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Review Articles

THE ORAL EFFECTS OF E-CIGARETTES – A LITERATURE REVIEW

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ABSTRACT

Background Because of regulations made against smoking, and the rising popularity of a healthy lifestyle there has been a visible change in the smoking habit of the population in the last 15 years. The negative impact on the attitude toward smoking forced the industry to develop new ways to satisfy the consumer's nicotine need. That is how heated tobacco products and a variety of ENDS (Electronic Nicotine Delivery System), such as electronic cigarettes) have been invented.
Objective This literature review aims to summarise the oral effects of consuming e-cigarettes which have been proven and publicised.
Data Sources The main source of the study has been the publications found through PubMed and NBCI (National Center for Biotechnology Information).
Study Selection Articles have been selected from the international literature if they had any information on the oral effects of e-cigarettes.
Data Extraction The information from the articles has been categorised based on the tissue and the time they last.
Data Synthesis Electronic cigarettes cause a change in saliva flow and its composition, a decrease in the blood supply of soft tissues and an immunosuppressed state in the said area, therefore the incidence of some diseases are higher among the users. Components of the e-liquid may cause damage to both soft and hard tissues, such as cancerous lesions, inflammation, chronic periodontitis and neurodegeneration. Nicotine may be absorbed by the surface of the teeth, causing patches, and some ingredients may be beneficial to the bacterial flora of the oral cavity.

KEYWORDS

E-Cigarette; Electronic Nicotine Delivery Systems; Oral Health; Nicotine; Smoking

1. INTRODUCTION

Over the last few years, electronic cigarettes (e-cigarettes) have gained greater and greater popularity. According to a 2011 survey by the WHO (World Health Organisation), 7 million people used e-cigarettes regularly worldwide at the time, and this number increased to 41 million by 2018 [1]. Some forecasts indicate that the popularity of e-cigarettes will not change; furthermore, as of 2021, there are an estimated 55 million daily users [1]. Concerning the health effects of e-cigarettes, they are thought to be a healthy alternative to smoking, a notion rooted in the marketing strategy and other factors of the tobacco industry. Another problem is that these products are accessible to a younger demographic: in 2020 alone in the USA, 19.6% of surveyed secondary school students used e-cigarettes, and 22.5% used them as a daily routine [2]. The harmful effects of traditional cigarettes are already established knowledge in people's awareness, thanks to widespread effort to combat the habit of smoking in the population; however, when it comes to e-cigarettes, no similar action has been underway, allowing their popularity to increase on and on. Over the last years worldwide, countless research studies have aimed to describe the health effects of electronic cigarettes, which indicates that there are many questions without answers. For this reason, this article aims to summarize present knowledge concerning the oral effects of using electronic cigarettes.

2. CHANGES IN THE SALIVA FLOW AND ITS CONSEQUENCES

Traditional cigarettes burn at almost 1000 degrees Celsius and produce quite toxic by-products at this high temperature, for instance, tar. In contrast, during the use of electronic cigarettes, there is no burning; instead, they vaporize liquid content at a much lower temperature, so the exhaled vapour is assumed to contain fewer toxic components [3]. The temperature of the vapour emitted by the e-cigarette depends on

