Lifestyle Risk Factors that Increase Chances of Developing Oral Cancer: Up to Date Review

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Abstract

1.Background/Objectives: Oral cancer is on the 6th most common cause of malignancies of the world. With higher prevention strategies, the 5-year survival rate of oral cancer is lower than 50% in some countries. Several risk factors that are linked with lifestyle behaviors have been identified in the occurrence of oral cancers. 2.Methods: Multiple database from 2014 to mid 2024. Applying filters were used to identify systematic reviews and meta-analyses, which investigated oral cancer incidence and risk factors. All published articles related to "behavior risk factors in oral cancer" were included in this review. 3.Results: The utilization of tobacco has reached

the proportions of a global epidemic; alcohol association even raises the risk of developing oral cancer. In recent studies, there has been an association between smoking and a higher HPV infection. In addition, Candida albicans disrupt the metabolism of epithelial cells, so they can evolve from leukoplakia to dysplasia or even carcinoma leading to association of chronic inflammation. Also a persisting chronic inflammation with the association of one more risk factors from above can lead to an increase chance of developing oral cancer. 4.Conclusion: Most oral cancer are due to behavior habits, the main risk factors in oral cancer are smoking, alcohol consumption and the presence of HPV). Improving lifestyle changes should be one of the goals in every patient's life. In addition, different strategy of public health information should be promoted in order to consider giving up smoking and excessive drinking of alcohol. A change in diet is also necessary. Therefore, public health campaigns are essential in determining a prevention of behavior lifestyle habits especially in younger adults because they represent the future adults.

Keywords: oral cancer; tobacco; HPV; risk factors; alcohol; lifestyle; Candida albicans

INTRODUCTION

There is global effort against cancer due to the higher prevalence of cases therefore, a behavior approach should be adapted for information of the population of good ways of living, early diagnostics, and modern treatment. The complexity of determinate causes of cancer comes due to the combination of behavioral-related lifestyles, environmental and genetics. Social, economic, and demographic factors are associated with developing certain lifestyles. Oral cancer is still on the 6th most common cause of malignancies of the world [1] with an expected number of new cases in US for 2024 of 34,850 and 6,380 of approximate deaths [2]. The central and eastern European regions have few of the highest rates of cancer of the oral cavity due to diverse social factors [3]. Even with higher prevention strategies, the 5-year survival rate of oral cancer is still lower than 50% in some countries [4]. Prevention by managing the risk factors is the main method that can assure the delay of the occurrence of the disease. Over time, several risk factors in the occurrence of oral cancers have been identified. The most frequently alleged were gender and behavior habits, smoking, alcohol consumption, nutritional deficiencies, irritations produced by prosthetic works and socio-economic environment. Papilloma virus infections, aging, careless oral hygiene and low-vegetable diets, candida albicans are also risk factors that merge into developing premalignant lesions and becoming a risk factor in oral cancer [5, 6]. Therefore, the continuous change of lifestyle behaviors can lead an individual to develop a possible oral malignancy. Lifestyle behaviors refers to how a person choose to live his life and how he manages problems and interpersonal relations. Lifestyle behavioral risk factors for oral cancer are tobacco usage, heavy alcohol drinking and dietary micronutrient deficiency.

Figure 1. Oral cancer risk factors

Aim and objectives

The aim of this review is to summarize the behavior risk factors that lead to serious consequences regarding an individuals health condition. Therefore, the awareness of public

and clinicians of the behavior risk factors and early signs of oral cancer has an important impact on prevention.

MATERIAL AND METHODS

A search was performed in multiple database from 2014 to mid 2024. Applying filters were used to identify systematic reviews and meta-analyses, which investigated oral cancer incidence and risk factors. All published articles related to "behavior risk factors in oral cancer" were included in this review. The research papers obtained from the study search were screened, resulting in the exclusion of 35 articles, while 63 articles were included for analysis. The next step was the scan of the titles and abstracts of the search results. Irrelevant topics of scope of the study were removed. Due to the discrepant defined anatomic subsites affected by oral cancer was in the literature, lead to the exclusion of many articles that included the oropharynx in their analyses. Secondary research studies and systematic reviews were also excluded.

