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Cigarettes Versus Electronic Cigarettes: The Effects on the Oral Cavity

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SYSTEMATIC REVIEW / *REVUE SYSTÉMATIQUE*

Oral Pathology / *Pathologie Orale*

CIGARETTES VERSUS ELECTRONIC CIGARETTES: THE EFFECTS ON THE ORAL CAVITY

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Objectives: To date, there is a large amount of scientific evidence on the effects of smoke-free products on oral health, highlighting their potential in reducing the risk of causing and progressing smoking-related diseases. In contrast to the last statement, other studies confirm the cytotoxic and tissue effects of nicotine-containing e-cigarette liquid. The purpose of this study was to review the literature and to evaluate the damage caused by cigarette smoking in comparison with that caused by e-cigarettes.

Methods: Our study considered the consultation of the bibliographic databases "Medical Literature Analysis and Retrieval System". The research was carried out by using the keywords: "Cigarette" AND "E-cigarette" AND "oral cancer caused by smoking" AND "cigarette toxicology" AND "cigarette toxicology".

Results: Research related to the impact on oral health of e-cigarette usage began in 2011 with the publication of 26 studies. Those studies were focused primarily on nicotine-related harms, subsequently evaluating the adverse effects on the oral cavity of other chemical components released during the inhalation.

Conclusions: The use of smoke-free products can negatively affect oral health when compared to abstaining from smoking. This confirms that smoke-free alternative products are not risk-free as they contain nicotine, an addictive substance, and the best choice for any smoker remains to stop using tobacco and nicotine-containing products.

Keywords: Electronic Nicotine Delivery Systems; Oral Cancer; Oral health; Periodontal Diseases; Smoking.

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The authors declare no conflicts of interest.

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CIGARETTES VERSUS CIGARETTES ÉLECTRONIQUES: EFFETS SUR LA CAVITÉ ORALE

Objectifs: Un nombre croissant de données scientifiques a étudié les effets des produits sans combustion sur la santé bucco-dentaire, certaines études suggérant une réduction du risque d'initiation et de progression des maladies liées au tabagisme. Toutefois, d'autres travaux rapportent des effets cytotoxiques, inflammatoires et délétères sur les tissus, associés aux liquides de cigarettes électroniques contenant de la nicotine. L'objectif de cette étude était de revoir la littérature actuelle et de comparer les dommages bucco-dentaires causés par le tabagisme conventionnel à ceux associés à l'utilisation des cigarettes électroniques.

Méthodes: Une revue narrative de la littérature a été réalisée par consultation de la base de données « Medical Literature Analysis and Retrieval System (MEDLINE) **».** La stratégie de recherche incluait les mots-clés et combinaisons suivants : *« cigarette », « e-cigarette », « oral cancer caused by smoking », « cigarette toxicology »* et *« electronic nicotine delivery systems »*. Les études pertinentes évaluant les effets des cigarettes conventionnelles et électroniques sur les tissus oraux ont été analysées.

Résultats: Les recherches évaluant l'impact de l'utilisation des cigarettes électroniques sur la santé bucco-dentaire ont débuté en 2011, avec l'identification d'au moins 26 études publiées. Les premières investigations se concentraient principalement sur la toxicité liée à la nicotine, tandis que les études ultérieures ont évalué les effets indésirables d'autres composés chimiques libérés lors de l'inhalation de l'aérosol. Les résultats rapportés incluaient une toxicité cellulaire, des réponses inflammatoires, des altérations parodontales et des effets potentiellement carcinogènes sur les tissus oraux.

Conclusions: Les produits sans combustion peuvent avoir un impact négatif sur la santé bucco-dentaire lorsqu'ils sont comparés à une abstinence totale de tabac et de nicotine. Bien que les cigarettes électroniques puissent réduire l'exposition à certains toxiques issus de la combustion, elles ne sont pas dénuées de risques en raison de leur teneur en nicotine et de leurs effets cytotoxiques associés. Ainsi, la stratégie la plus efficace pour préserver la santé bucco-dentaire et générale demeure l'arrêt complet du tabac et des produits contenant de la nicotine.

Mots-clés: Cancer oral; Maladies parodontales; Santé bucco-dentaire; Systèmes électroniques d'administration de la nicotine; Tabagisme.

Introduction

According to the World Health Organization (WHO) data, tobacco smoking is the greatest threat to health and the main risk factor for chronic non-communicable diseases worldwide, with approximately one billion smokers [1-15].

