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(Review Article)



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Abstract

Background: Electronic cigarettes are one form of cigarettes that are popular in society. However, their impact on health, especially oral health, is not better than conventional cigarettes because they can cause various health disorders and oxidative stress. Various lesions in the mouth can occur due to long-term use of electronic cigarettes.

Purpose: This study aims to systematically review previous research findings regarding oral lesions that can be found in patients who smoke electronic cigarettes or e-cigarettes.

Method: This research is a type of secondary literature research in the form of a systematic literature review (scoping review). This scoping review is compiled based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) method.

Result: The results of various studies were obtained from subjects with different frequencies and intensities of electronic cigarette use. So that different lesions were obtained in each observation. The lesions recorded were such as leukoedema, coated tongue, smoker's melanosis, hairy tongue, and nicotinic stomatitis.

Conclusion: Based on various studies, it has been shown that in e-cigarette users, oral lesions such as leukoedema, coated tongue, smoker's melanosis, hairy tongue, and nicotinic stomatitis can be found. The findings of these lesions depend on the frequency and intensity of e-cigarette use.

Keywords: E-Cigarette; Smokers; Oral Lesions; Oral Normal Varians

1. Introduction

Electronic cigarettes or (e-cigarettes) are electrically powered devices (battery) with various designs. Since the emergence of electronic cigarettes, the appeal and popularity of electronic cigarettes has increased significantly, especially among teenagers [1]. A survey by the National Youth Tobacco revealed an increase in e-cigarette use in 2011-2013 among teenagers with no previous history of smoking [2]. In general, electronic cigarettes (e-cigarettes) consist of 3 (three) parts, namely the battery (the part that contains the battery), the atmoizer (the part that will heat and vaporize nicotine), and the cartridge (containing nicotine solution). At the end of the electronic cigarette (e-cigarette) there is a chip that will light up when inhaled and then activate the battery that will heat the nicotine solution and produce vapor that will be inhaled by the user [3]. The electric device (battery) in e-cigarettes functions to heat e-liquid aerosols containing nicotine, propylene, glycol, glycerin and various flavoring additives to produce aerosols that can be inhaled [1].

Aldehydes produced by e-cigarettes can cause carbonyl/oxidative stress, DNA addition/damage, and cellular aging [1]. E-cigarettes can also cause respiratory disorders such as obstructive pulmonary disease and lung cancer [4]. Clinical

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studies have shown that the habit of smoking e-cigarettes can also cause disorders in the oral cavity, namely more plaque accumulation, gingiva loss of clinical attachment, and probing depth exceeding 4 mm compared to individuals who have never used tobacco in any form [5]. In addition, various oral lesions such as Leukoedema can appear with prolonged use of e-cigarettes [6]. Oral lesions can be caused by smoking and poor oral hygiene [7]. This study aims to systematically review previous research findings regarding oral cavity lesions that can be found in patients who smoke electronic cigarettes or e-cigarettes.

2. Material and methods

This research is a type of secondary literature research in the form of a systematic literature review (scoping review), which is a literature review compiled through a thorough search of studies relevant to the specific topic to be discussed and the assessment and synthesis of data carried out using established methods so that it can be used as a basis for evidence-based practice. This scoping review is compiled based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) method, which is a collection of evidence-based items that aim to report a systematic review or meta-analysis.

Data search was conducted during the period of September 2 - October 5, 2024 in the electronic databases ScienceDirect, PubMed, and Google Scholar. Phase search and Boolean operators (AND, OR) were used to determine the search for keywords that were in accordance with the Medical Subject Headings (MeSH). Keywords were based on the following: ("E-Cigarette" OR "Vape" AND "Oral Mucosa Lesions" OR "Oral Normal Variants") OR ("E-Cigarette" AND "Oral Mucosa Lesions") OR ("E-Cigarette" AND "Oral Normal Variants") OR ("E-Cigarette" AND "Oral Normal Variants") OR ("Yape" AND "Oral Normal Variants") OR ("Yape" AND "Oral Normal Variants"). The article selection process was carried out through four stages, namely identification, screening, eligibility assessment, and determination of inclusion articles. Data search was carried out using the PICO framework. The PICO framework is in accordance in (\leftarrow Table 1).

