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Electronic cigarettes and their impact on oral health - review

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ABSTRACT

INTRODUCTION
Nowadays, the popularity of e-cigarettes is growing rapidly. Manufacturers of e-cigarettes advertise them as a less harmful option than traditional cigarettes, suggesting that their use can help reduce nicotine dependence and reduce the risk of smoking-related diseases. However, studies indicate that inhaling the chemicals in liquids can carry serious health consequences, particularly concerning the oral cavity Many of these preparations contain substances about whose effects we do not yet know enough, which raises concerns among public health professionals. The aim of this study was to provide an overview of e-cigarettes, including their popularity, the origins of their development, the substances they contain and the impact they have on oral health, which is most at risk from the harmful effects of e-cigarettes.

SUMMARY
Smoking e-cigarettes is detrimental to oral health due to the harmful substances they contain and causes various oral diseases.

KEY WORDS: electronic cigarettes, oral health, smoking, vapers, nicotine, nicotine addicition, tobacco, dental caries, periodontits, carcinogenic potential

GENERAL INFORMATIONS ABOUT E-CIGARETTES

Electronic cigarettes (known as e-cigarettes) are increasingly popular both among people trying to quit smoking and as a replacement for classic cigarettes. They are perceived as less harmful than smoking traditional cigarettes, which is why they are mainly taken up by young people. Compared to traditional cigarettes, tobacco is not burnt in e-cigarettes. Nicotine is released by heating the liquid to approximately 200 degrees Celsius. This creates an aerosol, which is inhaled into the lungs by the user. Bystanders can also inhale this aerosol when the user exhales it into the air as visible smoke. E-cigarettes do not produce the so-called sideways smoke, which is characteristic of classic cigarettes and is a poison for passive smokers. Despite these advantages, they are not as safe as most people believe. [1]

THE GLOBAL POPULARITY OF E-CIGARETTES

In 2011, the number of e-cigarette smokers was 7 million, and in 2018 this figure has risen to 41 million. [2] In 2021, around 82 million vapers were reported, which is around 1% of the

population. This shows how quickly the popularity of e-cigarettes has grown and this trend is certain to continue.
Europe is the continent with the highest number of vapers (2.3% of the total population), while the lowest number occurs in Southeast Asia (0.7% of the total population).

E-CIGARETTES IN POLAND

Smoking e-cigarettes in Poland is becoming increasingly popular, especially among young people who are unaware of the health risks of this addiction. The amount of vapers is estimated at 4.8% of the country's population (4.0% among females and 5.6% among males). [3]

HISTORY OF E-CIGARETTES

The first attempts to create an alternative to traditional cigarettes were started in the 19th century in the United States. In 1965 Herbert A. Gilbert patented the ‘smokeless tobacco-free cigarette’, in which tobacco was replaced by flavoured air heated by a heating element. Another attempt was made with the introduction of the non-flammable Favor cigarette in 1986.

In 2003, Chinese pharmacist, Hon Lik, developed the modern e-cigarette after his smoker father died of lung cancer. The product was well received in the Chinese market as a smoking cessation device or alternative cigarette product. On the basis of this product, newer and newer devices with newer technologies have been developed to meet the expectations of users. [4]

CONSTRUCTION OF THE E-CIGARETTE

Picture 1. Operation and construction of the e-cigarette. „The E-Cig Quandary. Special Report by M. Blanding and M. Drexler, Harvard Public Health

The electronic cigarette consists of a battery, a cartridge or tank for e-liquids and an atomiser.
The battery is usually rechargeable, sometimes it needs direct connection to a contact, USB or car socket. As the e-cigarette is an electronic device, it does not work without power.
The cartridge is a replaceable container for liquid. The liquid in the cartridge can be refilled; liquids are available in different strengths depending on nicotine content and in many different flavours.
The atomiser is the ‘heart’ of the e-cigarette - the place where the liquid is heated and turns into an aerosol with flavouring ingredients, sometimes with fragrances.
Some e-cigarettes even have an LED light that imitates the glow of a cigarette.