RESULTS

Lifestyle risk factors related to oral cancer development.

3.1. Tobacco

Using tobacco has an increased risk of developing oral cancer that is correlated to the amount and length of time they smoked or chewed [7]. Tobacco is used as multiple forms-cigarettes, cigars, pipe and bidi etc. hookah or chillum (a clay pipe used to keep the burning tobacco) in some countries of Asia including India [3]. Nicotine is one of the substances of the tobacco and induces dependence among a type of persons with a genetically, mentally and socially predisposition [8]. The utilization of tobacco has reached the proportions of a global epidemic, with a consumption of 1000 cigarettes per year for every man, woman, and child on the globe [9]. In the literature, epidemiological research is highlighted that men are heavier smokers than women are, therefore, their risk on developing oral cancer is higher. The most concerning fact is that 15% of adolescents in the world embrace this lifestyle behavior and are estimated as daily smokers. They have even higher rates 25–35% and above in Eastern European and Latin American countries [10]. One of fourth of oral cancer cases are due to cigarette smoking, therefore, the risk levels are correlated with the quantity of cigars smoked per day [11]. The alcohol association even raises the risk of developing oral cancer. The factors that contribute in developing this type of behavior are coping with stress and personal resources but for young adults the main reason is the social influence of friends, family, publicity from tobacco industry that encourages smoking [12].

3.2. Alcohol

The incidence of cancer in the oral cavity is higher in chronic alcohol users, thus 7 out of 10 people suffering from chronic alcoholism develop at least one premalignant or malignant lesion of the oral cavity and the association with increased tobacco consumption elevate the risk of cancer development [13]. In the composition of alcohol are carcinogenic impurities such as polycyclic aromatic and nitrosamines. The combination of alcohol and other carcinogenic compounds increase the deterioration of the oral epithelium leading to an increase permeability of these compounds and intensify the penetration of carcinogens into target tissue [14]. High levels of alcohol have been associated with different types of Streptococcus species and Neisseria species, therefore, elevate the risk of develop oral squamous cell carcinoma [15]. The mechanism of alcohol at the mucosal level is represented of cell deterioration that facilitates the entry of carcinogens into the exposed cells, altering the metabolism of oral mucosal cells. Chronic alcohol users have a higher incidence of cancer of

the oral cavity cancer. In association with tobacco consumption have a possibility of developing one premalignant or malignant lesion of the oral cavity [13]. Unfortunately, observational studies have indicated a higher frequency of cervical and oral cancers due to nutritional deficiencies, which develop alcohol users because of the malabsorption of microelements and vitamins [16].

3.3. Human Papilloma Virus

In the past two decades, oral cancer diagnosis due to Human Papilloma Virus has increased among men and/or women in different European nations, such as United Kingdom, France, Germany, Denmark, and Sweden [17]. HPV status is an important risk factor due to sexual promiscuity. The difference between HPV + and HPV- is that the patients are middle aged caucasians, with no history of smoking, a high socio-economical state and a large number of exposure of different sexual partners[18]. In recent studies, there has been an association between smoking and a higher HPV infection [19], because smoking produces pro- inflammatory and immunosuppressive actions, which lead to an elevated risk of HPV infection [20]. Therefore, the treatment response studies reported that HPV related oral or oropharyngeal cancer have a better prognosis [22]. Dalla Torre et al. suggested that some factors related to oral epithelial wound can be a site entry that facilitate the oral infection of HPV [23]. Furthermore, a prior study found correlation between the number of extracted teeth and prevalence of oral HPV infection [24]. In addition, there is an initiation of prevention of cervical cancer associated with HPV16 and HPV18 within vaccination of young boys and girls [25]. The HPV vaccine is effective in preventing the occurrence of precancerous cervical lesions mostly with high risk of HPV16, 18. The protocol of the vaccine is two-dose administration best at 11 or 12 years and before 15 years of age, regardless of the patient's sex. In addition, asymptomatic HPV infection in men is thought to have a major part in progress of the transmission to female partners [26].

