



Editorial

## Synergistic Aggression to the Oral Mucosa: The Emerging Role of Vaping and Alcohol

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In 2020, 377,713 new cases of oral cancer were registered, with 177,757 deaths estimated, acquiring the eighteenth position of the most common malignancies worldwide<sup>1</sup>. This figure reflects a significant public health problem, compounded by the fact that many patients are diagnosed in advanced stages of the disease, which significantly increases morbidity and mortality rates<sup>2</sup>.

Currently, oral squamous cell carcinoma accounts for 90% of oral cancer cases, a statistic that cannot be ignored. These lesions may emerge spontaneously or be preceded by clinical conditions recognised for their malignant potential. However, the risk of progression to neoplasia is not uniform: it varies depending on patient-related factors and the specific characteristics of the lesion. Despite diagnostic advances, tobacco remains a crucial factor in this process, whether smoked or smokeless, by promoting both the development of cancer and the transformation of premalignant lesions<sup>2</sup>.



Consequently, although its oncogenic role is widely demonstrated, traditional consumption of tobacco has followed a downward curve in recent decades. According to data from the National Health Interview Survey, the prevalence of adult smokers in the United States fell from 20.9% in 2005<sup>3</sup> to 11.5% in 2021<sup>4</sup>, a decrease attributed to prevention campaigns, effective health policies, and greater access to cessation programs. This downward trend has been consistent across various population groups, although structural inequalities persist in vulnerable communities. If this trajectory continues, conventional smoking could reach historically low levels, but this does not mean that its impact on oral health has lost its validity<sup>3</sup>.

In contrast, electronic cigarettes (e-cigarettes) or vapes show a worrying upward trend in the adult population of the United States. According to data from the National Health Interview Survey, the percentage of adults using them increased from 4.5% in 2019 to 6.5% in 2023, with a particularly marked increase among young people aged 21 to 24, whose consumption reached 15.5%<sup>5</sup>. This is not a response to a harmless tobacco substitution, but rather to the rapid normalisation of vaping, driven by its attractive presentation and the misperception of lower risk. The growth pattern reveals that e-cigarettes are gaining ground not only among those who have quit traditional tobacco. The rising trend demands urgent public health attention, as vaping, far from being a passing fad, is consolidating as a powerful new vehicle for addiction<sup>5</sup>.

New evidence reinforces this concern: e-cigarette use is not safe for the oral mucosa. Recent studies have shown that exposure to aerosol or liquid from these devices can induce direct DNA damage in oral cells, including adduct formation, oxidative stress, double-strand breaks, apoptosis, and alterations in gene expression. In addition, biomarkers of genotoxicity have been identified in vaping users, such as elevated levels of nitrosamines and acrolein, as well as cellular abnormalities consistent with premalignant processes. Although longitudinal studies are needed to establish a definitive causal relationship, these findings point to vaping as a possible initiating agent in oral carcinogenesis.

In addition, various studies have shown that alcohol not only acts as a chronic irritant to the oral mucosa, but also enhances the carcinogenic effects of other agents such as tobacco or, in current contexts, e-cigarette vapour. Ethanol metabolism produces acetaldehyde, a highly mutagenic compound that directly interferes with cellular DNA, promotes repair errors, and alters the expression of genes involved in cell cycle control. Furthermore, alcohol increases epithelial permeability, facilitating the entry of environmental toxins and carcinogens into deeper layers of the epithelium, thus exacerbating tissue damage. The synergy between alcohol and other harmful agents results in an ideal microenvironment for the development of potentially malignant lesions and their subsequent transformation into cancer, especially in chronically exposed tissues such as the oral cavity<sup>6</sup>.

Despite the accumulation of preclinical evidence pointing to morphological, genetic, and functional alterations in the oral mucosa induced by the use of e-cigarettes, especially when combined with alcohol, the scientific community has yet to respond with the urgency that this phenomenon requires. The early onset of potentially malignant lesions in young individuals, many without a traditional history of tobacco use, poses a new epidemiological pattern that needs to be documented and thoroughly understood. However, the literature still lacks longitudinal studies, detailed clinical records, and case reports that reflect this alarming change. It is imperative to generate knowledge that allows for the construction of solid and contextualised evidence, capable of influencing clinical guidelines, public health policies, and preventive strategies. We cannot wait decades to confirm a suspicion that already shows sufficiently disturbing clinical, histopathological and molecular signs.

Recent developments in the clinical profile of oral cancer suggest a worrying shift: from a disease traditionally associated with older adults and chronic tobacco and alcohol use to an increasingly younger population, without a traditional history of risk, but with ongoing exposure to new aggressors such as e-cigarettes and recreational alcohol. It is an emerging trend, supported by case reports, *in vitro* studies and recent clinical observations, which allows us to propose an epidemiological transition model that warns of three key moments: a classic phase (older adults with cumulative harmful habits), a transition phase (young people exposed to new substances episodically but intensely), and a proactive surveillance phase (based on clinical records, targeted screenings and guidelines adapted to a new reality). This proposal seeks to call attention to the scientific community to recognise, document, and address the changing profile of oral cancer from a perspective of prevention, early detection, and timely intervention.

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