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REVIEW

Risk factors and preventive strategies in oral cancer: a comprehensive review

Factores de riesgo y estrategias preventivas en el cáncer oral: una revisión integral

Luis Miguel Quintana Sánchez[1], Yivelin Fernández Queija[1], Lourdes Hernández Cuétara[1]

[1]Universidad de Ciencias Médicas de La Habana, Facultad de Ciencias Médicas "Miguel Enríquez", Departamento de Estomatología General Integral. La Habana, Cuba.

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ABSTRACT

Introduction: oral cancer was identified as a global health problem due to its high morbidity and mortality. This malignant neoplasm, originating in the oral mucosa, affected structures such as the lips, tongue and hard palate, with squamous cell carcinoma being the most prevalent, representing 90 % of the cases. The main risk factors included tobacco and alcohol consumption, with a synergistic effect that facilitated carcinogenesis. Other elements, such as diets low in fruits and vegetables, exposure to radiation, immunosuppression and unfavorable socioeconomic conditions, also contributed significantly. Early detection of premalignant lesions, such as leukoplakias and erythroplasias, was crucial to prevent progression to advanced malignant stages.
Development: the study highlighted that tobacco consumption generated thermal, chemical and systemic damage to the oral mucosa, while alcohol promoted desiccation and immunodeficiency, increasing the risk of oral cancer. In addition, a diet rich in fruits and vegetables offered a protective effect, while excessive consumption of red meat and spicy foods increased exposure to carcinogens. Factors such as the use of ill-fitting dentures, viral infections, especially HPV, and prolonged radiation were relevant. Diagnosis by TNM classification allowed determining prognosis and directing effective treatments.
Conclusions: the article concluded that oral cancer control required a comprehensive approach based on prevention, education, early diagnosis and timely treatment. The active participation of stomatologists in early detection and education of the population was essential. The importance of implementing educational programs and strengthening primary care to reduce risk factors, improve survival rates and guarantee a better quality of life in vulnerable populations was emphasized.

Keywords: Oral Cancer; Risk Factors; Early Detection; Prevention; Squamous Cell Carcinoma.

RESUMEN

Introducción: el cáncer oral fue identificado como un problema de salud global por su elevada morbilidad y mortalidad. Esta neoplasia maligna, originada en la mucosa oral, afectó estructuras como los labios, la lengua y el paladar duro, siendo el carcinoma de células escamosas el más prevalente, representando el 90 % de los casos. Entre los principales factores de riesgo se incluyeron el consumo de tabaco y alcohol, con un efecto sinérgico que facilitó la carcinogénesis. Otros elementos, como dietas bajas en frutas y verduras, exposición a radiaciones, inmunosupresión y condiciones socioeconómicas desfavorables, también contribuyeron significativamente. La detección temprana de lesiones premalignas, como leucoplasias y eritroplasias, resultó crucial para prevenir la progresión hacia estados malignos avanzados.
Desarrollo: el estudio destacó que el consumo de tabaco generó daño térmico, químico y sistémico en la mucosa oral, mientras que el alcohol promovió desecación e inmunodeficiencia, aumentando el riesgo de cáncer oral. Además, una dieta rica en frutas y verduras ofreció un efecto protector, mientras que el consumo excesivo de carnes rojas y alimentos condimentados incrementó la exposición a carcinógenos. Factores como el uso de prótesis dentales mal ajustadas, infecciones virales, especialmente por el VPH, y radiaciones prolongadas fueron relevantes. El diagnóstico mediante la clasificación TNM permitió determinar el pronóstico y dirigir tratamientos efectivos.
Conclusiones: el control del cáncer oral requería un enfoque integral basado en prevención, educación, diagnóstico temprano y tratamiento oportuno. La participación activa de estomatólogos en la detección temprana y la educación de la población resultó esencial. Se enfatizó la importancia de implementar programas educativos y fortalecer la atención primaria para reducir factores de riesgo, mejorar los índices de supervivencia y garantizar una mejor calidad de vida en las poblaciones vulnerables.