3.4. Candidosis and dental hygiene

Candida albicans is a fungus that becomes opportunistic at immunocompromised patients [27], there have been studies that link to oral cancer. The relationship between oral candidosis and oral cancer is that Candida albicans produces leucoplastic lesions by adhering to the surface of tongue. The latest studies about the association between this pathologies is that oral carcinoma occurs more frequently on candida leukoplakias than on other types of leukoplakias encountered in practice by its presence on the surface of pre-existing oral dysplastic lesions. Moreover, chronic infections with Candida albicans disrupt the metabolism of epithelial cells, so they can evolve from leukoplakia to dysplasia or even carcinoma [27,28].

Another risk factor associated with oral cancer is oral health and oral hygiene especially in association with other risk factors, such as tobacco and alcohol. In an Indian case control study, it has been shown that 79% of the patients with oral cavity and oropharynx cancer oral cancer is decreased by 26% by dental visits [28]. Furthermore there were investigated also factors that maintain the oral hygiene like tooth-brushing, mouthwash use, and dentist visits. These investigations showed a beneficial correlation between oral cancer and tooth-brushing more than twice a day, mouthwash use, and dentist visits. In spite of that, an amount of studies suggested that mouthwash use may increase overall oral cavity cancer risk because of the alcohol ingredients. In contradiction, a recent meta-analysis including smoking and non-smoking patients didn’t managed to show this type of correlation between mouthwash exposure and the oral disease [29].

3.5. Diet and nutrition

The role of diet and nutrition in general health is already known to have beneficial effects, therefore in the literature review studies have shown that a diet rich in vegetables, fruits, carotenoids and other vitamins has an important role in lowering the risk of oral

cancer, while studies of evidence for different foods or nutrients is less convincing [30-34]. There have been studies that enhances that consumption of red meat more than once a week compared to white meat (chicken, fish) increases the risk of oral cancer [30]. This is also consistent with information from a few studies that analyzed the overall impact of diet in relation to oral and pharyngeal cancer using a priori defined scores (including the Mediterranean diet score) [35]. Moreover, the association of low consumption of fruit and vegetables or high consumption of meat along with increased exposure to tobacco and alcohol has been associated with an increase in risk for development of oral cavity cancer [31,36]. Lower intake of vitamin B, especially by reducing the concentration of folate and Vitamin B6, Vitamin B12, produces degenerative changes in the oral mucosa, which help the carcinogenic action of chronic irritant factors. In one study, experimental carcinoma of the oral mucosa was induced in riboflavin-deficient mice more easily than in the control group that did not have riboflavin deficiency. Similar results were obtained in experimental carcinogenesis in some studies in mice with deficiencies of vitamin A or Zinc [37]. Therefore, diet has the possibility to affect overall oral health and our organism inflammatory status. In a study whereas the Dietary Inflammatory Index (DII) was measured showed an association between DII and the risk of oral cancer [38].

3.6. Chronic Inflammation Associated

Chronic inflammation has an important role in the development of some epithelial cancers such as oral and neoplasms. Altering the mucosa from chronic inflammation leads to developing the first steps of tumorigenesis and are composed of alteration of different types of cells such as fibroblasts, myofibroblasts, adipose cells, immune and inflammatory forming tumor microenvironment [39]. Another role in chronic inflammation is regarding oral microbiota. It is known that inside a human mouth there are 700 different bacterial species involved in immune response, nutrient digestion, and carcinogen metabolism. The perturbation of this microbiota is due to gingivitis, periodontitis and poor oral health conditions, which promote chronic inflammation [40, 41]. There are different types of conditions, which lead to developing oral cancer: mechanical iritations, oral ulcerations, periodontitis tooth loos [43].

Prevention programs of oral cancer where premalignant lesions like leukoplakia, erythroplakia, submucous fibrosis, reverse smoking. The association between risk factors and premalignant lesions are showed in Table 1.