The basic principle of an e-cigarette is to heat a liquid (usually containing nicotine) to a temperature (200-300°C) where it becomes volatile and can be inhaled. No combustion takes place in the e-cigarette, so no strong odour is emitted and no by-products such as carbon monoxide are produced.[5]

E-LIQUIDS

The liquid consists of:

- glycerine,
- propylene glycol
- alternatively nicotine,
- a wide range of flavourings and fragrances, such as fruits, chocolate, cakes, vanilla, coffee, bubble gum and many others.

Nicotine is a pyridine alkaloid extracted from the leaves of tobacco (Nicotiana tabacum). It is a highly addictive substance whose content in e-cigarettes ranges from 0 to 3.6%.

Glycerine is the primary ingredient in e-liquid. Its content is 30%-99,6%. It belongs to the organic compounds of the sugar alcohols group. In the food industry it is a substance to keep the product moist and sometimes a sweetener. It is used to produce a vapour that mimics cigarette smoke very well.

Propylene glycol can also be a primary ingredient in e-liquid. Its content in the e-liquid and its function are the same as for glycerine (30-99,6%). It causes a sensation called “throat hit,” which is a great way to satisfy those trying to quit traditional smoking. It belongs to the diols and is readily used in the food industry to make beer, ice cream and coffee and also in cosmetics as a base in various products. [6] [7]

Glycerine and propylene glycol are classified by Food and Drug Administration (FDA) as “generally recognized as safe.”. However, when heated, they break down into toxic substances, including formaldehyde or acrolein, which are proven carcinogens. [8] [9]

The aerosol produced by e-cigarettes has been found to contain 18 of the 93 toxic compounds on the U.S. Food and Drug Administration (FDA) list that are found in tobacco and tobacco smoke. Their concentrations are lower than in conventional cigarettes. [1]

Aldehydes are most commonly used as flavoring substances. However, they have proven toxic effects and can damage cells and even cause mutations or cancer. The connection between the toxicity of liquids and the type of liquid flavor is confirmed. The risk of flavor toxicity increases as the chemical complexity of the flavor increases. Manufacturers already offer several thousand flavors, with each successive flavor being more complex, and new flavors will appear on the market. Vanillin and cinnamaldehyde, which have proven toxic effects on the body, are a special danger. [10]
Cinnamaldehyde interferes with cellular respiration and glycolysis in a dose-dependent manner. It decreases cellular ATP levels, thereby reducing cilia motility in airway epithelial cells. Proper cilia motility is an essential airway defense mechanism, so inhaling cinnamaldehyde may increase the risk of respiratory tract infections in e-cigarette users. [11] [12]
Vanillin causes changes in cellular physiology and impairs the ability of airway epithelial cells to maintain homeostasis. [13]

ARE E-CIGARETTES ADDICITIVE?

E-cigarettes are often used as an alternative to traditional cigarettes when quitting smoking. However, they are also addictive, as the liquid often contains nicotine, which is a highly addictive substance.

Nicotine binds to nicotinic receptors (acetylcholine receptor type) of the nerve connections of the autonomic ganglia of the nervous system, the adrenal medulla and the central nervous system, showing an excitatory effect on both the sympathetic and parasympathetic parts of the nervous system. Nicotine influences the increased release of dopamine. Dopamine, the feel-good hormone, is a neurotransmitter that is responsible for our well-being, contentment and sense of pleasure. [14]

Nicotine receptors are regularly irritated by smoking, and the body becomes accustomed to the effects of nicotine. With regular smoking, the number of nicotine receptors in the body increases. After a while, the body's tolerance to a dose of nicotine increases, and to stimulate more receptors, the smoker has to reach for even more cigarettes to achieve the former pleasure. This is the classic vicious cycle of the physical addiction mechanism. [15]

Nicotine withdrawal makes permanently active nicotine receptors unstimulated and this causes symptoms of withdrawal syndrome. This can manifest as the onset of irritability, anxiety, nicotine craving (a strong urge to reach for an e-cigarette), decreased concentration, fatigue, appetite and sleep disturbances. These symptoms can appear within just a few hours after smoking an e-cigarette. Withdrawal symptoms peak within the first few days of last smoking and usually subside within a few weeks. However, sometimes they can persist for months. [16]