Palabras clave: Cáncer Oral; Factores de Riesgo; Detección Temprana; Prevención; Carcinoma de Células Escamosas.

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INTRODUCCIÓN

Oral cancer is a global health problem due to its high morbidity and mortality rates. This malignant neoplasm originates in the oral mucosa, which includes structures such as the lips, mobile tongue, hard palate, and cheeks. These areas are lined with different types of mucosa (masticatory, specialized, and lining), each susceptible to various neoplastic alterations. Squamous cell carcinoma is the most common type, accounting for 90 % of cases.

Among the etiological factors, tobacco and alcohol stand out, whose individual and synergistic effects on the oral mucosa contribute significantly to the development of these neoplasms. In addition, diet also plays an important role; insufficient consumption of fruits and vegetables increases the risk, while a diet rich in these foods acts as a protective factor. Conversely, excessive consumption of red meat and spicy foods is associated with an increased risk of oral cancer.

Other factors include immunosuppression, poorly fitting dental prostheses, infections with viruses such as human papillomavirus (HPV), prolonged solar or ionizing radiation exposure, and certain unfavorable socioeconomic conditions. Genetic predisposition and DNA mutations are also determinants in the onset and progression of oral cancer.

Early diagnosis of premalignant lesions, such as leukoplakia or erythroplakia, is crucial for cancer prevention. If not detected and treated in time, these lesions can progress to malignant states. In addition, tumor staging using the TNM classification (size, lymph node involvement, and metastasis) allows the extent of the disease to be assessed and the prognosis to be determined.

The stomatologist's role in early detection is essential. This professional performs regular oral examinations and educates the population about the warning signs of oral cancer, such as persistent ulcers, red or white lesions, difficulty chewing or swallowing, and changes in tongue or jaw mobility.

A multidisciplinary approach to oral cancer management and the implementation of preventive and educational strategies can significantly improve patient outcomes, reduce mortality rates, and improve quality of life. Therefore, promoting healthy habits and timely access to medical care are essential to address this public health issue.

Objective: to describe the risk factors for premalignant oral cavity lesions present in Bernardo Posse Polyclinic patients.

DEVELOPMENT

Oral cancer refers to malignant neoplasms that develop from the oral mucosa, which includes the following areas:

- Lips and lip corners.
- Cheeks.
- Floor of the mouth and mobile tongue.
- Hard palate.
- Isthmus of the fauces.

Among the types of oral mucosa are the masticatory mucosa, which includes the gums and hard palate; the specialized mucosa located on the dorsal surface of the tongue; and the lining mucosa, which covers the inner surface of the lips, cheeks, vestibules, floor of the mouth, ventral surface of the tongue, and soft palate.

Etiology of oral cancer

Oral cancer is a multifactorial disease in which tobacco and alcohol play a vital role. The consumption of any type of tobacco, including cigarette smoking, is a potential risk factor for oral cancers, causing various effects on the oral mucosa, such as the physical effect of the heat produced by cigarette combustion, a chemical effect associated with the production of carcinogens such as benzopyrene and dibenzo anthracene, and systemic impact that decrease vascular irrigation and cause respiratory alterations. Excessive consumption of alcoholic beverages is also a significant risk factor for its appearance, which also has several effects on the oral cavity, such as drying due to mucosal astringency, the appearance of nitrosamines, and effects associated with liver damage, metabolic depression, immunodeficiency, and the production of secondary metabolites that promote carcinogenesis. Both consumption creates a synergistic effect, as alcohol solubilizes the polycyclic aromatic hydrocarbons from tobacco combustion, allowing them to penetrate the epithelia easily.

