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Oral cancer, potentially malignant disorders and prevention: an integrative review

Câncer bucal, desordens potencialmente malignas e prevenção: uma revisão integrativa

Cáncer bucal, desórdenes potencialmente malignas y prevención: una revisión integrativa

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Lucas Soares Fernandes Aires Furtado[1]
Jorge Luiz Alencar Miranda Sales[2]
Natasha Muniz Fontes[3]
Mara Ilka Holanda de Medeiros Batista[4]
Alessandra Albuquerque Tavares Carvalho[5]
Marcília Ribeiro Paulino[6]

This study aimed to carry out an integrative review about oral cancer. Articles were searched in PUBMED (descriptors in English), SCIELO and BVS (Portuguese descriptors) databases. The articles considered were from 2008-2018, in a total of 33 articles, two epidemiological bulletins and a reference book. The productions were divided into three thematic areas, namely: general aspects on oral cancer; potentially malignant disorders and the importance of early diagnosis; and, prevention strategies for oral cancer. The increased incidence of oral cancer sets the disease as a public health problem. The strategy for cases reduction is directly related to the knowledge and control of risk factors for developing the disease, as well as the early diagnosis. The dentist is the responsible for the early diagnosis of oral cancer, the population guidance on habits, risks and preventive actions and health promotion. It is necessary further training of professionals for prevention and recognition of lesions aiming the appropriate intervention.
Descriptors: Mouth neoplasms; Diagnosis, Oral; Erythroplasia; Leukoplakia.

Este estudo teve como objetivo realizar revisão integrativa sobre o câncer bucal**.** Os artigos foram pesquisados nas bases de dados PUBMED (descritores em inglês), SCIELO e BVS (descritores em português). Foram considerados artigos de 2008-2018. Foram considerados 33 artigos, dois boletins epidemiológicos e um livro de referência. As produções foram divididas em três áreas temáticas a saber: aspectos gerais sobre o câncer bucal; desordens potencialmente malignas e a importância do diagnóstico precoce; e, estratégias de prevenção voltadas para o câncer bucal. O aumento da incidência do câncer bucal configura a doença como problema de saúde pública. A estratégia de redução dos casos está diretamente relacionada ao conhecimento e controle dos fatores de risco para o desenvolvimento da doença, bem como ao diagnóstico precoce. O cirurgião dentista é responsável pelo diagnóstico precoce do câncer bucal, orientação da população sobre hábitos, riscos e realização de ações preventivas e promoção da saúde. É necessária maior capacitação dos profissionais para prevenção e reconhecimento das lesões visando a intervenção adequada.
Descritores: Neoplasias bucais; Diagnóstico bucal; Eritroplasia; Leucoplasia.

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Descriptores: Neoplasias de la boca; Diagnóstico bucal; Eritroplasia; Leucoplasia.

1. Dentist. Juazeiro do Norte, Ceará, Brazil. ORCID: 0000-0003-0774-7927 E-mail: lucassoares.f@hotmail.com
2. Dentist. Juazeiro do Norte, Ceará, Brazil. ORCID: 0000-0003-2752-5299 E-mail: jorge-amando@hotmail.com
3. Dentist. Specialist in Orthodontics. Specialist in Dentistry. Master's in Orthodontics. Professor at the Catholic University Center of Quixadá, CE, Brazil. ORCID: 0000-0002-0502-0364 E-mail: natashafontes@hotmail.com
4. Dentist. Specialist in forensic dentistry. Master's in Forensic Expertise. PhD in dentistry. Professor at the of Dentistry course of the University Center of João Pessoa, PB, Brazil. ORCID: 0000-0002-7314-0595 E-mail: marailka@hotmail.com
5. Dentist. Doctorate in Dentistry. Professor of the Pos-Graduation in Dentistry, Federal University of Pernambuco (UFPE0, Recife, PE, Brazil ORCID: 0000-0003-0390-3611 E-mail: alessandra.atcarvalho@gmail.com
6. Dentist. Master's in Dentistry. Doctorate student in Dentistry at UFPE. Professor at the University Center Dr. Leão Sampaio, Juazeiro do Norte, Ceará, Brazil. ORCID: 0000-0002-3924-4251 E-mail: marcilia.paulino@yahoo.com.br

INTRODUCTION

Oral cancer (OC) is a multifactorial disease resulting from the interaction of genetic and environmental factors. Factors such as alcohol abuse, smoking and ultraviolet radiation are well elucidated on the oncogenic action; but human papilloma virus (HPV) infection and diet are subject of further studies to establish its association with neoplasia[1,2].