Table 1 Ulasan hasi	mengenai temuan d	ata lesi pada	pasien perokok
		ata iooi paaa	paoren perenen

P (Population)	Smokers
I (Intervention)	Smoking electronic cigarettes
C (Comparison)	Nonsmokers, ex-smokers, and conventional cigarette smokers
0 (Outcome)	Oral Mucosa Lesions

The papers selected for this evaluation were chosen based on precise inclusion and exclusion criteria. To ensure that the study accurately represents the latest developments in the field, only papers published in the last ten years (2014-2024) were considered. To ensure relevance to the subject of the study, articles were required to include at least one related phrase in the title, such as "E-Cigarette", "Vape", "Oral Lesions", or "Oral Normal Variants". In addition, only primary research papers or research studies were considered, as they present new data and findings, while review articles or editorials were excluded. The selected papers were required to provide results that were closely aligned with the intended purpose of the study, namely the finding of lesions in e-cigarette smokers.

Conversely, items that did not meet the inclusion criteria were removed. These included review papers, meta-analyses, case reports, and other publications that did not include original data or primary research findings. These publications were not directly relevant to the study's aim of investigating what lesions could be caused by e-cigarettes. Excluded from consideration were articles published before 2014 to avoid the influence of outdated data on the findings. Additionally, studies that lacked clear or comprehensive data reporting, such as those that did not offer sufficient information on sample characteristics, treatment procedures, or outcome measures, were excluded from consideration. Furthermore, any papers with unclear, contradictory, or insufficient intervention methods were removed to ensure that the included studies adhered to the criteria.

3. Results and discussion

3.1. Study Selection

This screening resulted in 10753 articles. Initial exclusion criteria required that the journal not be published for more than 10 years, reducing the selection to 10166 articles. Subsequent exclusion criteria included duplication and deletion for other reasons (inappropriate keywords) and resulted in 552 articles. The next criterion required that the articles be

included in the fields of Medicine and Dentistry, reducing the selection to 104 articles. Furthermore, the criterion that only original articles be included further narrowed the selection to 37 articles. The next exclusion criterion required that the articles specifically address e-cigarettes with oral lesions or oral normal variance or vaping with oral lesions or oral normal variance, leaving 15 articles. The final exclusion criteria focused on articles that specifically and specifically addressed lesion findings in e-cigarette smokers, resulting in a final selection of 5 articles.

3.2. Study Characteristics

This studies used a case-control study, Experimental laboratory (quantitative), and a cross-sectional study design with a period from 2018 to 2021. This study was held in various countries such as Italia [8], São Paulo [9], Brazil [10], Indonesia [11, 12]. Discussion of selected journals is in (\succ Table 2).

3.3. Outcome

The prevalence of lesions in each study varies. In the conclusion of the study, it can be seen that each lesion listed is related to the habit of using electronic cigarettes according to (\succ Table 3).

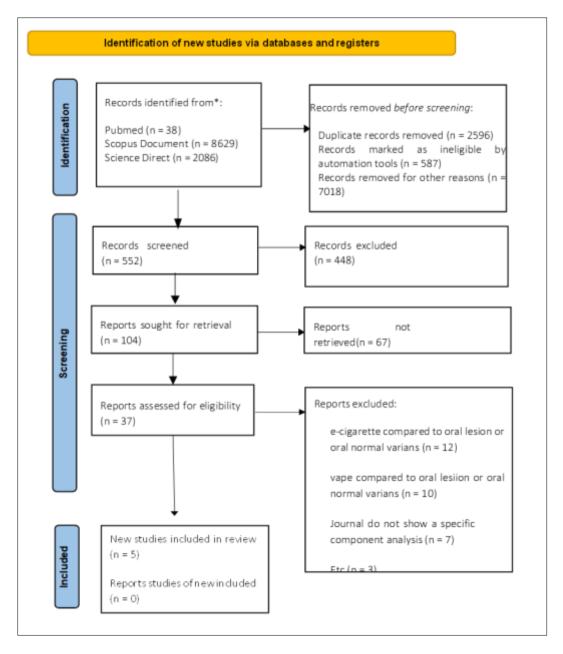


Figure 1 PRISMA *diagram flow* literature search.