Diet Certain nutrients and eating habits are associated with the development of many diseases, such as oral cancer:[22]

- Fats are not linked to oral cancer, but they are related to cancer of the intestine, pancreas, and liver.
- Fruits and vegetables are rich in micronutrients and have an antioxidant and protective effect against oral cancer. Several studies have been conducted on lycopene, a substance found in tomatoes that is released when they are cooked and acts as an antioxidant.[23] There is considerable evidence from clinical studies that a diet rich in vegetables (cruciferous, green, and yellow) and fruits, especially citrus fruits, may prevent the development of these neoplasms due to their rich content of carotenoids, vitamin C, and vitamin E.
- Excessive consumption of red meat fried or cooked with spicy seasonings promotes the development of oral cancer, as they release carcinogenic substances such as heterocyclic amines.
- Immunosuppression: the increase in oral cancer in young people could be explained by the problem of chronic immunosuppression associated with HIV.[24]
- Dental factors: studies support a link between poor dental health, poorly fitting dentures, old dentures, broken or chipped teeth, and the presence of oral cancer.[25,26]

Infection with the human papillomavirus, which is transmitted through sexual contact (specifically HPV type 16), has been

associated with oral cancers. The risk increases with age, is more common in patients aged 50 years and older, and in many countries, is more common in men than women.

A link has been found between bacterial infections and syphilis and syphilitic glossitis, but this is more likely due to the drugs used to treat these conditions, such as arsenic salts or other heavy metals.[13] In relation to fungal infections, it is unclear whether candida is a superinfecting agent of the lesion or a specific agent that causes it.[13]

People with slight skin pigmentation exposed to prolonged occupational sun exposure are at increased risk of developing squamous cell carcinoma of the lip. The lip undergoes a series of pre-neoplastic changes that progress more intensely as the dose of actinic radiation accumulates and as the lip ages. These changes are called actinic cheilitis. If exposure continues, squamous cell carcinoma may eventually develop.[27] On the other hand, a relationship has been found between ionizing radiation and an increased risk of salivary gland neoplasms.[13] Socioeconomic and occupational factors A prevalence of oral cancer has been observed in textile workers, alcohol merchants, printing workers, handlers of phosphorescent material for the manufacture of clock faces, and also in the most disadvantaged social classes and divorced individuals due to malnutrition problems.[27]

Genetics

An associated predisposition is observed in cases of:

- Syndromes (mutations);
- Increased DNA mutations;
- Difficulty in metabolizing carcinogens;
- Difficulty in repairing DNA.[27]

Classification of malignant tumors of the oral soft tissues

Depending on the tissue from which they derive, we find:

Malignant tumors derived from the epithelium

- Squamous cell or epidermoid oral carcinoma (90 %).
- Verrucous carcinoma.
- Spindle cell carcinoma.
- Melanoma.
- Adenocarcinoma, mucoepidermoid carcinoma.
- Basal cell carcinoma.[28,29,30]

Squamous cell carcinoma or epidermoid carcinoma is cancer that begins in the squamous cells found in the skin, lining the body's hollow organs, and in the passages of the respiratory and digestive tracts. It accounts for 4 % of all cancers in the body and 90 % of all oral cavity cancers.[31,32]

Verrucous carcinoma is a type of squamous cell carcinoma that is described separately because of its different behavior. It is less malignant, grows slowly, and is non-invasive.[33,34,35,36,37]

Spindle cell carcinoma comprises a biomorphic tumor that shows foci of squamous cell carcinoma on the surface and spindle cells deeper down. Melanoma is a highly malignant neoplasm of the melanocytes, which is rare but essential because it can be confused with pigmentation of the oral mucosa.[38,39]

Adenocarcinoma, or mucoepidermoid carcinoma, is a cancer that affects the salivary glands. Basal cell carcinoma originates in the deepest layer of the epidermis (basal layer), especially in areas exposed to the sun.[40,41]

Malignant tumors derived from connective tissue.[42,43]

Depending on the connective cells from which they derive, they are divided into:

- Fibrosarcoma: derived from fibroblasts.
- Malignant fibro histiocytoma: derived from fibroblasts and malignant histiocytes.
- Liposarcoma: derived from adipocytes.
- Angiosarcoma: derived from the endothelial cells of blood and lymphatic vessels.
- Neurosarcoma: derived from the covering of peripheral nerves.
- Rhabdomyosarcomas: derived from striated muscle cells.
- Leiomyosarcomas, which are derived from smooth muscle cells, are rare in the oral cavity.