In 2003, Hon et al. had the idea of using piezoelectric ultrasound to vaporize a forced flow of nicotine-containing liquid, designed as vapor, similar to cigarettes and filed his first patent in China, in the United States and the in the European Union [11-34].

The name "electronic cigarette" (e-cig, abbreviated from the English e-cigarette) identifies all the electronic devices capable of inhaling vapor without using combustion and its utilization in the population is an increasingly widespread habit [1-48].

To date, there is a large amount of scientific evidence on the effects of smoke-free products on oral health, highlighting their potential in reducing the risk of causing and progressing smoking-related diseases [1-32].

In contrast to the last statement, other studies confirm the cytotoxic and tissue effects of nicotine-containing e-cigarette liquid [25-48].

The present review differs from existing meta-analyses on tobacco/e-cigarettes and oral health because of the inclusion of both cytotoxic and periodontal effects together.

Therefore, the purpose of this study was to review the literature and to evaluate the damage caused by cigarette smoking in comparison with that caused by e-cigarettes.

Materials and methods

The present review was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines. The research question was about cigarette and e-cigarette use and their effect to the oral cavity. A literature search between 2015 and 2022 was conducted in February 2024 in four electronic databases (Medline / PubMed, Scopus, Embase, and Web of Science) using the combination of the terms "Cigarette" OR "E-cigarette" AND "dental" OR "oral health" OR "oral cancer" OR "cigarette toxicology". Articles not in English language were excluded; observational, cross-sectional, and interventional studies were all eligible. PICO inclusion and exclusion criteria were adopted. Eligibility was judged by two reviewers, with an inter-rater agreement of 100%.

PICO criteria used to select studies were as follows. As for Population, studies involving patients smoking traditional cigarettes or e-cigarettes were included. As for Intervention, studies involving the cytotoxic and periodontal effects of cigarettes and e-cigarettes were included. As for Comparison, the results of the cytotoxic, genotoxic, oncogenic features, as well as periodontal effects associated with e-cigarettes or cigarettes were compared. The expected Outcome was to obtain indication about the effects and damages and/or potential damages associated with e-cigarettes or cigarettes. ROBIS tool checklist was adopted for included studies. The Newcastle–Ottawa Scale (NOS) was used for assessing the quality of the included non-randomized studies within the present systematic review.

Criteria for excluding studies were (a) experimental analysis conducted on animals or in vitro; (b) letters to the editor, or conference abstracts. Studies regarding animals or in vitro were excluded in order to have uniform results regarding humans.

Based on the abstracts of the articles, the articles were included or excluded in the review. Finally, data were extracted from the selected articles. The PRISMA statement was adopted during data assessment and extraction.

Results

A total of 26 articles resulted eligible. The selection process of the articles is resumed in the flowchart of Figure 1.

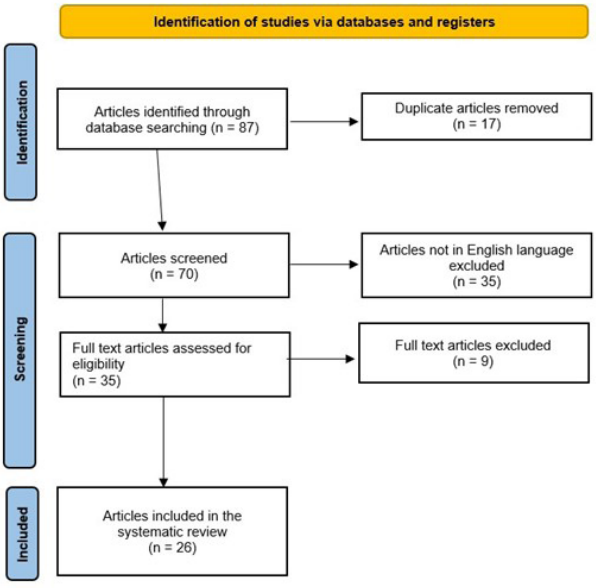

Figure 1. PRISMA flowchart

The initial electronic search yielded 87 articles. Then, 17 duplicate articles were excluded. Following abstract screening, 35 articles were excluded. A total of 35 articles were eligible for full-text evaluation. Following the full-text assessment, 26 articles were included for the present systematic review analysis.

Table 1 resumes cytotoxic, genotoxic, oncogenic features, whereas Table 2 resumes periodontal effects associated with e-cigarettes or cigarettes. They show a statistically significant relationship between smokers of conventional cigarettes and periodontitis and smokers of electronic cigarettes and cell destruction.

Table 1: Cytotoxic, genotoxic, oncogenic features.