The oral cavity is an easily exposed part to the effects of cigarettes because the oral cavity is where the absorption of substances resulting from cigarette combustion occurs. Toxic components in cigarettes can irritate the soft tissue in the oral cavity and can cause mucosal infections, slow wound healing, dry socket, suppress osteoblast proliferation, increase phagocytosis ability, and can also reduce blood flow to the gingiva [13]. Various oral lesions such as Leukoedema can appear with prolonged use of e-cigarettes [6]. Oral lesions can be caused by smoking and poor oral hygiene [7]. The results of the selection discussion based on journals, abstracts, and full texts were carried out and produced 5 main journals to be discussed as follows:

Table 2 Review of results regarding	g lesion data findings	in smoking patients
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No.	Author	Year	Title	Study Design	Location	Result
1	Bardellini, E., et al.	2018	Oral mucosal lesions in electronic cigarettes consumers versus former smokers	Case-control study	Italia	It was found that nicotine stomatitis, hairy tongue and angular cheilitis were significantly more common in e-cigarette users
2	Carvalho, B. F. D. C., et al.	2024	Oral Mucosa and Saliva Alterations Related to Vape	Experimental laboratory (quantitative)	São Paulo	The development of hyperkeratosis lesions on the oral mucosa in electronic cigarettes is significant, one of which is nicotinic stomatitis
3	Garcia, B. D. F. S. et al.	2024	The use of electronic cigarettes and other tobacco products among university students and their potential relationship with oral health: A cross-sectional study	A cross- sectional study	Brasil	When e-cigarette use was combined with other forms of tobacco use, additional oral changes were more prevalent, including coated tongue and nicotinic stomatitis.
4	Amtha, R., et al.	2024	Profile of oral mucosa changes and perception of e-cigarettes smoker	A cross- sectional study	Indonesia	This study found that approximately 21.1% of subjects experienced nicotine stomatitis, 11.4% of subjects experienced leukoedema, 13.2% of subjects experienced smoker's melanosis, and 28.9% of subjects experienced smoker's keratosis lesions
5	Yohana, W. et al.	2021	Characteristics of Dental Health, Salivary Viscosity, pH and Flow Rate, Gum Hyperpigmentation, Malocclusion, Blood Pressure and Pulse Related to Body Mass Index of Vapers	Case-control study	Indonesia	Smoking is also associated with periodontal disease. The consequences of the longer duration time of smoking that occurs in the oral cavity is gum hyperpigmentation.

No.	Author	Population	Assessment criteria	Lesion Findings	Prevalence of lesion	Conclusion of the Research
1	Bardellini, E., et al.	A total of 90 patients were examined, 45 were former smokers (group A) and 45 were EC consumers (group B)	The research was conducted based on the results of observations on former smokers and consumers of electronic cigarettes	Nicotinic stomatitis	13,3%	Nicotine stomatitis is more common in e-cigarette smokers
				Hairy Tongue	15,5%	Statistically greater prevalence of lesions in e- cigarette smokers
2	Carvalho, B. F. D. C., et al.	A vape user patient, who showed white plaques on the posterior area of the hard palate	Analyzing patients with clinical examination, sialometry, pH evaluation, and white lesion excision biopsy. Molecular changes in saliva and vape fluid were also analyzed by vibrational spectroscopy	Nicotinic stomatitis	100% (The research samples were detected to have these lesions)	In the middle third of the palate, there were papules with a reddish central area, compatible with nicotinic stomatitis
3	Garcia, B. D. F. S. et al.	Of the 620 participants, 57.1% reported using tobacco in some form, with 47.4% reporting electronic cigarette (e- cigarette) use. stage admin electro questi partici deterr preval tobacco secono involv exami	conducted in 2 stages: the first	Coated tongue	P < 0.05 (Statistically	When e-cigarette use was combined with other forms of tobacco use, additional oral changes were more common, including coated tongue and nicotinic stomatitis (P < 0.05)
			participants to determine the prevalence of tobacco use and the second stage involved a physical examination of participants	Nicotinic stomatitis	significant lesion findings)	
		of Trisakti validated University questionnaire a students who intraoral clini	This study used a validated	Nicotinic stomatitis	21,1%	Mucosal changes were observed in e- cigarette smokers
4	Amtha, R., et al.			Leukoedema	11,4%	
			examination of the subjects	Smokers Melanosis	13,2%	
5	Yohana, W. et al.	Observational descriptive study involving 30 vapers in Bandung	Intra oral examinations such as DMF-T, calculus, stain, gum hyperpigmentation, malocclusion; salivary viscosity, pH and flow rate.	Smokers Melanosis	Severe : 23.33% Mild : 50% Fair : 13.33%	Active vapers can experience smokers melanosis which is seen as gum hyperpigmentation.