Metastasis in the soft tissues of the oral cavity:[44]

These are rare in the oral mucosa since of all the neoplasms in the body, only 1% metastasize to the oral mucosa, 90 % to the jaw bones, and 10 % to the soft tissues. Primary tumors are usually located in the lung, kidney, and liver.

Neoplasms of the immune system with oral involvement:[45,46]

- Non-Hodgkin's lymphoma: a neoplasm of lymphocytes and their precursors.
- Multiple myeloma: a malignant hematological neoplasm with the proliferation of plasma cells and multiple bone marrow involvement.

Clinical manifestations of oral cancer

Oral cancer, in its most common clinical manifestation, squamous cell carcinoma, can develop in one of two ways:[47,48]

- "De novo," developing directly from healthy mucosa.
- Following the sequence: premalignant lesions and states (epithelial dysplasia)-carcinoma.

Approximately 50 % of squamous cell carcinomas develop on a previously altered epithelium. We understand a precancerous lesion to be morphologically altered tissue in which the appearance of cancer is more likely than in its standard counterpart.[49]

- Leukoplakia: Any whitish patch or plaque that cannot be removed by scraping cannot be classified clinically or histopathologically as another entity.
- Erythroplakia: Any erythematous patch or plaque that cannot be removed by scraping and cannot be characterized clinically or histopathologically as another entity.
- Inverted smoker's palate: These are whitish-red lesions that appear on the palatal mucosa of patients who have a habit of smoking with the flame directed inward.

Premalignant states are general conditions or diseases associated with an increased risk of cancer in any location of the body:

- Lichen planus: This chronic inflammatory mucocutaneous condition is characterized by very itchy lesions with a marked autoimmune character.
- Nevus: These are limited formations of skin and mucous membranes associated with deposits of melanocytes in the different layers of the epidermis and dermis.
- Atrophic mucous membranes: These conditions are characterized by structural defects in the quality and quantity of the mucous lining of the oral cavity, which makes it more susceptible to the action of carcinogens.
- Oral papillomatosis: This is a rare condition of the mucous membrane of the oral cavity consisting of multiple confluent and exuberant projections with a broad base resembling cauliflower. Many consider it a premalignant condition, and others consider it a variant of verrucous carcinoma.
- Submucosal fibrosis: This is a rare alteration of the mucosa of the mouth characterized by epithelial atrophy accompanied by hardness or stiffness of the submucosa and a particular discoloration.
- Actinic cheilitis: This inflammatory reaction of the mucosa and submucosa of the lips is associated with excessive exposure to solar radiation.[50,51,52]

The potential for malignancy of these conditions, known as "premalignant lesions and conditions," is determined by the presence of epithelial dysplasia, which is understood as a variable combination of a series of microscopic phenomena indicative of a disorder of epithelial maturation and an alteration in cell proliferation. In the biology of tumor growth, four well-defined phases can be distinguished:

1. Malignant alteration of the target cell: transformation.
2. Growth of the transformed cells.
3. Local invasion.
4. Metastasis.[53,54,55,56,57]

The size of the tumor depends on the production/loss ratio. The more cells there are in the division, the greater the sensitivity to chemotherapy. The growth of transformed cells is carried out thanks to blood vessels, which, on the one hand, release growth factors and growth factor-releasing cells and, on the other hand, serve as a source of nutrition. Local invasion depends on the aggressiveness and malignant potential of the tumor. Cancer appears through the malignant transformation of a single cell. Over time, "tumor heterogeneity" will occur, which refers to the appearance of subclones with different phenotypes from the original cell, giving rise to various cell types. Tumor metastasis can be summarized as follows:[58,59,60]

e. Invasion of the extracellular matrix.
f. Circulation through the bloodstream.
g. Secondary deposits in distant sites.