Squamous cell carcinoma (SCC) of head and neck is a malignancy that affects the sites of the oral cavity, such as lip, tongue, palate, floor and the gingival edge and the oropharynx. Among the types of malignancies involving the craniofacial region, this corresponds to 90-95%, causes about 130,000 deaths worldwide each year, configuring itself as a public health problem[1,3,4].

The process of carcinogenesis is complex and difficult to identify in the early stages, however, there are lesions said as malignant or potentially malignant that are revealed, in some cases, as the first clinical conditions of this process. The main premalignant lesions are leukoplakia, erythroplakia, actinic cheilitis and lichen planus, with the latter having its malignant potential not clearly established yet and, for some studies, there is no relationship with the OC[5,6].

Strategies towards the intervention for the risk factors, as well as the clinical examination by the qualified dental surgeon (DS), together with the patients' orientation, are seen as the best ways to reduce the incidence and morbidity and mortality of the disease[7]. Diagnosis of precursor disorders or cancer in early stages allows a better prognosis and treatment with less invasive procedures and with lower mutilation, with greater survival[8].

In Brazil, the Primary Health Care (PHC), represented by the Family Health Strategy (ESF) is established as the gateway of patients in the Unified Health System (SUS), and with regard to assistance to cancer patients, control actions, health promotion, early diagnosis and support to the needs of the patients in treatment are promoted. These actions are developed by the multidisciplinary team and, above all, the oral health team[9]. In this context, this study aims to conduct an integrative review of the literature on oral cancer.

METHOD

This is an integrative review whose method allows synthesize results from research on a topic or issue in a systematic way, orderly and comprehensive, providing further information on a subject/issue[10].

For this work, the electronic databases of the Virtual Health Library (VHL) and Scientific Electronic Library Online (SciELO) were accessed using the search terms in Portuguese, in addition to the US National Library of Medicine platform (PUBMED), whose search terms were searched in English, as table 1.

Table 1. Search terms by databases and language. Juazeiro do Norte/CE, 2018.

VHL and SciELO (Portuguese)	PubMed (English)
Diagnóstico de câncer bucal	Oral cancer diagnosis
Lesões orais potencialmente malignas	Potentially malignant oral lesions
Leucoplasia	leukoplakia
Eritroplasia	erythroplakia
Quelite actinica	actinic cheilitis
Líquen plano	lichen planus

Articles published from 2008 to 2018 were considered, available for full reading (free access). Portuguese language and type of documents "article" for the VHL and SciELO databases were used as additional filters. For the database PUBMED used the additional filter "article" for the types of documents sought.

From that point, all the titles and abstracts of the registers found were read, the items whose thematic relevance was established by reading the title and abstract