Author and year	Type of study	Sample analysed	Descriptive data	Effects/symptoms	Exams/ tools/ tests
Bustamante et al. (2018)	Descriptive comparative	Conventional Smokers (N=20) E-cigarette smokers (n=20) Non-Smokers (N=19)	N = 59	16/20 e-cigarette users had levels of N0-nitrosonornicotine in their saliva	- LC-MS/MS
Sun et al. 2019	in vitro	BLU Classic tobacco 2.4% nicotine 2.4% nicotine 35mL puff/minute with a duration of 4s at 30s intervals	Human keratinocytes orally	Enhanced metabolism of ba pto genoto metabolites	- Hplc - qPCR - Western blot
Franco et al. 2016	Descriptive comparative	E-cigarette smokers Conventional smokers(n=23) E-cigarette smokers(n=22) Non-smokers(n=20)	N=65	The prevalence of micronuclei decreased in the group of cigarette consummaters compared to conventional smokers [p<0.005]	Micronuclei dosing test
Flieger et al. 2019	Descriptive comparative	Conventional smokers(n=8) E-cigarette smokers(n=8) Non-smokers(n=8)	N = 24	Thiocyanate saliva levels in e-cigarette users similar to those of conventional smokers and significantly higher than those of non-smokers	HPLC - UV
Willershausen et al. 2014	in vitro	Fibroblasts of the human periodontal ligament	Smoker Shop Smoking Liquids Hazelnut Flavor (20mg/ml Nicotine) Lime Flavor (20mg/ml Nicotine) Menthol Flavor (22mg/ml Flavor) Incubated for up to 96 hours	The result was exposure to menthol fluid: Reduced cell proliferation(p<0.001) Reduced DETECTION of ATP(p<0.001)	- PrestoBlueCell ViabilityAssay - - - ApoGlowBioassay Municipality - Microscopy - Migrationassay, Yon

Sundar et al. 2016	in vitro	Increased carbonilation of proteins and pro-inflammatory responses in HPdLF and HGEPp Increased inflammation and DNA damage markers in HPdLF and HGEPp and 3D model of human epigenic tissue	Human Periodontal Ligament Fibroblasts (HPdLF) Human Gingival Epithelium Progenitors (HGEPp) 3D Model of Human Epigengival Tissue	Bleeding at survey sites and gum grow fluid increased after vaporization Minimum variation in plaque levels	- Essay Comet test Protein carbonylation / oxyblot - ELISA for cytokines - Western blotting
Duggar et al. 2018	in vitro	E- grape-flavored liquid	Cultivated oral keratinocyte model	Negative effect on cell growth, regardless of absence or presence of nicotine	Colorimetric asage
Welz et al. 2016	in vitro	Culture of mucosal tissue from fresh tissue samples of healthy oropharyngeal mucosa	Happy Liquid brand (each with 12mg/ml nicotine) apple flavor, cherry flavor, tobacco flavor. Incubated with 250 ll liquid for various lengths of time	All liquids caused a reduction in cell vitality. Fruit flavors showed greater toxicity than tobacco flavor. DNA fragmentation increased in fruit flavors, but not in tobacco flavor	- Tetrazole - 8 water soluble Alcaline electrophoresis in microgel
Sancilio et al. 2016	in vitro	E-liquid from Halo Company (0e24mg/ml nicotine)	Human gum fibroblasts	Exposure to e-cigarette liquid increased ROS production and Baxex pressure followed by apoptosis	MTT Flow cytometry test in Fluorescence microscopy microscopy

Table 2. periodontal effects associated with e-cigarettes or cigarettes

Author and year	Type of study	Descriptive data	Sample analysed	Effects/symptoms	Exams
Jeong et al 2019	Comparative descriptive	N = 13,551	Smokers of e-cigarettes(n=222) Conventional smokers (n=2320) Ex-smokers(n=2667) Non-consumers(n=8,342)	Periodontal disease more likely for: E-cigarette smokers than non-consumers (OR=2.34, CI: 1.52-3.59) Conventional smokers compared to non-consumers (OR=2.17, CI:1.76-2.68)	Population survey
BinShabaib et al 2019	Comparative descriptive	N=135	Conventional cigarette smokers(n=46) E-cigarette smokers(n=44) Non-smokers(n=45)	Higher levels of gum crevicular fluid in conventional smokers than in e-cigarette users or non-smokers($p<0.05$) Higher levels of pro-inflammatory cytokines in conventional smokers than in conventional smokers e-cigarette and non-smoking consumers($p<0.05$) No difference in gum crevicular fluid or pro-inflammatory cytokines among groups of e-cigarette smokers and non-smokers	Clinical and radiographic examination
Farsalinos et al 2013	Almost experimental	N=111	Exclusive e-cigarette users (former conventional smokers)	Gingival hemorrhage (<5%)	Face-to-face interview
Alqahtani et al 2019	Comparative descriptive	N=102	E-cigarette smokers (33). Water pipe smokers (34). Conventional smokers (35).	The plaque index and survey depth were higher in all smokers than in non-smokers($p<0.05$)	Questionnaire for clinical examination
Wadia et al 2016	Longitudinal descriptive	N=20	Conventional smokers switching to e-cigarettes	Bleeding at survey sites and gum grow fluid increased after vaporization	Clinical and laboratory examination (for the detection of cytokines and GCF fluids)
Ismail et al 2019	Longitudinal descriptive	N=45	E-cigarette users at baseline and 6 months	Periodontal health measures decreased to 6 months ($p<0.05$)	Clinical examination