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several factors such as battery voltage, resistance, atomiser condition, mouthpiece size, and e-liquid composition (mainly the level of propylene glycol (PG) and glycerine content); furthermore, some devices have adjustable voltage, so the temperature can vary quite widely. Generally, it can be stated that the average temperature of vaporizing is about 157 to 266 degrees Celsius [3]. The result of the extremely high-temperature vapour (mainly of PG-based liquids) may be the formation of substances containing a carbonyl group such as formaldehyde or acetaldehyde, which cause inflammation in the oral mucosa [4,5]. The most common and important condition that the vapour-induced temperature increase causes is xerostomia. The change in the saliva flow is assessed by measuring the resting and stimulated saliva flow. Symptoms of xerostomia may be a sticky or burning sensation in the oral cavity, increased thirst, difficulties in talking, swallowing, and tasting, and halitosis. Furthermore, the dried-out mucosa has a greater risk to develop oral infections such as oral candidiasis, which can recur from time to time. Besides these, the user's oral hygiene deteriorates [6], and the saliva's washing effect is compromised, therefore the incidence of caries rises [7]. Using an electronic cigarette changes not just the quantity of saliva but the quality as well. Oral pH is driven into the acidic range by nicotine; however, nicotine-free liquids move oral pH into the basic range and the saliva's buffer capacity is not affected [8]. Changes to the saliva's composition are also notable: the amount of secretory IgA, lysozyme, and lactoferrin is different from the physiologic level. Secretory IgA is a specialized antibody for the oral cavity containing saliva. The lysozyme content of saliva is detrimental to the immune processes: because of its proteolytic function, it breaks down antibodies. B-lymphocytes that have met antibodies migrate to one of the salivary glands and transform into plasma cells. In addition to monomer IgA, these cells produce a protein called J-protein, which connects IgA molecules by their Fc regions to form a dimer; this way, the lysozyme recognising the Fc regions becomes ineffective against these IgA dimers [9]. After the use of an electronic cigarette, it is proved by ELISA testing that the amount of IgA is decreased, which leads to a weakened oral immune response [10]. Lysozyme is responsible for breaking the bond between N-Acetylglucosamine and N-Acetylmuramic acid; these being the components of the bacterial cell walls, the action causes the lysis of bacteria. The substance also has antiviral and antifungal functions. As an effect of using e-cigarettes, the amount of lysozyme decreases, causing a downturn in oral protection [10]. Lactoferrin is an iron-binding glycoprotein, a multifunctional molecule participating in numerous physiological processes. Concerning the oral cavity, it is produced by the serous cells of the salivary glands; like lysozyme, it has antibacterial, antiviral, and antifungal effects, and is also an important immunomodulator. As an effect of using e-cigarettes, its level increases; the extra quantity may be considered an indicator of oral inflammation [10].

3. CHANGES CAUSED BY VACUUM

During the use of an electronic cigarette, there is suction in the oral cavity, the size of which depends on the type of equipment, and its duration on the user's habits. The suction power is produced by the mimic muscles, and its consequence is a relative vacuum in the oral cavity. In a University of California 2010 study, the researchers ran tests on the most popular e-cigarettes of that time, assessing the level of effort needed to use an e-cigarette and the health effects of the arising vacuum. They measured the pressure by a manometer attached to a machine mimicking smoking and found that the user needed to generate greater suction power with any type of e-cigarette than with traditional ones. In the first ten suction cycles, the density of the vapour did not change; after the tenth suction cycle, however, it started to decrease continuously. The longer the e-cigarette had been used the greater effort was needed for the same amount of vapour. The generated vacuum, the density of the vapour and the required effort varied across device types [11]. There is no unified medical position yet on the health effects caused by the vacuum; further studies are needed, but the presumed consequences are the overload of the tongue and mimic muscles. The result of the greater suction power is that the vapour travels to the distal parts of the lung, reaching deeper regions, with all associated disadvantageous consequences [12].

4. EFFECTS ON DIFFERENT ORAL TISSUES

4.1 Soft Tissues: Acute Changes

As an effect of e-cigarette vapour, the blood supply of the soft tissues decreases, which can be traced back to two reasons. On the one hand, the chronic nicotine supply has a vasoconstrictor effect; on the other, the use of nicotine-free e-cigarettes decreases the blood supply as well. This is explained by glycerine and propylene-glycol inducing endothelial inflammation, which decreases the ability of veins to dilate so they stay constricted [13]. A decrease in blood flow can have numerous consequences such as decreased tissue defence and a hypoxic milieu, which can cause changes in the bacterial microbiome, leading to the proliferation of anaerobic species. Periodontal index values become higher, and the tendency to regenerate decreases, which leads to slow or failed wound healing [8].

Propionaldehyde, which appears in the aerosol during the decomposition of propylene-glycol, leads to the irritation of the oral cavity and the throat, with sensitivity, redness, and dry cough [14]. The symptoms of irritation tend to alleviate with continued use. Nicotine can cause a burning sensation by the activation of the TRPA1 (transient receptor potential ankyrin) channel [15].