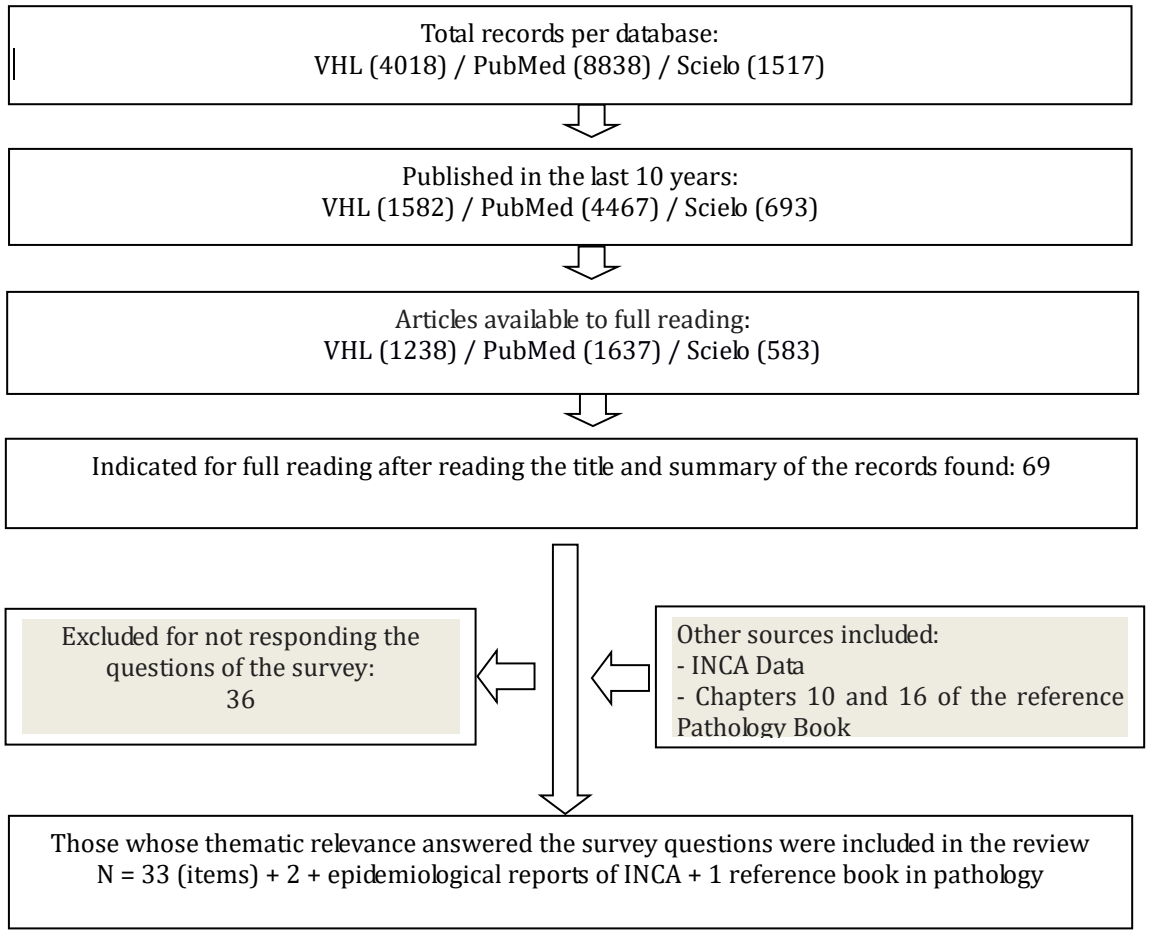
were selected for full reading. The articles read in full that responded to the survey questions were part of the literature review.

Data from the National Cancer Institute (INCA) were also considered and the book Neville Oral and Maxillofacial Pathology. - 4th Ed 2016 was used, as it is a theoretical reference regarding this issue. Articles of opinion, theses, dissertations and case reports were excluded from the review. The search strategy is detailed in Flowchart 1.

RESULTS

The flow chart 1 shows the documents considered in the study, which included 33 articles, 2 epidemiological bulletins and a reference book. In turn, these productions were divided into three thematic areas, namely: general aspects of oral cancer; potentially malignant disorders and the importance of early diagnosis; and, prevention strategies for oral cancer.

Flowchart 1. Methodological research design. Juazeiro of the North / EC, 2018.



DISCUSSION

General aspects of oral cancer

The malignant tumors of the oral cavity located in the lips, oral cavity, salivary glands and oropharynx are regarded as malignant tumors. The terms mouth cancer or oral cancer are also used. There is a strong association of CB with the socioeconomic status of people living in the social risk areas[11].

Multicenter studies show that the CB has increasing rates around the world and especially in developing nations. Data indicate that 60% of new cases occur in these countries, at about 275,000 every year[9]. Surveys show that direct exposure to risk factors such as alcoholism and smoking, associated with social vulnerability factors, directly contribute to the increased incidence of malignancies, among them the squamous cell carcinoma[12].

At about 90% of head and neck cancers are represented by epithelial tumors of the squamous cell carcinomas (SCC), which

has a very aggressive behavior, other types are distributed in salivary glands cancer, melanomas, osteosarcomas and non-Hodgkin lymphomas[3 13].

The risk factors most commonly associated with the development of oral cancer, which can be modified, are tobacco, alcohol and solar exposure[1]. The consumption of alcohol and smoking increases the risk of potential form depending on the quantity used, and are related to more than 80% of the cases, being considered as synergists in enhancing the risks[1,12].