Yao et al 2017	Descriptive correlational	N=533	Current adult users of conventional cigarettes and e-cigarettes in the United States	Gum haemorrhage linked to increased spending on e-cigarettes	Tobacco and belief survey
Huilgol et al 2019	Comparative descriptive	N=456,343	Good oral health (n=221,336) Poor oral health (n=234,977)	Daily use of e-cigarettes associated with increased likelihood of oral ill health	Telephone survey
Al-Aali et al 2018	Comparative descriptive	N=92	- E-cigarette users(n=47) - Non-smokers(n=45)	Plaque index, survey depth, peri-implant bone loss and pro in higher inflammatory cytokines in e-cigarette users Less bleeding during survey of e-cigarette users	Clinical and radiographic examination

Discussion

Specifically, with regard to periodontal effects, studies have suggested that daily e-cigarette usage is associated with a worst oral health. They have linked poor oral health to the number of permanent teeth removed. Tooth loss is a complex measure of oral health, as it can be caused by multiple factors. However, considering that two of the main factors contributing to tooth loss are periodontal disease and dental caries, the results of these studies were considered relevant to both the periodontal and dental effects categories [30-48].

The results on cytotoxic, genotoxic and oncogenic effects were different, establishing a high heterogeneity between the results of different liquids, but agreeing on the fact that cells of oral cavity in e-cigarette users had a prevalence of micronuclei (as a predictor of increased risk of tumor degeneration), similar to that of non-smokers and significantly lower than that of conventional smokers [35-45].

Most of the mouth and throat symptoms experienced by e-cigarette users in previous studies were of lesser magnitude and temporary duration than those reported by conventional smokers. In addition, such studies also found an interesting attenuation of the above symptoms in conventional smokers who switched to e-cigarettes with a reduction in oral health damage. It is important to note, however, that these studies were not designed to test the effects of e-cigarette utilisation on the oral cavity, but were mostly cross-sectional and descriptive studies that did not always take into account factors such as age, general health status, duration of previous conventional smoking and medication use. These limitations have therefore severely hampered the quality of the evidence provided [25-43].

Chemicals and carcinogens present in conventional cigarette smoke are known risk factors for various diseases including oral cancer and periodontal disease.

Switching from conventional cigarettes to e-cigarettes may improve some oral health parameters (bacterial plaque on teeth's surface, bleeding index, probing depth, etc.) and also have an overall benefit on the general health of patients.

The available evidence shows that patients who smoked both conventional and electronic cigarettes (with nicotine) have: inhibition of osteoblast proliferation, inhibition of osteoclast proliferation and production stimulation of inflammatory cytokines by human gingival fibroblasts, impediment of neutrophil phagocytosis in different measures between electronic and conventional cigarettes. However, the reduction of cell proliferation and the cytotoxic effect of electronic cigarettes appear to be less than that of conventional cigarettes.

Conclusion

The analysed studies show that the use of smoke-free products can negatively affect oral health when compared to abstaining from smoking. This confirms that smoke-free alternative products are not risk-free as they contain nicotine, an addictive substance, and the best choice for any smoker remains to stop using tobacco and nicotine-containing products.

However, for those who are unwilling or unable to stop smoking, smoke-free products are a much better option and hold the potential of reducing the harmful effects of smoking on oral health.

E-cigarette aerosol is less compositionally complex than conventional cigarette smoke and contains significantly lower levels of toxic substances.

Therefore, it is desirable that subsequent scientific confirmation can further evaluate the harms and benefits of e-cigarettes.

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"All authors have made substantive contribution to this study and/or manuscript, and all have reviewed the final paper prior to its submission."

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