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Non Tobacco Induced Oral Cancer

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ABSTRACT

Tobacco is one of the most important risk factors for premature death globally. More than 60 toxic chemicals in tobacco can invade the body's various systems. Oral squamous cell carcinoma (OSCC) is a pathological type of oral cancer, accounting for over 90% of oral cancers. A vast quantity of scientific, clinical and epidemiological data shows that tobacco is associated with the development of oral squamous cell carcinoma, and its carcinogenic pathways may be complicated. It is widely accepted that tobacco is one the most important carcinogenic factors of OSCC, and its carcinogenic pathways may be multifaceted. However many cases of squamous cell carcinoma has been reported in person with no history of tobacco use especially in females. The purpose of this review is to summarize the possible mechanisms of non tobacco etiologies that promote the development of OSCC, on the basis of relevant research, so as to provide directions and ideas for future related research.

Keywords: Tobacco; Cancer; Chemicals

INTRODUCTION

Oral cancer is the eleventh most common cancer globally. There is a wide geographical variation in the incidence of oral cancer, with approximately two-thirds of patients in the developing countries of Southeast Asia, Eastern Europe and Latin America. In India, the gingival–buccal complex (alveolar ridge, gingiva, buccal sulcus, buccal mucosa) forms the most common subsite for cancer of the oral cavity, in contrast to cancer of the tongue that is more common in the western world.[1]India has one of the highest incidences of oral cancer (age-standardized rate of 9.8 per 10 000) making it the most common cancer among men (men:women ratio 2:1) and accounts for about 30% of all new cases annually. A recent survey of cancer mortality in India shows cancer of the oral cavity as the leading cause of mortality in men and responsible for 22.9% of cancer-related deaths.

These cancers are associated with the use of tobacco, betel quid, areca nut, smoking, and alcohol consumption. In addition to these, long‐standing irritation, viruses (HPV), premalignant conditions, immunosuppresion has been postulated as a risk factor.[2]

Tobacco is one of the most important risk factors for premature death globally. More than 60 toxic chemicals in tobacco can invade the body's various systems. Oral squamous cell carcinoma (OSCC) is a pathological type of oral cancer, accounting for over 90% of oral cancers. A vast quantity of scientific, clinical and epidemiological data shows that tobacco is associated with the development of oral squamous cell carcinoma, and its carcinogenic pathways may be complicated.[3,4] It is widely accepted that tobacco is one the most important carcinogenic factors of OSCC, and its carcinogenic pathways may be multifaceted. However many cases of squamous cell carcinoma has been reported in person with no history of tobacco use especially in females.[5,6] The purpose of this review is to summarize the possible mechanisms of non tobacco etiologies that promote the development of OSCC, on the basis of relevant research, so as to provide directions and ideas for future related research.

Some of the suspected non tobacco etiologies of oral cancer are:

Chronic irritation

It may result from poor oral hygiene, poor dentition, missing teeth and ill‐fitting dentures.

Mechanism of Carcinogenesis Following Mucosal Trauma

Experimental animal studies have suggested that chronic trauma may result in cancer formation by two mechanisms. It has been proposed that persistent mechanical irritation causes DNA damage and may eventually result in cancer formation.[7,8] This has been proven by increased activity of poly‐ADP‐ribose polymerase. in cases with chronic trauma. According to second proposed mechanism, chronic mucosal trauma results in inflammation, thereby releasing chemical mediators such as cytokine, prostaglandins, and tumor necrosis factor. Such an inflammation leads to oxidative stress.[9,10]This could induce genetic and epigenetic changes damaging DNA, inhibiting its repair, altering transcription factors, preventing apoptosis, and stimulating angiogenesis, thus resulting in carcinogenesis.[11,12]

Site of Oral Cancer Associated with Dental Trauma

In a retrospective study from Australia, it was found that the lateral border of tongue was the most common site of tumor occurrence in both smokers and nonsmokers. The incidence of tumor occurrence in lateral border of tongue was twice as common in nonsmokers as compared to smokers. This suggests that lateral border of tongue could be a site for chronic dental trauma.[13,14]

Ill- fitting Denture and Oral Cancer

In a multivariate analysisconducted in Brazil, it was found that ill‐fitting denture‐associated sores were associated with oral cancer with adjusted OR = 4.58; CI = 1.52–13.76 (P = 0.007). They concluded that chronic physical irritation of oral mucosa contributes to the topical carcinogenic effect of tobacco. In a meta‐analysis, the use of

dentures by itself was associated with an increased risk of developing cancer w(OR = 1.42, 95% CI = 1.01–1.99) while ill‐fitting dentures appeared to substantially increase the risk of developing cancer by almost four times (pooled OR = 3.90, 95% CI = 2.48–6.13).[15,16]