Chronic alcoholism is one of the risk factors for the development of oral cavity cancer; however, the phenomena involved in the biological commitment generated by alcohol are poorly understood. It is estimated that alcohol has the ability to stimulate epithelial cell proliferation as well as change their maturation process. Other changes such as the decrease in DNA repair, immune and nutritional disorders can contribute in their relationship with the development of the CB14.

There is also evidence that smoking and alcohol consumption may influence the results of anticancer therapies. Smokers may be less likely to respond to treatment if they consume tobacco, resulting in lower survival rate, and has a greater chance of suffering from side effects of the drugs used, while patients continuing to consume alcohol appear to have a higher risk of recurrence and or to evolve with metastasis[15].

Some epidemiological studies relate the participation of HPV in the process of oral oncogenesis, particularly type 16, which, in many cases, may be associated with squamous cell carcinoma of the oral cavity and oropharyngeal, especially among young people and the non-smoking ones[16].

With regard to the epidemiology of the disease, there is prevalence for males, in a ratio of 2:1 with the female, being the fifth and sixth decades of life the age groups with the highest incidence[17]. Studies indicate that the most affected by the CEC are lip (40%), tongue (20%) mouth floor (16%), RetroMolar trigone (7%) and gum (6%)[18].

The risk profile for oral cancer is associated with smokers, drinkers, with a history of chronic exposure to ultraviolet rays, either by work activities or high incidence regions, linked to the lack of protection and social factors of frailty, such as low income, poor access to health services and low education level[19,20,21].

CB is about 3% of all cancer cases in world.[4]. The most recent epidemiological record regarding the CB in Brazil comes from INCA's research bases. It is estimated 11,200 new cases of oral cancer in men and 3,500 in women for each year of 2018 and 2019, being the 5th most common cancer in men and the 12th most common among women[22].

The diagnosis can be facilitated by anatomical features of their own oral cavity that favors the direct visualization of the structures, eliminating the need of more complex instruments and generating minimal or no discomfort to the patient during the examination[2,23].

However, the diagnosis of this cancer has been performed later, resulting in high rates of morbidity and mortality of this condition and the institution of more invasive therapies for patients[24]. Failures in professional training, lack of continuing education and/or qualification of the dentist, contribute to this picture, since this professional is the most responsible agent in the early diagnosis and the formulation of actions to health promotion[23].

Late diagnosis of CB leads to a poor prognosis with a higher degree of mutilation therapies, causing deformities and even death cases, in addition to high social and economic cost[25]. That is the reason cancer is considered as a public health problem and it is up to the dentist to act directly in actions aimed at prevention and diagnosis of the cases[13].

Potentially malignant disorders and the importance of early diagnosis

The World Health Organization (WHO) in 2005 changed the term referring to the pre cancer lesions, calling the lesions with malignant potential or DPMs that set up as tissue changes with potential for transformation into malignant neoplasms over, with leukoplakia, the Erythroplakia,

actinic cheilitis and lichen planus[26] fitting this classification. They appear as changes in the epithelium lining the oral cavity, with leukoplakia being the most frequent lesion[5].

Leukoplakia is a predominantly white plate-shaped lesion of the oral mucosa, non-detachable to scraping, which cannot be identified clinically or histologically as any other lesion[27]. The injuries that most commonly make differential diagnosis with leukoplakia are: lichen planus, leukoedema, frictional keratosis, white spongy nevus and morsicatio[5].

Leukoplakia, regarding surface, presents it surface as smooth shape, rough or verrucous. The more committed intraoral sites are the buccal mucosa, lip commissure, buccal floor, tongue, palate and alveolar ridge. The malignant potential can vary from 0 to 20%, with an average of 5%[26.28]. There are no specific histological findings for leukoplakia; so, the diagnosis is made by exclusion of other changes that appear morphologically similar to it[26].

The main factors that support leukoplakia to be considered precursor of oral carcinoma is their presence in the tissue surrounding tumors with dysplastic changes in buccal epithelium in longitudinal studies[29]. The main factor associated with the development of this DPM is tobacco; however, other factors are recognized, such as alcohol, radiation, trauma and microorganisms such as HPV[1].

