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The influence of tobacco and alcohol in oral cancer: literature review

A influência da associação de tabaco e álcool no câncer bucal: revisão de literatura

Rafaella B. Leite; Ana Carla O. Marinho; Beatriz L. Costa; Maria Beatriz V. Laranjeira; Kleyber D. T. Araújo; Anaícla F. M. Cavalcanti

Universidade Federal do Rio Grande do Norte, Natal, Rio Grande do Norte, Brazil.

ABSTRACT

In Brazil, smoking and drinking are more common in male patients, less frequently affecting female patients. The most diagnosed type of lesion is squamous cell carcinoma. This article aims to understand the literary references associated with the influence of tobacco and alcohol on the development of oral cavity cancer. In order to elaborate an analytical and thematic literature review, using the Literatura Latino-Americana e do Caribe em Ciências da Saúde (Lilacs), Scientific Electronic Library Online (Scielo), US National Library of Medicine National Institutes of Health (PubMed) and Medline databases, articles from the English and Portuguese literatures published between 2007 and 2019 were searched with the help of the terms: *prognostic factors and indicators*, *tobacco*, *alcohol* and *oral carcinoma*. Proper knowledge of the disease and its etiological and prognostic factors should make professionals able to prevent, identify and control oral cancer.

Key words: carcinoma squamous cell; prognosis; tongue neoplasms.

RESUMO

No Brasil, o fumo e a ingestão de bebidas alcoólicas são mais comuns em homens. O tipo de lesão mais diagnosticada é o carcinoma epidermoide. Este artigo tem como objetivo realizar um levantamento das referências literárias já publicadas associadas à influência do tabaco e do álcool no desenvolvimento do câncer na cavidade bucal. Para elaborar uma revisão de literatura, do tipo analítica e temática, utilizamos a Literatura Latino-Americana e do Caribe em Ciências da Saúde (Lilacs), o Scientific Electronic Library Online (Scielo), o US National Library of Medicine National Institutes of Health (PubMed) e o Medline. Nessas bases de dados, foram pesquisados artigos das literaturas inglesa e portuguesa publicados entre 2007 e 2019, com auxílio dos seguintes termos: fatores e indicadores prognósticos, tabaco, álcool *e* carcinoma bucal. *O conhecimento adequado da doença e dos seus fatores etiológicos e prognósticos devem capacitar os profissionais para prevenir, identificar e controlar o câncer de boca.*

Unitermos: *carcinoma de células escamosas; prognóstico; neoplasias da língua.*

RESUMEN

En Brasil, el humo y la ingestión de bebidas alcohólicas son más comunes en hombres. El tipo de lesión más frecuente es el carcinoma. Tuvimos como objetivo hacer un inventario de referencias literarias publicadas acerca de la influencia del tabaco y del alcohol en el desarrollo del cáncer en la cavidad oral. Para la revisión de literatura, de tipo analítica y temática, la búsqueda de artículos en las lenguas inglesa y portuguesa publicados entre 2007 y 2019 se realizó en las bases de datos Literatura Latino-Americana e do Caribe em Ciências da Saúde (Lilacs), Scientific Electronic Library Online (Scielo), US National Library of Medicine National Institutes of Health (PubMed) y Medline, con los siguientes términos: factores e indicadores pronósticos, tabaco, alcohol, *y* carcinoma oral. *El conocimiento adecuado de la enfermedad y de sus factores etiológicos y pronósticos debe capacitar a los profesionales de salud para prevenir, identificar y controlar el cáncer oral.*

Palabras clave: *carcinoma de células escamosas; pronóstico; neoplasias de la lengua.*

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INTRODUCTION

Disorderly growth of cells that invade the mucous epithelial tissue causes malignant neoplasms in the oral cavity; lower lip, tongue and floor of the mouth are the most affected regions[1]. Annually, around 6.4 million cases of malignant tumors are diagnosed worldwide; oral cancer is responsible for 10% of them[2, 3]. In Brazil and the United Kingdom, the squamous cell carcinoma (SCC) accounts for 90%-95% of malignant tumors of the mouth; the association of tobacco and alcohol is the major cause of oral cancer[2, 3].