Viruses and Human Cancers

About a fifth of all human cancers worldwide are caused by infectious agents. In 12% of cancers, seven different viruses have been causally linked to human oncogenesis: Epstein-Barr virus, hepatitis B virus, human papillomavirus, human T-cell lymphotropic virus, hepatitis C virus, Kaposi's sarcoma herpesvirus, and Merkel cell polyomavirus

The notion that viruses have a role in the etiology of malignancy originated from the studies published in 1911 by Peyton Rous, who reported a filterable agent (Rous sarcoma virus [RSV]) in cell extracts of a chicken tumor that could transmit the tumor into healthy chickens . The discovery of this retrovirus opened up the field of tumor virology, demonstrating that some cancers could have an infectious etiology and eventually leading to the discovery of oncogenes . In the 1930s, two tumor viruses were described in mammals, suggesting the possibility that viruses may play a similar causal role in human cancers.[17,18]

Precancerous lesions of oral mucosa, as potentially malignant disorders

Oral leukoplakia, oral submucous fibrosis, and oral erythroplakia are the most common oral mucosal diseases that have a very high malignant transformation rate .Actinic cheilitis, some miscellaneous inherited diseases such as xerodermapigmentosum and Fanconi's anemia, and immunodeficiency are another potentially malignant disorders for oral carcinoma as well as these three diseases.

The etiology of precancerous lesions of oral mucosa is not well-known. Some risk factors such as tobacco chewing, tobacco smoking, and alcohol play an important role in development of potentially malignant oral conditions. While tobacco chewing is a major risk factor for oral leukoplakia, OSMF, and erythroplakia, tobacco smoking may be a risk factor for oral leukoplakia. Alcohol drinking may increase the risk by 1.5-fold for oral leukoplakia, by 2-fold for OSMF, and 3-fold for erythro-plakia. According to Thomas et al, while alcohol drinking and tobacco chewing may possibly be risk factors for multiple oral premalignant lesions, smoking was not associated with the risk of multiple oral premalignant lesions.[19]

Various studies reported about etiopathogenesis of precancerous lesions of oral mucosa. Vlkováet alanalyzed saliva markers of oxidative stress and reported that salivary thiobarbituric acid reacting substances and advanced glycation-endproducts were significantly higher in patients than in control. They also reported that no significant differences were found in salivary advanced oxidation protein products, vascular endothelial growth factor, sialotransferase, and neuraminidase. Total antioxidant capacity and expression of superoxide dismutase were lower in patients than in age-matched controls.[12]

Oral cancer after prolonged immunosuppression

Here we disscused it for multiorgan chronic graft-versus-host disease.Chronic myeloid leukemia (CML) is a clonal myeloproliferative disorder characterized by the presence of a reciprocal translocation between chromosomes 9 and 22 (Philadelphia chromosome), which leads to the appearance of a new hybrid gene (BCR-ABL) with tyrosine kinase activity. Current initial therapy is the administration of the tyrosine kinase inhibitor, imatinibmesylate, but in some cases, particularly for refractory or advanced phase disease, hematopoietic stem cell transplantation (HSCT) can be indicated as a curative treatment. However, there is concern about late complications of this procedure, such as chronic graft-versus-host disease (cGVHD) and the development of malignancies secondary to radiotherapy, chemotherapy, and prolonged immunosuppressive treatment.[13]

Immunosuppressive drugs are believed to cause SCC by a carcinogenic effect or by increasing the carcinogenic effect of other agents combined with its immunosuppressive effect.Azathioprine has been reported as a mutagenic agent, and associated to the promotion of secondary malignancies when used in GVHD treatment. On the other hand, cyclosporine is not directly associated to an increased risk of SCC, but is believed to induce phenotypic changes, and promote tumor growth, including invasiveness.[14]

CONCLUSION

It is widely accepted that tobacco is one the most important carcinogenic factors of OSCC, and its carcinogenic pathways may be multifaceted. However many cases of squamous cell carcinoma has been reported in person with no history of tobacco use especially in females.[5,6] The purpose of this review was to summarize the possible mechanisms of non tobacco etiologies that promote the development of OSCC, on the basis of relevant research, so as to provide directions and ideas for future related research.

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