Any region of the oral cavity can be affected by leukoplakia; however, tongue and mouth floor lesions, for being the most affected areas for oral cancer, require a more careful look by the surgeon dentist[5].

Clinically, leukoplakia can be classified as homogeneous, granular, verrucous and proliferative verrucous. When in the presence of histologic diagnosis of dysplasia it is classified according to severity, as follows: mild, moderate and severe epithelial dysplasia, when all the epithelium is involved uses the term used is carcinoma in situ[27].

The conduct facing these conditions depends on the biopsy and histopathologic diagnosis. Mild to moderate dysplastic lesions may be periodically monitored, along with the guidance regarding the withdrawal of tobacco use by the patient. The severe lesions and carcinoma in situ are indicated to total removal, through total ablation, cryosurgery, electrocautery and periodic longitudinal monitoring[26].

Erythroplakia, another DPM, is described as an oral epithelial tissue change, presenting itself in a plate form or reddish-colour macula that cannot be identified histologically as other lesion[29]. Erythroplakia may be associated with leukoplakic areas being called leucoeritroplasia. Despite having less effect than leukoplakia, it has a greater malignancy rate, around 14 to 50%. In addition, in 90% of the cases, it is characterized as moderate or severe dysplasia[26].

The real erythroplakias often have major epithelial dysplasia, in situ carcinoma or invasive squamous cell carcinoma. The pathogenesis of Erythroplakia remains elusive, but it is assumed that it is associated with the same causes of CEC[29]. Histologically, the affected epithelium may present lack of keratin layer, atrophy and hyperplasia, the absence of keratin layer exposes the microvasculature of the tissue giving it a reddish appearance, often painful[27].

Actinic cheilitis, also known as actinic lip keratosis, is also part of the group DPM, its malignant capacity occurs because of prolonged and continuous exposure to sunlight, specifically ultraviolet radiation, primarily affecting the lower lip; however, tobacco is also a factor related to its etiology[30].

The inflammatory process generated by sun overexposure and chronic, with no protection, causes injuries that can be white, red, desquamative and ulcerated. Clinically, healing processes that alter the boundary between the skin and lip rouge can be identified, with the malignization rate of these lesions ranging from 10 to 20%[31].

The actinic cheilitis has a predilection for males, aged 40-50 years and presents chronic evolution, which leads some patients to not showing the initial changes, whose clinical aspect can be observed by the edge of the atrophy of the lower lip vermilion, with whitish patches of smooth surface. With the

evolution of the injury, rough and desquamative areas appear[23].

Histologically, actinic cheilitis has an atrophic stratified squamous epithelium, with great production of keratin, there is epithelial dysplasia, presence of chronic inflammatory infiltrates and collagen fibers changes occur generated by the ultraviolet light[5]. The treatment protocol of actinic cheilitis is since topic local actions as, lip sunscreen (to prevent progression) to surgical treatments for injuries to the presence of malignancy, such as vermilionectomy, which is a procedure by which is carried out the excision of the red part of the lip and/or affected parts affected by ulcerations[26,32].

With regard to lichen planus (LP), studies have been conducted in order to assess a possible relationship between this lesion and oral cancer, some showing evidence of there being a probability of up to 6.51% of Lichen planus alone suffer malignization along the years, that is why WHO classifies the LP as a potentially malignant condition[17].

Lichen planus is a chronic skin disease that often affects the oral mucosa, and presents itself in two forms, reticular and erosive, and its prevalence of 0,1 to 2,2% in population[5]. Reticular Lichen planus is characterized by the presence of white crossing streaks (Wickham striae), which may also be presented in the form of a papule.

The erosive form is symptomatic, with ulcerated areas being clinically observed. Currently, the malignant potential remains undefined, with disagreement in the literature because of few studies showing this condition associated with the CB[27]. The studies that show the lichen planus malignant transformation into squamous cell carcinoma are related to erosive form, so that the atrophic epithelium may be susceptible to carcinogen agents[5].

Several factors contribute to low rates of early diagnosis of DPM, such as the absence of symptoms in patients, imprecise location of the lesions, poor performing of diagnostic tests, low level of population's knowledge about the disease and the risk factors, in addition to few educational activities that address the risk factors for oral cancer[12].