Based on the similarity or lack of similarity to the Malpighian epithelium from which they derive, oral carcinomas can be classified into three grades:

- Well differentiated: Histologically, they are very similar to the Malpighian squamous epithelium from which they derive. The tumor cells retain the ability to form keratin, forming pearls or horny globules within well-defined limits. Mitosis is moderate, and there is slight cellular atypia. A peritumoral infiltrate frequently appears.
- Moderately differentiated: The number of mitoses increases, and cell keratinization decreases, with corneocytes no longer forming and cells keratinizing in isolation. The tumor infiltrate decreases.
- Poorly differentiated or undifferentiated: Keratoblastic activity disappears. Cell clones lose their resemblance to the cells they derive, and intercellular adhesion breaks down, facilitating metastasis.[61,62,63,64]

The most common clinical finding in the oral cavity is a hardened ulcer with everted edges that is sometimes painful and is usually accompanied by cervical lymphadenopathy. In more advanced stages, squamous cell carcinoma can present in three clinical forms:

- Endophytic morphology: forming an irregular ulcer with everted edges and a dirty base.
- Exophytic morphology: vegetative tumor growth, irregular and indurated on palpation.
- Mixed type: formed by a combination of the two previous forms.

Diagnosis of oral cancer[55,56,57,60,62]

The warning signs of oral cancer that dentists and patients should look out for during oral examinations or self-examinations are ulcers that do not heal, persistent red or white lesions, lesions that bleed easily, difficulty chewing or swallowing, and difficulty moving the tongue or jaw. Pain and irritation may or may not be present in early lesions.

To facilitate clinical and therapeutic follow-up of patients, the TNM classification is used: T (size of the primary tumor); N (presence of lymph nodes); M (distant metastasis). In more detail, the corresponding subdivisions are:

a. T1: Tumor less than or equal to 2 cm; T2: Tumor greater than 2 cm but less than 4 cm; T3: Tumor greater than 4 cm; T4: The tumor invades adjacent structures.

b. N0: No lymph node metastasis; N1: Metastasis in a homolateral lymph node less than or equal to 3 cm; N2a: Metastasis in a homolateral lymph node greater than 3 cm but less than 6 cm; N2b: Metastasis in multiple homolateral lymph nodes, less than 6 cm; N3. Metastasis in a lymph node greater than 6 cm.

c. M0: No distant metastasis; M1: Distant metastasis. The most important survival factor is the disease stage at diagnosis. In practical terms, tumor staging is established as follows:

- Stage 1: T1 M0 N0.
- Stage 2: T2 M0 N0.
- Stage 3: T3 N0 M1; T1 N1 M0; T2 N1 M0; T3 N1 M0.
- Stage 4: T4 M0 N0; Tx M2-3 N0; Tx Nx M1.

Stages I and II encompass the initial period, during which the survival rate is usually high, while stages III and IV represent the advanced stages of the disease, during which the prognosis worsens dramatically.[63,64]

Functions of the stomatologist: The treatment of cancer patients is multidisciplinary, and it is more aggressive and less conservative the later the disease is diagnosed.

1. Perform a comprehensive oral examination of all individuals requesting stomatological services.
2. Record the stomatological visit and PDCB examination in the patient's medical record.
3. Perform a comprehensive oral examination at least once a year on all patients aged 35 and over who live in the area covered by the service.
4. Examine the population of assigned nursing homes annually.
5. Refer all patients suspected of pre-neoplastic or malignant lesions of the oral complex to the Maxillofacial Surgery consultation and fill out the front of the referral form to the Maxillofacial Surgery Service.
6. Provide dispensary care and follow-up on all patients aged 15 years and older referred to Maxillofacial Surgery.
7. Actively collaborate in locating patients who do not attend their Maxillofacial Surgery appointments.
8. Actively participate in scientific activities to improve the quality of oral cancer control measures.
9. Actively participate, in coordination with mass organizations, in the educational tasks of the Program and advise the Family Physician on the examination and pathologies of the oral complex.
10. Comply with the established procedures for filling out the Statistical System forms.
11. Provide priority dental treatment to patients referred with oral cancer, premalignant lesions, or who have received cancer-specific treatment.
12. Refer all patients confirmed with benign, premalignant, and malignant lesions of the oral complex for risk factor control, prioritization of prosthetic rehabilitation, and annual follow-up.
13. Participate in the discussion of deaths from oral cancer.