Tobacco contains more than 70 cancer-causing agents, for example, nitrosamines and polycyclic hydrocarbons, such as benzopyrene[4], which, in contact with the oral mucosa, causes thermal aggression, inducing a chronic inflammation that favors the formation of predisposing lesions[5, 6]. In Brazil, preponderance of smoking changed from 20.2% to 12.8% among men and from 13% to 8.3% among women, between 2006 and 2015. Although there has been a reduction in tobacco use among the general population, it is still linked with the highest cancer rates in the country[2, 7, 8].

Alcohol, in its turn, helps dissolve chemicals in the cigarette, leaving them in high concentration[6, 9]. On the other hand, alcoholism alone is poorly understood as a cause of oral carcinoma; however, associated with smoking, is the most common etiologic form. Evidence of cancer in the oral mucosa emerges from the occurrence of white or red plaques (leukoplakia or erythroplakia); some lesions are asymptomatic[10]. The dental surgeon plays an important role in prevention and diagnosis of this type of disease, as well as treatment and rehabilitation of the affected patient[4, 11].

Treatment is based, in general, on tumor histology, location, and stage, and the patient's physical conditions[12]. Treatment options, either curative or palliative, are divided into these modalities: surgery, radiation therapy, and chemotherapy, or a combination of them[14]. The establishment of a previous diagnosis is essential, because it preserves the individual's functions, besides improving survival[15].

Therefore, knowledge of this disease, with its varied clinical presentations and their consequent implications in the disease course, is fundamental for health professionals dedicated to prevention, early detection, and treatment of head and neck cancer, especially oral SCC. This literature review aims to show the influence of the association between smoking and alcoholism upon the development of oral cancer.

MATERIAL AND METHODS

The originals used in this review were obtained by a search of scientific articles published between 2007 and 2019 and indexed in the databases Literatura Latino-Americana e do Caribe em Ciências da Saúde (Lilacs), Scientific Electronic Library Online (Scielo), US National Library of Medicine National Institutes of Health (PubMed) and Medline, Instituto Nacional do Câncer (Inca) and World Health Organization (WHO). We also conducted searches in books dealing directly with oncology. The words used as key words were: squamous cell carcinoma, precancerous conditions and tongue neoplasms. The choice of books and publications was made with the highest levels of relevance and richness of details; in contrast, those that did not contribute positively for the development of the article were discarded. Inclusion criteria: articles in the Portuguese and English languages addressing the association of tobacco and alcohol in oral cancer, published between 2007 and 2019; articles addressing tobacco and alcohol alone and that did not meet methodologic criteria for the conduction of this study were excluded.

RESULTS AND DISCUSSION

Cancer, tumor and neoplasm are words with close meaning to refer to a group of a hundred diseases that affect any organ, whose common aspect is the rapid excessive abnormal cell replication, inducing the formation of tumors in cells[15-17]. Hence, the human body carefully controls the growth of each type of cell in the body, as insufficient or too many divisions will produce, or not, cancer. This, in turn, is predictable, because tumors are caused by exogenous factors. The exogenous causes of cancer are chemical carcinogenesis, radiation, and specific viruses[18]. One of the main reasons for the development of cancer is the association between smoking and alcohol abuse[19]. Tobacco comes from a plant scientifically named *Nicotiana tabacum*, from which a substance called nicotine is extracted; it is originated from South America and one of the oldest and most commonly used drugs nowadays, in cigarette form[15]. It acts directly reducing users' immune response, leaving them prone to systemic oral diseases[20].