One of the best strategies to prevent oral cancer is early detection of premalignant oral lesions and prevention of its neoplastic transformation[33]. The current dentistry should be geared not only to cure diseases, but also for their prevention, through health strategy promotion[13]. However, if the injury is developed, the treatment will vary according to clinical staging, establishing surgical treatment, radiotherapy and chemotherapy, associated or isolated[33].

Prevention strategies towards oral cancer

In Brazil, INCA[22] estimated 14,700 new cases of oral cancer from 2018 to 2019. These data is growing, making oral cancer a public health problem that needs more effective action to its control[8,9]. It is known that socioeconomic status and the possibility of access to health services influence the variation in the incidence of CB in the world, as in developed countries the incidence rates and mortality resulting from CB are smaller than in developing countries[34].

Early diagnosis and education activities aimed at the population and, especially, the risk group represent effective strategies to reduce the incidence of DPM and the emergence of carcinomas[7]. The direction carried out by qualified professionals fosters the acquisition of protection habits and encourages individuals to seek appropriate assistance before oral changes that may arise and be identified[2].

From the National Oral Health Policy it was determined that the FHSs next to oral health services institute prevention and control actions of oral cancer, aiming to carry out detection tests routinely in the health unit in home visits and health campaigns, track cases suspected and confirmed guaranteeing the system of reference and counter reference, establish partnerships for diagnosis and prevention and health education measures with universities and research centers[9].

In addition, specialized dental clinics (CEO) compose frames of reference and counter reference with the Family Health Units where patients should be welcomed,

guided and directed according to their needs and case complexity[35].

For this to be possible, skills geared towards the management of the CB must be incorporated into the dentist's training, such as knowledge of the disease (incidence, lesions with malignant potential, diagnostic techniques and rehabilitation, monitoring of patients on therapy) and the development of educational activities for the population[19,25].

Among strategies that should be adopted by the oral health teams, there are: the completion of the clinical examination, guidance of self-examination, health promotion, identification of suspected cases and referral to services with high level of complexity to define the diagnosis, as well as follow-up of cases in treatment[36].

The visual-tactile examination, which involves palpation and inspection of the oral cavity, is the precursor oral lesion screening maneuver most commonly used, the management is made easier by direct access to the oral structures, it does not depend on devices and instruments of greater complexity, has high specificity, at about 98%[7]. The test is noninvasive, inexpensive, and its effectiveness depends on the professional experience, their knowledge and clinical experience, setting up as a secondary prevention approach, which can increase the chances of patients' healing in up to 90%[12].

With regard to self-examination, from a clear professional guidance, timely and the individual's perception of the acquisition of healthy habits, it favors the adherence to prevention and search measures for health care in the early stages of the disease[37]. The mouth self-examination routinely adopted by the individuals becomes a self-care action, enables the identification of changes in the oral cavity at an early stage and, therefore, the search for professional care[36].

The self-examination, the disclosure of the determining factors for the emergence of oral cancer and the clinical examination of the cavity performed by a trained professional, are measures that should be adopted and encouraged by professionals and institutions linked to primary health care, through well-structured and interconnected tools, as isolated actions and campaigns of little consistency do not generate satisfactory and replicable results[36].

Professional training is a primary intervention measure in the CB issue, it must be strengthened at all levels, especially at graduation, giving the surgeon dentist knowledge to promote health in the population, working in clarifying the disease, acquisition of protective measures and early diagnosis, as well as the formulation and articulation of public policies aimed at this pathology[2,19].

Health education measures should also be directed to the community, the dissemination of information of the determinants of oral cancer, such as risk factors, harmful habits, diet and lifestyle must be addressed and clarified for the inclusion of self-care and prevention[37]. Conducting periodic campaigns, dissemination in the media and the guidance given to patients are very well accepted maneuvers[7].

Other factors that corroborate the need for investment in health promotion, especially in the acquisition of healthy habits and knowledge by the population, are given by the characteristics of oral cancer, which in the early stages do not show symptoms. Another factor is the low demand for dental services for check-ups, contributed to the late diagnosis in which treatment becomes costly and with poor prognosis[37].

