oral epithelial cells and periodontal fibroblasts. *Oncotarget.* 2016 Nov 22;7(47):77196-77204 <https://doi.org/10.18632/oncotarget.12857>
9. Drummond MB, Upson D. Electronic cigarettes. Potential harms and benefits. *Ann Am Thorac Soc.* 2014 Feb;11(2):236-42. <https://doi.org/10.1513/annalsats.201311-391fr>
10. Orellana-Barrios MA, Payne D, Mulkey Z, Nugent K. Electronic Cigarettes—A Narrative Review for Clinicians. *Am J Med.* 2015 Jul;128(7):674-81. <https://doi.org/10.1016/j.amjmed.2015.01.033>

11. McKee M. Electronic cigarettes: peering through the smokescreen. *Postgrad Med J*. 2014 Nov;90(1069):607-9. <https://doi.org/10.1136/postgradmedj-2014-133029>
12. Ramôa CP, Eissenberg T, Sahingur SE. Increasing popularity of waterpipe tobacco smoking and electronic cigarette use: Implications for oral healthcare. *J Periodontal Res*. 2017 Oct;52(5):813-823. <https://doi.org/10.1111/jre.12458>
13. Spindle TR, Talih S, Hiler MM, Karaoghlanian N, Halquist MS, Breland AB, Shihadeh A, Eissenberg T. Effects of electronic cigarette liquid solvents propylene glycol and vegetable glycerin on user nicotine delivery, heart rate, subjective effects, and puff topography. *Drug Alcohol Depend*. 2018 Jul 1;188:193-199. <https://doi.org/10.1016/j.drugalcdep.2018.03.042>
14. Ratajczak A, Feleszko W, Smith DM, Goniewicz M. How close are we to definitively identifying the respiratory health effects of e-cigarettes? *Expert Rev Respir Med*. 2018 Jul;12(7):549-556. <https://doi.org/10.1080/17476348.2018.1483724>
15. Alanazi H, Park HJ, Chakir J, Semlali A, Rouabhia M. Comparative study of the effects of cigarette smoke and electronic cigarettes on human gingival fibroblast proliferation, migration and apoptosis. *Food Chem Toxicol*. 2018 Aug;118:390-398. <https://doi.org/10.1016/j.fct.2018.05.049>
16. Shin JW, Jo SH, Kim KH, Song HN, Kang CH, Bolan N, Hong J. Are glass fiber particles released during the use of electronic cigarettes? Development of a semi-quantitative approach to detect glass particle emission due to vaping. *Environ Res*. 2018 Aug;165:267-273. <https://doi.org/10.1016/j.envres.2018.04.032>
17. Cho JH. The association between electronic-cigarette use and self-reported oral symptoms including cracked or broken teeth and tongue and/or inside-cheek pain among adolescents: A cross-sectional study. *PLoS One*. 2017 Jul 11;12(7):e0180506. <https://doi.org/10.1371/journal.pone.0180506>
18. McGraw D. Current and future trends in electronic cigarette use. *Int J Psychiatry Med*. 2015;48(4):325-32. <https://doi.org/10.2190/pm.48.4.g>
19. Motooka Y, Matsui T, Slaton RM, Umetsu R, Fukuda A, Naganuma M, Hasegawa S, Sasaoka S, Hatahira H, Iguchi K, Nakamura M. Adverse events of smoking cessation treatments (nicotine replacement therapy and non-nicotine prescription medication) and electronic cigarettes in the Food and Drug Administration Adverse Event Reporting System, 2004-2016. *SAGE Open Med*. 2018 May 21;6:2050312118777953. <https://doi.org/10.1177/2050312118777953>
20. Willemsen MC, Croes EA, Kotz D, van Schayck OC. De elektronische sigaret: Gebruik, gezondheidsrisico's, en effectiviteit als stopmethode [Electronic cigarettes: use, health risks, and effectiveness as a cessation method]. *Ned Tijdschr Geneeskd*. 2015;159:A9259. Dutch. <https://doi.org/10.1016%2Fj.drugalcdep.2018.03.042>