In addition to physical dependence, there is also psychological dependence on nicotine, which is the result of the constant repetition of the smoking ritual. If an addict uses an e-cigarette in stressful and uncomfortable situations, then he associates smoking with a method of relieving stress. Unfortunately, nicotine has a stimulating effect, so it is not an effective form of de-stress. Whereas the ritual of smoking an e-cigarette distracts the smoker from his problems, which deceptively brings relief and comfort. [17]

E-CIGARETTE IMPACT ON HUMAN HEALTH

E-cigarettes are considered by many people as a healthier alternative to traditional cigarettes, but this is not true. They have been proven in many studies to negatively affect many systems in the body, and some of the effects are not yet known. The main hazard to the human health from e-cigarettes is the toxic effects of nicotine, formaldehyde and aroma compounds. [18]
Studies conducted by Kucharska et al. have shown discrepancies between the composition of the liquid declared by manufacturers and the actual composition. [19] The presence of metals (nickel, aluminium, cadmium, silicon) was also found. Therefore, the information provided by the manufacturer cannot be fully trusted and we do not know what harmful substances may be present in e-cigarettes. [18]

ORAL HEALTH

The oral cavity is the first part of the body that is exposed to direct contact with the vapour produced by e-cigarettes. [20]
However, evidence of the direct impact of e-cigarettes on oral health is difficult to obtain, because the occurrence of diseases can only be assessed after a long period of exposure.
The most serious hazard to oral health is the development of periodontitis or oral cancer.
In a clinical study, it was found that e-cigarette smokers can struggle with dry mouth, increased tooth sensitivity, and mouth ulcers. There may also occur the increase in gingival

bleeding. The evaluation of clinical parameters (plaque index (PI), bleeding on probing (BoP), probing depth (PD), clinical attachment loss (CAL)), which where increased and radiographic parameters of inflammation shows that e-cigarette smokers are at lower risk of periodontitis than traditional cigarette smokers, but more so than non-smokers. [21]

PERIODONTITIS

It is proved that the use of e-cigarettes interfere with the oral microbiome and in this way disrupts the oral bacterial flora, leading to a prevalence of periodontal pathogens. The oral bacterial flora of e-cigarette smokers was similar to the flora of traditional cigarette smokers. Bacteria that were present in high numbers in both groups of smokers were Selenomonas, Leptotrichia and Saccharibacteria. Bacteria that were particularly prevalent in e-cigarette smokers were Fusobacterium and Bacteroidales, which are associated with gum disease. [22]

Periodontal disease occurs as a result of a disruption in the homeostasis between the oral bacterial flora and the organism, resulting in an increased immune-inflammatory response. [23] E-cigarette smokers may have significantly increased levels of TNF-α, the pro-inflammatory cytokines responsible for inflammation. On the other hand, levels of the cytokines IL-4 and IL-1β may be reduced, as there is a tendency for these cytokines to decrease in people with gum disease and increase due to treatment, indicating a suppression of the immune response by certain bacteria.

In a study by Cichońska it has been observed reduced antioxidant capacity in the saliva of vapers and cigarette smokers compared to non-smokers. A decrease in the content of uric acid, hypoxanthine and xanthine in saliva may result in the formation of free radicals and reactive oxygen species, which accelerate the process of periodontitis. [22]

There are also studies showing the effect of e-cigarette smoking on periodontal treatment. Periodontal treatment is less effective in vapers compared to non vapers because more patients require surgical treatment after professional mechanical plaque removal. Though conventional smokers need more complex periodontal treatment than vapers. However, these studies were conducted on a small sample size, so they cannot be relied on completely.

Studies have shown three processes in which the negative impact of e-cigarettes on periodontal health manifests itself. These are:
- a change in the bacterial flora of the oral cavity with a predominance of periodontal bacteria,
- impairment of the immune-inflammatory response,
- disruption of soft tissue healing.

These changes are similar to those caused by smoking conventional cigarettes. [24]

DENTAL CARIES

The use of e-cigarettes is also associated with changes in oral flora in regard to the occurrence of tooth decay. There is a correlation between smoking e-cigarettes and tooth decay.
Vapers have an estimated 79.1% risk of developing tooth decay, compared to 59.6% group. [25]

The main components of e-liquid, glycerol and propylene glycol, increase the viscosity of the aerosol, which adheres more easily to tooth enamel. This promotes biofilm formation on the tooth surfaces.
Cariogenic sugars such as sucrose, fructose and glucose are added to improve the flavor of the e-liquid. They exhibit toxicity to commensals of the oral flora - Streptococcus gordoni, Streptococcus mitis, Streptococcus intermedius and Streptococcus oralis.