Faced with this panorama, and because of the rates of new cases of oral cancer that are increasingly greater each year, treatment costs are high and quality of life of patients during and after treatment is significantly compromised, the development of public policy health should include actions on professional-staff community-triad, the agreement between the severity of the disease and the need for intervention should guide the execution of more effective policies[36].

The oral cancer is a malignant neoplasm that affects the oral cavity tissues, with greater preference for the tongue, floor of the mouth and inferior lip, with lesions that may be their precursors, such as leukoplakia, erythroplasia, actinic cheilitis and Lichen

planus, changes that can be controlled, which can be managed with less invasive procedures, and in the context of potentially malignant lesions, should be addressed in conjunction with preventive and educational actions[26].

The most qualified professional to carry out prevention and early diagnosis of CB is the dentist; however, aspects such as failures in the training process can result in difficulty of working preventive actions and the formulation of health education strategies aimed at risk groups[11].

In a study to assess the level of knowledge of 70 surgeons dentists about oral cancer, through the use of questionnaires, it was evident that most of the sampling had adequate knowledge about the disease; however, they reported difficulty in transmitting information to patients[2].

Other research also focused on the knowledge of professionals about oral cancer elucidated other deficiencies in the conduct of professionals, such as: lack of early diagnosis, work failures as a team, few importance of the population for the health selfcare, miscommunication between professionals of different levels of attention[36].

Similarly, another study with questionnaires applied to dentists revealed that 69.5% of them do not feel confident to perform diagnostic maneuvers of oral cancer, and in addition, only 3.7% of respondents had adequate knowledge about this neoplasia[24].

Besides the lack of professional training, other factors contribute to the maintenance of high rates of incidence of oral cancer in Brazil, among them: the lack of reference flow and counter reference for monitoring of confirmed and suspected cases, lack of continuous actions to the risk population and low adherence of the population to the existing actions[7].

The reduction in rates of malignant tumors of the oral cavity should be grounded on two principles: early diagnosis and health education for intervention in risk factors. Education actions are part of measures of primary prevention to health, seeking to intervene in the conditioning factors for the development of oral cancer (smoking, drinking, sun exposure and diet) before installing biological changes. Early diagnosis highlights recovery measures aimed at detecting DPMs, as these have the greatest potential for the emergence of malignant oral cancer[12].

Although not all DPM turn into CB, and not every CB is preceded by DPM, professionals must have greater knowledge about the injuries that precede the carcinoma, even if not all of them develop into malignancies, for the recognition of these and risk factors associated promote a better prognosis and, consequently, the institution of more conservative treatments[6].

CEC can have its oncogenesis process related to DPMs. The transformation rates of dpm for malignant neoplasia can range from group to group and may be associated with the histopathological diagnosis of epithelial dysplasia, the location of the lesion and its type[33].

Several factors contribute to the high incidence of DPMs and CB and are mainly linked to lack of information on preventive measures and failure in early diagnosis. There are failures in the prevention process and the control actions proposed by the health system are perennial and do not reach all the society layers[18].

Several strategies are adopted to control the CB, considered a public health problem throughout the world; however, the effectiveness of actions is directly related to the knowledge of the disease, diagnostics, professional training and involvement of the risk group. Joint actions with other health campaigns can be beneficial to extend the reach of the population at risk for oral cancer and help reduce cases of disease[20].

CONCLUSION

The increased incidence of new cases of mouth cancer indicate that this disease is a public health problem and the possibility of reduction is directly related to knowledge and control of risk factors that lead to development of neoplasia.

It is very important an increasing role in the oral health team in the early diagnosis and clearing population to decrease the

incidence of new cases. The dentist is the professional responsible for conducting early diagnosis and educating the population about habits, risks and actions of disease prevention and health promotion.

Therefore, it is necessary additional dentists' training in management and recognition of DPMs of the oral cavity, given that these, when intervened appropriately and with periodic monitoring has a chance of malignization decreased, resulting in less invasive and/or mutilating treatments.

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CONTRIBUTIONS

Lucas Soares Fernandes Aires Furtado and **Jorge Luiz Alencar Miranda Sales** worked in the conception, design and writing. **Natasha Muniz Fontes** and **Mara Ilka Holanda de Medeiros Batista** worked in review and writing. **Alessandra Albuquerque Tavares Carvalho** and **Marcília Ribeiro Paulino** participated in orientation and review.

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