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As a result of the immunosuppressed state in the oral cavity, the incidence of infectious mucosal diseases, mainly candidiasis caused by Candida albicans, increases among e-cigarette users. It has been proved by in vitro experiments that in candida cells exposed to e-cigarette vapour, the expression of chitin and SAP-2,3,9 (secreted aspartic protease) increases, and a change takes place in the phenotype: the hyphae become longer. These changes help the adhesion of candida to the oral mucosa [16].

Upon exposure to some components of the vapour such as carbonyls, reactive oxygen radicals, and different types of aldehydes, the cytokine secretion of epithelial cells increases, which causes inflammation [17]. The components of e-liquid may cause an allergic reaction depending on one's immune system.

The prevalence of some mucosal diseases is higher among e-cigarette users. One such disease is stomatitis nicotina palati; induced by nicotine, the lesion mainly occurs on the hard palate, appearing as hyperkeratotic patches. Another disease occurring more often is lingua villosa nigra (black hairy tongue), causing the enlargement of the tongue's papillae and a change in colour to black. The risk of the disease cheilitis angularis also increases; this is a state associated with the bilateral drying and cracking of the anguli oris, which can be superinfected by some candida species [18].

4.2 Soft Tissues: Chronic Changes

Several components of e-liquids may damage the epithelial cells, which can cause the death of these cells, leading to ulcerative areas and wounds. During the use of an e-cigarette, metal particles may get into the aerosol from the atomiser or the cotton wool, including cadmium, nickel, and arsenic. Metal particles cause cancerous lesions, inflammation, chronic periodontitis, and neurodegeneration. As a result of heat and atomizing, flavouring substances decompose to carbonyls such as diacetyl. The main ingredients (propylene glycol and glycerine) decompose because of the heat, and among the decomposition products there are molecules containing a carbonyl group (formaldehyde, acetaldehyde) and reactive oxygen species (ROS). These molecules are cytotoxic regardless of the nicotine content; they induce DNA damage in the oral epithelium. They decrease the cells' defence via antioxidants, which would protect the cell against the reactive radicals; apoptosis and inflammation are induced. Carbonyl compounds cause protein carbonylation and oxidative stress. The consequence of all the above is a decrease in proliferative capacity and viability [15].

The volatile organic compounds with the potential for carcinogenicity in the e-cigarettes' vapour have a genotoxic effect [19]. Compared to traditional cigarettes, e-cigarettes have fewer carcinogenic substances at lower levels, but further studies are needed to find out if e-cigarettes can cause malignant transformations. The difficulties to judge the situation include the lack of long-term experiments and participant recruitment challenges since the ideal subject would be a person who has never smoked and does not have any risk factors. Despite the shortage of clinical proof, current medical opinion states that because there are carcinogenic components and adverse changes induced in cells, using an e-cigarette could have a carcinogenic effect [20].

4.3 Hard Tissues: Teeth

Nicotine can be absorbed by the surface of the teeth, causing yellowish-brown patches [21]. During the degradation of propylene-glycol, which is one of the components of the e-liquid, acidic substances such as acetic acid or lactic acid are produced, which can directly damage the enamel [22]. Furthermore, propylene-glycol is a quite hygroscopic substance: it binds the water from saliva and soft tissues, further increasing the rate of xerostomia already developed, along with all the adverse consequences [22]. During a 2018 research, enamel was incubated in flavoured and non-flavoured e-cigarette vapour; measuring their hardness, the researchers found that the enamel treated with flavoured vapour was 27% softer than the other preparation. Considering these results, flavours may promote the demineralisation of enamel. The pathomechanism of this process is that triacetin (traditional tobacco flavour), hexyl acetate (apple flavour), and ethyl butyrate (pineapple flavour) are all esters, sources of nutrients for cariogenic bacteria, manly for Streptococcus mutans. They facilitate the extracellular polymer formation of bacteria, which is the main process of biofilm generation, and they promote bacterial growth. During the degradation of carbohydrates, acids are generated, mainly lactic acid, decreasing pH and causing the demineralisation of teeth [23].