The oral homeostasis becomes impaired, which promotes an increase in the amount of cariogenic bacteria, Streptococcus mutans, which are the main cariogenic pathogens. Bacteria break down the sugars in e-liquid and lower the pH of the oral cavity. [23] [26]

The decomposition products of sugars are organic acids, which demineralize the inorganic substances of the tooth, and then proteolysis of organic substances occurs.
Enamel that comes into contact with flavored e-cigarette aerosol has less hardness compared to enamel affected by non-aromatized aerosol. [23]

ORAL LESIONS AND OTHER DISEASES

Studies have shown that vapers are more prone to suffering from certain oral diseases, such as: smoker's melanosis, nicotine stomatitis, hyperplastic candidiasis, angular cheilitis and a hairy tongue. [27]
One of the most common lesions is smoker's melanosis. The polycyclic amines (nicotine and benzopyrene) present in tobacco stimulate melanocytes to increase melanin production. Melanin has antioxidant activity, so hyperpigmentation is a tissue defense response. Smoker's melanosis is a benign pigmented lesion that occurs mainly in the attached mandibular gingiva on the labial side of the canines and incisors. These lesions are reversible, tobacco-dependent and regress after smoking cessation. [28]

Nicotine stomatitis (smoker's keratosis) is another disease entity specific to vapers. It is characterized by the appearance of gray-white lesions resembling cobblestones on the palatal mucosa. The palate becomes thickened, hyperkeratotic. Often red, papular elevations surrounded by white rings of keratosis (inflamed openings of salivary gland ducts) develop on the surface. The cause may be heat concentrated in the mouth during smoking or liquid ingredients such as nicotine, artificial flavorings, propylene glycol and glycerol, which have a toxic effect on the oral mucosa and cause keratinization which is the body's defense mechanism. Smoking cessation causes the mucosal lesions to regress. [29] [30]

Hairy tongue (lingua villosa nigra) is the next oral lesion whose occurrence is associated with vaping. Bardellini et. al reported a higher frequency of hairy tongue in vapers compared to ex-smokers in their study. [27] Hairy tongue is characterised by abnormally keratinisation of the dorsal part of the tongue and it causes elongation of the filiform papillae. It may appear brown, green, yellow or black. [31] Changes in the oral flora in favour of bacteria or fungi producing chromogenic porphyrins are responsible for the colour change. The colouration may also be due to the accumulation of food colourings in the affected area. Hairy tongue is directly related to vaping, as it disappears when using e-cigarettes is stopped and returns with the resumption of vaping. The initiating factor for this lesion is the pH change associated with e-cigarettes. Other factors that intensify this disorder include dry mouth, increased temperature in the mouth during vaping, and impairment of the immune-inflammatory response. [32]

Hyperplastic candidiasis is a common lesion among vapers. According to Bardellini et al., this disease affected 17.8% of the examined patients who smoked e-cigarettes. It presents as white patches in the oral mucosal retro-commissural area, which cannot be removed by gently scraping. As with hairy tongue, the main pathogenic factor is the change in pH to acidic caused by the components of e-liquids. Candida secrete aspartyl proteinases and lipases, which break down protective proteins found in saliva, such as lactoferrin, lactoperoxidase, and immunoglobulins. The acidic environment and low content of protective proteins in saliva favor the proliferation of Candida. Associated diseases are often diabetes and an immunocompromised state. [27] [32]

A lesion that may be related to e-cigarette use is lichen planus. It usually appears as a symmetrical white lace-like pattern on buccal mucosa called Wickham striae. Its aetiology is not fully known, but it is thought to be related to the functioning of the immune system. It is likely that these lesions in vapers are more like an oral lichenoid reaction rather than pure lichen planus. However, it is very difficult to detect on clinical examination and can only be determined by biopsy. [32]

THE ORAL CARCINOGENIC POTENTIAL OF E-CIGARETTES

The most serious and dangerous effect that the use of e-cigarettes can cause is the process of carcinogenesis and the occurrence of tumour.
The cytotoxicity of the substances present in e-liquid, leading to oral mucosal damage and cell carcinogenesis, is confirmed by the studies conducted in 2018 and 2021. [9] [33] More recent studies are not available as they are only at the study design phase and the date of completion and publication of results is not yet known. [34]

The most common oral malignancy is oral squamous cell carcinoma, accounting for approximately 90% of these diseases. [35]

There are three mechanisms by which components of e-cigarettes have a harmful effect on cells. These are oxidative stress, immune-inflammatory response and DNA damage.