Smoking is considered the chief preventable death cause in the whole world, according to WHO. Researches prove that approximately 47% of the male population and 12% of the female population smoke[15]. Oral cancer and smoking use have a well-established relationship in the world literature[15, 21]. Tobacco use is an independent risk factor for the development of cancer, for it increases the relative risk seven- to tenfold when compared

with a non-smoker. Smoking significantly increases the risk of cancer, however this increase depends on both the amount of daily consumption and the duration of use, being a dose-dependent effect[15, 21]. Around 90% of the patients with mouth or throat cancer smoke cigarettes, cigars, pipes or chew tobacco[15, 22]. The habit of chewing tobacco considerably increases the possibility of developing oral cancer, for the chewing tobacco has formulations with alkaline pH, what eases nicotine absorption through the oral mucosa[15, 21].

Alcohol, in its turn, is the most widely used drug in the world, according to WHO; around 2 billion individuals consume alcoholic beverages[20]. There is no evidence about a specific type of alcohol that is harmful, but the most important etiologic factor is the amount of alcohol consumed[4]. However, there are studies confirming that beer and wine increase the risk of developing cancer[23].

Ethanol is a substance present in almost all beverages; it is not carcinogenic, but, when it is metabolized to acetaldehyde (ethanal), it helps exert multiple mutagenic effects on deoxyribonucleic acid (DNA)[4]. Ethanol increases permeability of the oral mucosa, facilitating the absorption of carcinogenic substances in the epithelial tissue[4, 24], posing detrimental effects to systemic and oral health[20]. Studies suggest that individuals that consume alcohol, but do not smoke, perhaps do not present a risk of oral carcinogenesis[4].

The incidence of carcinogenesis in the oral mucosa of smokers that consume alcohol is high, as alcohol acts as a solvent, and the cigarette, when in contact with the oral mucosa, releases toxins and thermal aggressions when lit[5]. Thus, it causes a decrease in mucosal immunity and, consequently, provides the entry of carcinogenic agents present in tobacco into tissues[25], increasing metabolism of carcinogenic substances, with the resulting increase in prostaglandins and Langerhans cells[4, 23].

Precancerous lesions are neoplasm precursors and divide into leukoplakia and erythroplakia[4, 10].

Leukoplakia, the most common lesion, is six times more frequent in smokers than in non-smokers[4]. It is a lesion with several different aspects: from white or whitish plaques that can be thickened, smooth, corrugated or hardened, or even raised verrucous plaques[10], which occur due to the increased keratin production, enhancing hydration of tissues by saliva, resulting in the whitish aspect. Regarding location, it exhibits predilection for buccal mucosa, ventral surface of the tongue and floor of the mouth; in patients that chew tobacco, the lesion is more common in the buccal mucosa[4].

Erythroplakia is similar to leukoplakia[10]. The difference resides in the velvety red plaques that can easily bleed, as well as in the possible erosions and the surface level with the surrounding mucosa[4]. In this lesion, epithelial changes are atypical, increasing the risk of malignancy[10]; it is considered a high-risk lesion[4]. The patient presents symptoms, with pain and sensitivity at the affected site. In oral erythroplakia, alcohol, smoking and *Candida* infection are etiologic factors of the disease that affect many oral cavity sites; the floor of the mouth is the most common[4].

Ninety-five per cent of cancers of the oral cavity are composed of SCC[10], also called epidermoid carcinoma[26]. It is the most frequent cancer in patients that make use of tobacco and alcohol. Smokers that do not drink present lower risk of manifesting cancer than individuals using both substances associated. SCC tends to affect more males[10] and, according to the National Cancer Institute (NCI) (2004), in relation to age group, 90% of patients with oral SCC were older than 45 years. Clinically, initial manifestation of the cancer resembles much leukoplakia and erythroplakia[10]. Over time, lesions grow rapidly (exophytic) and produce masses or suffer necrosis, forming an irregular and rough ulcer (endophytic), with reddish borders (erythroplakia) or white stains (leukoplakia)[27]. This cancer appears as in situ lesions for containing surrounding areas of atypia or epithelial dysplasia, with more direct sites of metastases – mediastinal lymph nodes, such as lungs, liver and bones[10, 13].