The metal content of e-cigarette vapour is beneficial for the bacteria as well because it contains iron, copper, and magnesium ions, which are the cofactors of some of the essential enzymes in Streptococcus mutans, and help the bacteria survive the attacks of the immune system. Researchers think e-liquid flavours are like fizzy drinks considering all things above, because of their cariogenic potency [23]. E-liquids usually contain glycerine as well, which is a desiccant like propylene-glycol. In the food industry, it is used as a sweetener, but cariogenic bacteria cannot break it down, meaning it does not facilitate the development of caries this way. On the other hand, through its viscosity, it helps bacterial adhesion to the surface of teeth; with the flavours in the e-liquid, it quadruples microbial adhesion to enamel, and the bacterial biofilm's size becomes twice as large [23]. The result of dental tissue weakening may be the fracture of enamel or fracture of an entire tooth. During a 2016 cross-sectional study, 11.4% of young respondents reported such damage to their teeth, proving the scientific position that with the use of e-cigarettes, the number of cracks and fractures of teeth increases [24].

4.4 Hard Tissues: Bone

Some ingredients of e-liquids are harmful to bone cells, affecting the cells' viability, differentiation, proliferative capacity, and matrix production. Cadmium found in e-liquid causes a decrease in the lifetime of osteoblasts even at a small concentration; furthermore, it increases the risk of certain musculoskeletal diseases such as rheumatoid arthritis and osteoarthritis [25,26].

In a 2019 experiment series, the effect of different flavouring substances of e-liquids on bone cells was assessed: osteoblasts were exposed to the most popular flavoured e-liquids, both nicotine-containing and nicotine-free, for 48 hours, then the cells' viability and their main osteoblast markers were evaluated. Results showed an increase in the expression of type I collagen, and the conclusion was that e-cigarettes are osteotoxic: all e-liquids decreased the viability of the cells, which was explained by oxidative stress and a higher level of reactive oxygen radicals. The rate of osteotoxicity was determined by the dosage and the flavour but was unrelated to nicotine content. Considering these findings, flavourless e-liquid is the least harmful, and cinnamon flavoured is the most cytotoxic [25].

The negative effects of e-cigarettes cause a change in the bone's features, and a decrease in its density and mineral content, which is dangerous mainly in childhood because this period is crucial in proper bone growth and development, this being the time when 90% of the bone mass develops. A long-time consequence of the change in the bones' condition might be osteoporosis [25], thus bone fractures might occur more frequently; furthermore, as an effect of nicotine, the regeneration of bone fractures is disturbed as well [27]. The changes in the bone's condition start in about two months of e-cigarette use; upon quitting, the alveolar bone recovers to its original, healthy state [28].

4.5 Effects on the Periodontium

The duty of the periodontium is anchoring, and fixing the teeth in the tooth ridge. The inflammation of periodontal tissues may lead to losing all the teeth, meaning that a healthy periodontium is necessary to keep and maintain one's teeth. Traditional cigarettes are well known for leading to periodontitis; the question here is if e-cigarettes have this consequence, too. Because of the vasoconstrictor effect of nicotine, the gingiva's oxygen and nutrition supply decrease. The consequence is a decrease in local white blood cell count, followed by these cells' inability to fulfil their defensive role, reinforced by low levels of lysozyme as a result of reduced saliva flow. On the other hand, there are consequential changes to the microbiome of the oral cavity, creating perfect circumstances for anaerobic periodonto-pathogenic bacteria to multiply, such as Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans and Prevotella intermedia. As a result of weakened defence and bacterial colonisation, inflammation, gingivitis, and periodontitis may develop [4]. The symptoms of such gingivitis include pain, redness and bleeding-while-brushing of the gingiva [17].

It is quite interesting that according to research on the microbiome of the saliva, done on 119 participants, some gram-negative bacteria such as periodonto-pathogenic Porphyromonas and Veillonella occur in a greater quantity in e-cigarette users' saliva than in that of traditional smokers, showing e-cigarettes' potential harm leading to periodontitis [29].