A correlation between periodontitis and oral cancer has also been detected. The existence of chronic inflammation as a result of periodontits can affect the contol of cell growth and induce carcinogenesis. [36]

Precancerous lesions from which oral squamous cell carcinoma can develop include oral lichen planus, leukoplakia and oral submucous fibrosis.

Oxidative stress is a condition in which there is an imbalance between the amount of harmful free radicals and the antioxidants that are designed to neutralise free radicals. An important defence element in the body is the antioxidant system of saliva, which contains peroxidase, catalase, superoxide dismutase, glutathione peroxidase, glutathione, vitamins E and C.
The components of the e-cigarette (especially nicotine) cause a reduction in antioxidant activity, which in turn can be responsible for the appearance of structural changes and DNA damage. Substances from e-cigarettes also disrupt mitochondrial function, leading to cellular stress. Oxidative stress leads to faster ageing of the body and is a very important risk factor for conditions such as atherosclerosis, heart attack, stroke, coronary heart disease, type 2

diabetes, autoimmune diseases (e.g. rheumatoid arthritis), neurodegenerative diseases (e.g. Parkinson's disease, Alzheimer's disease) and cancer. [37]

There are studies that confirm the link between inflammation and the process of carcenogenesis. The cytokines found in saliva are IL-6, IL-8, IL-1β and TNF-α. Cytokines play a key role in the processes of cell proliferation, differentiation, migration and apoptosis. They are involved in all stages of tumourigenesis and can initiate the inflammatory process. [38] [39] Increased inflammatory responses can result in changes in the mucosal epithelium causing keratinisation and metaplasia. [38] It has been proven that increased levels of IL-8 can enhance carcenogenesis, as can TNF-α, whose higher levels have been reported in a group of vapers. [36]

DNA DAMAGE

E-liquids contain many substances with proven cytotoxic effects. The components of e-cigarettes inhibit the proliferation of gingival fibroblasts, inducing their apoptosis. [40] Experimental studies conducted on oral cell lines have shown DNA strand breaks after exposure to e-cigarette vapour and gene dysregulation regardless of nicotine content. Flavouring ingredients in e-liquids (vanillin, ethyl vanillin, ethyl maltol) and aldehydes (acetaldehyde, fomaldehyde) cause DNA strand breaks. [41] Disruption of the cell cycle has also been observed in a group of vapers, which may be indicative of tumour growth. It has been shown that nicotine can increase the proliferation and the viability of cancer cells and reduce the effect of chemotherapy drugs. [21]

There are also studies which found that periodontal pathogens (Porphyromonas gingivalis, Fusobacterium nucleatum, Prevotella intermedia) play an important role in carcinogenesis. Studies have shown that repeated periodontitis was associated with an increased risk of oral squamous cell carcinoma. Proteases produced by bacteria can degrade human cells and modulate the host immune-inflammatory response, ultimately contributing to the emergence and progression of cancer. [42] [43]

Many studies report that there is limited clinical evidence and no long-term studies have been conducted to conclusively confirm that e-cigarette smoking is a carcinogenic factor. However, there are many indications that the use of e-cigarettes has serious health consequences that cannot be underestimated. [36] [40] [43]

SUMMARY

E-cigarettes, often erroneously perceived as a less harmful alternative to traditional cigarettes, are gaining popularity among adolescents and adults. E-cigarettes are addictive due to the nicotine they contain, and other ingredients such as glycerine, propylene glycol and various metals can lead to irritation of the oral mucosa, resulting in oral lesions and disease. The negative impact of e-cigarettes on oral health in the form of increased incidence of periodontitis, tooth decay and oral cancer has been proven. Based on the increasing amount of evidence of the harmful effects of these products, educational and regulatory action is needed to reduce their use in order to prevent negative oral health effects.

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