Annually, approximately 6.4 million cases of malignant tumors are counted in the world; 10% of them are oral cancer[26]. In all Brazilian states, 11,200 new cases were expected in 2018 for males, while the incidence for females was 3,500 new cases in the same year[28]. About mortality indices, between 2010 and 2015, among the 6,176 death cases verified, 378 were related with the lips, 1,239 with the floor of the mouth, 1,625 with the palate, and 2,925 with the base of the tongue[29].

The physician and the dental surgeon are responsible for the detailed analysis of the oral cavity, in case the patient presents a symptom that can lead to the diagnosis of oral cancer. It is necessary to verify the palate and the floor of the mouth, besides the interior part of the lips and the cheeks, the posterior part of the throat, lymph nodes and the extension and the lateral areas of the tongue[30].

If the diagnosis is positive for carcinoma, it is fundamental to ascertain the neoplasm stage, to begin treatment. It is also fundamental to verify if carcinogenic cells reached other organs (it is called metastasis when the carcinoma spreads to beyond where it began). Radiograph, computed tomography (CT), magnetic resonance (MR) imaging, and endoscopy are the exams

that can diagnose metastasis. Conversely, in case the diagnosis is negative, but there is continuity of symptoms, it is recommended to refer the patient to an otorhinolaryngologist[30].

The type of treatment depends directly on the size of the primary tumor, the affected region of the oral cavity, and the spread to the cervical lymph nodes. These factors will guide the choice of surgery, radiation therapy, or association of both procedures[19].

Chemotherapy associated with these treatments must be the option of choice in considerably advanced cases, which do not respond positively in its entirety when exposed just to the already cited methods. However, whenever possible, there must be a character of therapeutic protocol[19]. The treatment that has more colateral effects is chemotherapy. Some of them are: oral inflammations, alopecia, appetite loss, hematomas or hemorrhages due to the decrease in platelets, and fatigue due to the decrease in erythrocytes[31]. They affect directly and negatively the patient's quality of life, resulting in non-acceptance of his condition, exacerbated discomfort and shortening of social life[5].

In the anterior region of the oral cavity, lesions are located that present a better prognosis when compared with a similar lesion, but which is located at a more posterior portion. However, even though the affected site is a relevant factor, the clinical stage has a greater influence on prognosis[19].

The mortality and morbidity resulting from this type of cancer makes primary prevention a relevant factor. The major goal of primary prevention is to stop disease progression; to do so, it is necessary to limit the use of tobacco, presenting ways to discourage the habit of chewing it, besides providing stimuli to avoid alcohol abuse. It is also necessary to encourage the patient to adopt a healthier diet, as eating healthy foods lowers the risk of sarcoma[10].

Secondary prevention is the early recognition of malignant disease, so that it is possible to cure it or significantly reduce mortality and morbidity. Lastly, tertiary prevention involves prevention of relapse after a definitive treatment, and thus, reduction of disease-related adversities[10].

FINAL CONSIDERATIONS

The association of tobacco use and alcohol intake is the main cause of oral cancer. By means of the diagnosis of those lesions, we verify that the most frequent types of lesions are leukoplakia and oral SCC, with the tongue being the most affected site. Furthermore, in the literature analysis, no report mentioning alcohol alone was found as a cause of lesions or of any specific type of cancer in the mouth. We also observe that the smoking habit has decreased in Brazil; however, the number of cases of oral neoplasms annually diagnosed in smokers does not follow this reduction.

Dental surgeons should understand and, more than that, take on their role as professionals that have the opportunity to be faced with the initial signs, many times asymptomatic, of mouth cancer. An adequate conduct, aimed at the early diagnosis of those lesions, has impacts on survival and quality of life of the individual with a mouth neoplasm.

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CORRESPONDING AUTHOR

Rafaella Bastos Leite 0000-0002-3304-120X
e-mail: rrafaella_bastos@hotmail.com