The dentist's fulfillment of this responsibility will increase the survival rate for our patients and significantly reduce global morbidity and mortality ratesl.[65,66,67]

CONCLUSIONS

Oral cancer is a complex and multifactorial disease that poses a significant challenge to public health due to its high prevalence, mortality, and predisposing risk factors. This article has highlighted several key aspects of oral cancer's etiology, risk factors, diagnosis, and management, emphasizing the importance of multidisciplinary and preventive action for its effective control.

Among the most prominent risk factors are tobacco and alcohol use, which together enhance carcinogenesis by facilitating the penetration of carcinogens into oral tissues. In addition, poor dietary habits, such as excessive consumption of red meat and lack of fruits and vegetables, also increase the risk. Factors such as immunosuppression, viral infections, poor dental health, and prolonged exposure to solar or ionizing radiation contribute significantly to the development of this disease.

Squamous cell carcinoma remains the most common type of oral cancer, and its incidence is associated with conditions such as leukoplakia, erythroplakia, and premalignant states such as lichen planus or submucosal fibrosis. Early detection of these lesions is essential to prevent progression to advanced malignant stages. However, late diagnosis remains a significant obstacle, as advanced stages of oral cancer have a considerably worse prognosis.

The role of the stomatologist is crucial in this context. In addition to performing regular examinations for early detection, their active participation in educating the population about warning signs and risk factors is essential to promote prevention. TNM classification and tumor staging are indispensable tools in diagnosis and management, allowing prognosis to be determined and effective therapeutic strategies to be designed. This article highlights the importance of implementing educational programs that encourage healthy lifestyles and promote the reduction of risk factors, especially in vulnerable populations. It also underscores the need to improve access to primary and specialized care services, strengthening intersectoral collaboration between health, education, and other agencies. In conclusion, oral cancer control requires a comprehensive approach that combines prevention, education, early diagnosis, and timely treatment. Only through concerted and sustained action will it be possible to reduce the burden of this disease, improve survival rates, and ensure a better quality of life for affected patients.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORSHIP CONTRIBUTION

Conceptualization: Luis Miguel Quintana Sánchez, Yivelin Fernández Queija, Lourdes Hernández Cuétara.
Data curation: Luis Miguel Quintana Sánchez, Yivelin Fernández Queija, Lourdes Hernández Cuétara.
Formal analysis: Luis Miguel Quintana Sánchez, Yivelin Fernández Queija, Lourdes Hernández Cuétara.
Research: Luis Miguel Quintana Sánchez, Yivelin Fernández Queija, Lourdes Hernández Cuétara.
Methodology: Luis Miguel Quintana Sánchez, Yivelin Fernández Queija, Lourdes Hernández Cuétara.
Project management: Luis Miguel Quintana Sánchez, Yivelin Fernández Queija, Lourdes Hernández Cuétara.
Resources: Luis Miguel Quintana Sánchez, Yivelin Fernández Queija, Lourdes Hernández Cuétara.
Software: Luis Miguel Quintana Sánchez, Yivelin Fernández Queija, Lourdes Hernández Cuétara.
Supervision: Luis Miguel Quintana Sánchez, Yivelin Fernández Queija, Lourdes Hernández Cuétara.
Validation: Luis Miguel Quintana Sánchez, Yivelin Fernández Queija, Lourdes Hernández Cuétara.
Visualization: Luis Miguel Quintana Sánchez, Yivelin Fernández Queija, Lourdes Hernández Cuétara.
Writing – original draft: Luis Miguel Quintana Sánchez, Yivelin Fernández Queija, Lourdes Hernández Cuétara.
Writing – review and editing: Luis Miguel Quintana Sánchez, Yivelin Fernández Queija, Lourdes Hernández Cuétara.

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