3.4. Leukoedema

Leukoedema is one of the most common oral lesions in smokers [14]. The etiology of leukoedema is unknown, but it is noted that leukoedema is often associated with smoking habits, poor oral hygiene, and certain races that are common in black people [6]. Histologically, the lesion shows hyperparakeratosis and is often elongated with irregular retepegs and intracellular edema in the malpighian layer [15]. Clinically, leukoedema appears as epithelium covered with a diffuse edematous layer and appears like a velvety veil [6]. Leukoedema is a lesion in the form of a white plaque that is generally located on the buccal mucosa. Leukoedema was once considered a premalignant lesion, but this statement has been removed because it has been proven to have no potential to become malignant [14]. As in the journal Amtha, R., et al 2024, leukoedema was found in e-cigarette smokers, namely 11.4% [11].

3.5. Coated Tongue

Coated tongue or webbed tongue is a clinical appearance of tongue abnormalities that appear on the dorsum of the tongue as if covered by a layer that is usually white or another color according to the type of food consumed. In normal individuals, the tongue is coated by mucus, desquamated epithelial cells, organisms, and debris [16]. Risk factors that can increase coated tongue include oral hygiene, antibiotic consumption, alcohol, smoking, drugs, hypothyroidism, diabetes, syphilis, a weak immune system, oral trauma, dehydration, and xerostomia [17]. Cigarettes can cause dry mouth, which inhibits the function of saliva as a bacterial buffer and causes excess keratin production. Excessive and accumulated keratin production will facilitate the retention of debris on the papillae of the tongue [18]. Smoking can change the morphology of the tongue and can contribute to a higher prevalence of coated tongue in smokers [19]. According to the research results of Garcia, B. D. F. S. et al. 2024, e-cigarette use was common among college students, and when e-cigarette use was combined with other forms of tobacco use, additional oral changes were more common, including coated tongue [10].

3.6. Smokers Melanosis

Smoker's melanosis is a picture of a darker color change than normal gingival. Clinically, smoker's melanosis appears as a diffuse brown patch with no elevation. Smoker's melanosis is also associated with the consumption of the number of cigarettes smoked per day, the duration of smoking habits and aspects of intensity, and the frequency of smoking, the degree of occurrence of smoker's melanosis will increase [20]. In nicotine, smoker's melanosis may be caused by the effect of nicotine (a polycyclic compound) on melanocytes located along the basal cells of the oral mucosal epithelium. Nicotine appears to directly stimulate melanocytes to produce more melanosomes, resulting in increased deposition of melanin pigment as bacillary melanosis with varying amounts of melanin incontinence. Polycyclic amines in tobacco, such as nicotine and benzpyrene, stimulate melanocytes to increase melanin production [6]. The most common locations for Smoker's Melanosis are the anterior labial mandibular gingiva, buccal mucosa, lips, hard palate, and tongue. In general, several brown macules appear and appear light brown to dark brown, depending on the duration and amount of tobacco smoking. Microscopically, melanin production can be observed in the basal layer of the epithelium. The accumulated melanin and melanophages will be bound to the superficial connective tissue. The histopathology of smoker's melanosis is microscopically identical to physiological pigmentation or melanotic macules so that clinical examination is needed to diagnose this condition [21]. Cigarettes can stimulate melanocytes of the oral mucosa to produce excessive melanin which is then deposited in the basal cell layer of the mucosa, resulting in brown pigmentation of the buccal mucosa and gingiva [22]. This proves that cigarette use is associated with changes in the oral mucosa, one of which is gum hyperpigmentation. This finding is in accordance with research in Saudi Arabia, that active smokers can experience smoker's melanosis (43.28%) which is seen as gum hyperpigmentation [12]. The results of the study by Amtha, R., et al. 2024 also found that mucosal changes were observed in e-cigarette smokers, namely 13.2% of the total sample [11].