Furthermore, nicotine is antiproliferative to fibroblasts: as a result of prostaglandins and matrix metalloproteases released upon exposure to nicotine, myofibroblast and mesenchymal stem cell differentiation are blocked, holding back wound healing. Osteoblast functions and new vessel growth are similarly suppressed, negatively impacting the success rate of implant dentures, osteointegration, and the regeneration of papillae. Decreased osseointegration has been confirmed by animal experiments: around implants in rats getting a nicotine injection, the size of BIC (Bone Implant Contact), i.e., the contact surface between bones and implants, was lower than in the control group [27].

The components of the periodontium – gingival fibroblasts, periodontal ligaments, and epithelial cells – develop and maintain inflammation as a response to specific stimuli or stress caused mainly by cytokines. Some components of the vapour of e-cigarettes such as reactive oxygen substances, aldehydes and compounds containing a carbonyl group, are among the triggers of inflammation. The potential inflammatory effects of carbonyl compounds include carbonylation of proteins, leading to autoantibody production and periodontal destruction [30]. Furthermore, the stress caused by these compounds gives rise to DNA damage, which translates to early cell ageing. In vitro experiments have proved that gingival fibroblasts exposed to e-cigarette vapour face a greater risk of necrosis and apoptosis [30].

Periodontitis is a multifactorial disease where the presence of bacteria is a necessary but not sufficient condition; the effects of e-cigarette vapour provide a favourable medium for the development of this disease. The depth of an e-cigarette user's periodontal sac increases, the developed gingivitis may cause sensitivity and bleeding, and the plaque index increases.[17] The risk of periodontitis increases, which leads to tissue and bone destruction, tooth mobility and, in the worst case, tooth loss.

5. CONCLUSION

The main purpose of inventing e-cigarettes was to find a less harmful alternative to traditional cigarettes; it is therefore useful to compare the health effects of these two harmful habits. In numerous cases, the e-cigarettes' harmful effects on the oral cavity are milder than those of traditional cigarettes; however, they have several adverse effects and may cause

severe diseases. A further danger of e-cigarettes is that there are various types of devices and e-liquids, making the uniformity of regulations and medical research more difficult. Even though much research has been done in this area, there are still numerous unanswered questions and statements awaiting proof. Despite our lack of knowledge, the opinion on e-cigarettes' health effects are clear: they may be a useful assistive device while quitting traditional cigarettes, but they are unadvised to use in other cases due to their negative effects on oral tissues.

AUTHOR CONTRIBUTIONS

All authors agree to be accountable for the content of the work.

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Dr. Áron Imre Györkös, DMD, graduated from the Faculty of Dentistry, Semmelweis University, Budapest, Hungary in 2021. He is currently working as a dentist in Érd, next to Budapest, both in the public and private sector. The title of his research is The oral effects of e-cigarettes - a literature review. He started exploring this topic as his thesis and tried to summarise today's knowledge of e-cigarette health effects. He is currently working on something similar with IQOS and other heated tobacco products.

Questions

1. Generally, what temperature range do e-cigarettes vaporise the e-liquid?

❑a. 57 to 66 degrees Celsius;
❑b. 157 to 266 degrees Celsius;
❑c. 200 to 400 degrees Celsius;
❑d. 800 to 1000 degrees Celsius.

2. Which statement is true about the changes on the saliva because of e-cigarette usage?

❑a. The pH of the saliva rises by the usage of nicotine-free liquids;
❑b. The pH of the saliva decreases by the usage of nicotine-free liquids;
❑c. The pH of the saliva rises by the usage of nicotine containing liquids;
❑d. The vapour-inducted temperature rise causes more saliva secretion.

3. According to a 2011 survey by the WHO, how many people used e-cigarettes regularly worldwide at the time?

❑a. 1 million;
❑b. 34 million;
❑c. 7 million;
❑d. 1 billion.

4. Which component of the e-liquid can cause yellowish-brownish patches on the surface of the teeth?

❑a. Propylene-glycol;
❑b. Glycerine;
❑c. Sweeteners;
❑d. Nicotine.