Table 1. Association between behavior risk factors and premalignant lesions

Risk factor	Lesion	Mechanism	References
Alcohol drinking	Leukoplakia	The effects of ethanol are due to the reactive metabolites and the metabolic stress which is generated by the oxidative and non-oxidative metabolism of ethanol. Acetaldehydethe represents the first metabolite of ethanol, that has been recently linked with several adverse consequences of alcohol abuse.	44- 46
	Submucous fibrosis	Because of the alteration of the colllagen disposition when exposed to carcinogens the compact tissue supresses with an induced DNA damage, as well as malfunction of cellular proliferation, survival, differentiation, and the DNA repair. The microenvironment around the fibrosis tissue is also a malignant promotion factor where the collagen deposition alters in oral mucosa, therefour, the capillaries block the blood flow leading to an hypoxic environment suitable for the promotion of malignant cell growth .	45, 47, 48

Risk factor	Lesion	Mechanism	References
	Erythroplakia	The alcohol dehydrogenase 3 gene (ADH3) is involved in the alcohol–acetaldehyde pathway, and a growing number of molecular epidemiologic studies have evaluated the role of ADH3 in oral cancer risk. These results were mixt.	49, 50
Tobacco smoking	Leukoplakia	The alteration in mucosa may lead to the thickening of the epithelium and increase in pigmentation. Tobacco has an irritating effect on the minor salivary gland. Due to the modification that are taking place in the oral epithelium there are alterations in the morphology of exfoliated cell.	51-53
Vitamin/iron supplements and body mass index	Oral submucous fibrosis	Through the induction of oxidative stress, iron deficiency produces free radicals and re-active oxygen species that potentially cause cellular injury.	54-56
Chronic Inflammation Associated	Periodontitis Gingivitis	Because of an increase in neutrophil accumulation, the neutrophil-to-lymphocyte ratio in the oral cancer microenvironment. Also in saliva of oral cancer patients were found elevated inflammatory markers, particularly TNFα	57, 58
Diet and nutrition	Different degrees of inflamation	Production of biomarkers such as CRP, IL-6, and homocysteine cell metabolism, growth, and proliferation, can lead to the production of nitrogen compounds and catalyze the formation of free radicals that are responsabile of cell damage	59, 60
Human Papilloma Virus		The existing of various risk factors that contribute to the alteration of the oral musosa leading to changes in the keratinocytes from the basal layer to the surface of the epithelium. This malfunction provide a suitable micro-environment for productive cell replication, responsible for transformation of the keratinocyte into a permissive Cell and the entry of HPV. Viral replication is a process, depending both on select viral proteins codified by the viral genome and on the degree of infected cell differentiation	61, 62
Candidosis and dental hygiene	Leukoplakia	Production of IL1β, which activates the production of proinflammatory cytokines. The molecular investigation data have also identified, in C. albicans genotype A, as a important presence in oral squamous cell carcinoma lesions	63

The importance of screening test for oral cancers is a systematic clinical examination of the oral cavity and includes a visual inspection of the face, neck, lips, labial mucosa, buccal mucosa, gingiva, floor of the mouth, tongue, and palate as well as palpating the regional lymph nodes. Therefore individuals witch choose a lifestyle that include this associated behavior risk factors should benefice at least once a year of a proper medical consultation through dentists, otorhinolaryngology, general medicine and family medicine practitioners. Moreover, we have to take in consideration that any abnormality lasting for more than 2 weeks is reevaluated and considered for a biopsy.

CONCLUSIONS

Most oral cancer are due to behavior habits, the main risk factors in oral cancer are smoking, alcohol consumption and the presence of HPV, nevertheless the association with other minor risk factors represent a higher possibility of developing oral cancer. Chronic inflammation and infection have been suggested to contribute to carcinogenesis of the oral

cavity because of the presence of persistent inflammatory factors (cytokines, chemokines, prostaglandins, and free radicals). Improving lifestyle changes should be one of the goals in every patient's life. In addition, different strategy of public health information should be promoted in order to consider giving up smoking and excessive drinking of alcohol. A change in diet is also necessary, the role of diet and nutrition in general health is already known to have beneficial effects on human body despite tobacco being the strongest established risk factor for oral cavity cancer therefore it is considered that maintaining a good oral hygiene and treating all oral problems promotes a balanced lifestyle. Therefore, public health campaigns are essential in determining a prevention of behavior lifestyle habits especially in younger adults because they represent the future adults.

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Conflicts of Interest

The authors declare no conflict of interest.

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