3.7. Stomatitis Nikotina

Nicotinic stomatitis is also called smoker's palate and nicotina palatine [23]. This lesion is most often found on the roof of the mouth that is exposed to heavy cigarette smoke [6]. Nicotine stomatitis is a condition characterized by thickening or hyperkeratosis of the palatal mucosa. In nicotine stomatitis, there will be an increase in red papules due to inflammation of the minor salivary ducts which are sometimes accompanied by fissures on the palatal surface [24]. On the palate, there will be a homogeneous discoloration with many erythematous spots. In some cases, the palatal keratin becomes thickened, giving a gap or appearance like a dried mud appearance. The thickening that occurs will surround the salivary gland ducts which appear as white umbilicated nodules with a red center. The epithelial lining of the minor salivary glands often shows squamous cell metaplasia and hyperplasia [6].

According to the study of Bardellini, E., et al, 2018, Nicotine stomatitis is more common in e-cigarette users compared to former smokers. Many irritants, toxins, and carcinogens, naturally found in tobacco, cause typical rashes or

keratinization of the palate that appear as red dots surrounded by a white keratosis ring. Although e-cigarettes do not contain as many ingredients as conventional tobacco, they are vaporized by heat starting from a liquid solution (a mixture of propylene glycol, glycerin, nicotine, and flavorings). It can be speculated that nicotine stomatitis in e-cigarette users may depend not only on the exposure of the palatal mucosa to nicotine but also on some of these chemical compounds. For example, a recent study found that the product characteristics of electronic nicotine delivery systems, including flavorings, can induce inhalation toxicity, with strawberry flavored products being the most cytotoxic [8]. Other research results also found that vape use was associated with the development of hyperkeratosis lesions on the oral mucosa and significantly changed the patient's saliva pattern because vape fluids present carcinogenic and cytotoxic components in their composition. In the results of the sample observations, the middle third of the palate, papules were found with a reddish central area, compatible with nicotinic stomatitis [9]. The use of alternative forms of tobacco consumption is common among college students, with e-cigarette use being the most common form, and can cause adverse effects on the oral cavity, such as caries and gingivitis, especially when used in combination with other tobacco products. When e-cigarette use is combined with other forms of tobacco use, additional oral changes are more common, including nicotinic stomatitis [10]. The results of the study by Amtha, R., et al., 2024, found that mucosal changes were observed in e-cigarette smokers, namely 21.1% of the total sample population [11].

3.8. Hairy Tongue

Hairy Tongue is a benign condition resulting from elongation of the filiform papillae due to keratin accumulation. This can result from inadequate exfoliation (from decreased oral intake, poor oral hygiene, or dry mouth associated with anticholinergic medications) and accelerated keratinization (as can occur with irritation from smoking) [25]. In a Turkish study, the frequency of black hairy tongue increased in males, older age, smoking, individuals with a habit of drinking large amounts of hot tea, and poor oral hygiene. One of the predisposing factors for black hairy tongue is smoking. Smoking, drinking excessively hot beverages, and using mouthwashes can trigger the production of excess keratin. This keratin accumulation is produced by epithelial cells that express hair-type keratin and are located specifically at the tips of the filiform papillae. Keratin discoloration has been noted with smoking, e-cigarette use, colonization with chromogenic bacteria or fungi, use of oxidizing mouthwashes, radiation therapy, chemotherapy, and drug use [21]. Colonization of chromogenic bacteria can give various colors such as green, yellow, and brown to black [6]. Based on (► Table 3), Hairy tongue resulted in a statistically greater prevalence among e-cigarette users than former smokers. There are many initial or predisposing factors for abnormal coating on the dorsal surface of the tongue, especially with the pH changes associated with smoking. We can speculate that mucosal changes may also arise from other factors, namely the drying effect of the mucosa, high intraoral temperature, changes in intraoral pH, local changes in the membrane barrier and immune response, or changes in resistance to fungal and viral infections [8].

4. Conclusion

The use of e-cigarettes has many impacts, one of which is on the oral cavity. The reviewed studies showed an increased risk of oral lesions due to exposure to chemicals in e-cigarettes. In the oral cavity e-cigarettes smokers, lesions such as leukodema, coated tongue, smoker's melanosis, hairy tongue, and nicotinic stomatitis can be found. This shows that the use of e-cigarettes can have a negative impact on oral health. Further research is still needed to understand the exact mechanism of the effect of e-cigarettes on these lesions and to determine the long-term impacts. However, this scoping review emphasizes the importance of awareness of the oral health risks for e-cigarette users and the need for education and regulation to limit the negative impacts of their use.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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