Systematic review on correlation between chronic mechanical irritation and oral cancer

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Abstract:
Oral cancer is the sixth most common type of cancer that prevails world wide. There are about 3 lakh cases reported annually. This systematic review is aimed to assess the risk of chronic mechanical trauma leading to oral squamous cell carcinoma (OSCC). **Methods:** Systematically evidences were collected from Medline, Pubmed, Embase, Scopus and Web of science. The review includes only case- control, cross sectional, cohort studies that done in comparison with chronic mechanical trauma and OSCC. **Results:** Only 124 articles described chronic mucosal trauma as risk factors for oral cancers and were considered in this review. **Conclusions:** The review shows that chronic mucosal irritation resulting from ill-fitting dentures may be considered a risk factor for the development of oral cancer, such cancers occur commonly over the lateral border of the tongue.

Introduction:

Oral cancer is the sixth most common type of cancer that prevails world wide. There are about 3 lakh cases reported annually. The 5 year survival rate ranges from 55 to 60% that decreases to 30 to 40% in advanced oral cancers. The main causes are smokeless and smoking type of tobacco, Areca nut and alcohol contributes in majority cases with deleterious habits. High risk oncogenic human papillomaviruses (HPV) are also associated with oropharyngeal squamous cell carcinoma, with increasing incidence in developed countries. In addition to these well-recognized risk factors, patients immunosuppression, malnutrition or dietary deficiency, poor oral hygiene and predisposing genetic factors have been proposed to be significantly involved in the genesis of OSCC Lazos (2017).

Others become prey to cancer due to chronic irritation from sharp tooth, ill fitting denture, poor oral hygiene and genetic predisposition. The role of deleterious habits have been discussed over years in literature. We therefore, discuss systematically the role of chronic irritation resulting in oral cancer.

Methodology:

Systematically evidences were collected from Medline, Pubmed, Embase, Scopus and Web of science. The search was conducted for a period of past 40 years 1982 to march 2022. The keywords used for search were " Sharp cusp trauma and Oral cancer", "Dental trauma and mucosal injury,""Chronic oral mucosal irritation", "Potentially malignant disorders", Oral squamous cell carcinoma and risk factors". These words were used in combinations or alone to derive evidences for the study. Only articles that are in English language were used. 245 articles were selected by using the search words. Case- control, cross sectional, cohort studies were included in the study. Totally 124 articles were finally sorted after excluding those that are not fitting to the criteria.

Results:

A total of 124 articles were selected as per inclusion and exclusion criteria including 64 from PubMed, 36 from Scopus, and 24 from Web of Science were retrieved using the keywords. Screening the titles and abstracts of the identified articles revealed that 245 articles were not related to the topic of interest and thus were excluded from the study. Only 1 fulfilled the eligibility criteria and that were included in the systematic review. Cross references

of these 9 articles were checked manually and another four articles were included which gave a total count of 124 articles that were included in the systematic review. The workflow of systematic review has been summarized. k value of 0.98 and 0.96 was obtained for the review process indicating a good overall inter-observer reliability.

Discussion:

The role of inflammation in carcinogenesis is often underplayed, despite its inclusion as the 7th hallmark of cancer since 2009. CMI of the oral mucosa is the result of repeated, low-intense action of an oral deleterious agent such as sharp teeth, ill- fitting dentures, and functional alterations, separately or in combination causing sustained trauma Ariyawardana (2014). There are three types of CMI factors: Dental (malpositions, sharp/broken teeth, and/or rough or defective restorations); prosthetic (ill-fitting dentures, rough/sharp/overextended flanges, and lack of retention/stability); and functional (swallowing, occlusal, and other dysfunctional disorders). Thus, it is plausible that the chronic inflammation caused by intra-oral factors such as ill-fitting dentures, sharp teeth could be associated with increased risk of oral cancer. Thus, the present article was formulated to qualitatively and quantitatively review original studies evaluating the potential association between CMI and OSCC Manoharan (2014).

Efforts are made to study the role of chronic trauma as a carcinogen. Animal studies have suggested that chronic trauma may result in cancer formation by two mechanisms. Persistent mechanical irritation causes DNA damage and results in cancer formation. Increased activity of Poly-ADP-ribose polymerase is seen cases with chronic trauma Perry BJ (2014).

The second proposed mechanism, chronic mucosal trauma results in inflammation, thereby releasing chemical mediators such as cytokine, prostaglandins, and tumour necrosis. Genetic and epigenetic changes leads to damaging DNA , repair inhibition, prevents apoptosis, promotes angiogenesis resulting in angiogenesis. Inflammation causes oxidative stress. Chronic mechanical irritation is presents with erythema, atrophy, keratosis, hyperplasia, fibrosis in direct contact with mechanical agents Jain P and Jain (2015).

The presence of chronic mechanical irritation (CMI) is detected in any case of erythema, atrophy, ulceration, keratosis, hyperplasia, indentation or fibrosis in direct contact with a 'mechanical agent' (e.g. teeth or denture), during functional/parafunctional movements or decubitus position. This means that most if not any mucosal lesion of the border of the tongue can be associated with CMI: in rest position, the whole border of tongue is in direct contact with teeth or denture if present. Similar considerations apply to large part of the vestibular mucosa. Most of the oral mucosal surfaces have physiological contacts with teeth or dentures during functional movements or in rest position, so that the required direct contact between the traumatic agent and the lesion can be easily observed and even more in the presence of OSCC often implying altered mucosal surfaces due to an increased volume. In the presence of OSCC, a trivial contact with teeth or denture represents a CMI, but when assessing control patients, the same light contact is considered a CMI only in the presence of an objective clinical lesion Bernardes (2017). As any kind of light contact (due to interposition in the presence of diastema, or to lingual inclination of teeth, or to the habit of stabilising the denture using the tongue) implies very rare (if any) clinical lesions, this results in overestimation of CMI in OSCC patient and underestimation of CMI in control subjects. Additionally, all sources of trauma were jointly included, without considering the different impact of dental/prosthetic trauma when compared to parafunctional habits Gilligan (2017).

Previous studies dealing with the relationship between oral cancer and CMI employed dental or prosthetic variables, but without assessing them together. Thus, it is essential to define a clear and reproducible criterion for CMI that includes all the potential CMI factors. We applied one based on the protocol proposed. Identifying CMI offered a high a correlation coefficient, which suggests that the proposed method is repeatable.

Chronic inflammation results in the production of multiple factors such as infiltration of leukocytes, production of cytokines such as tumor necrosis factor-alpha (TNF-alpha), interleukins and chemokines such as cyclooxygenase-2 (COX-2), matrix metalloproteinases (MMP), reactive oxygen, and nitrogen species (ROS and RNS), and an activated nuclear factor B (NF-B). These factors promote carcinogenesis by stimulation tumor growth and modulation of the tumor microenvironment. The four major pathways of modulation are by promoting angiogenesis,

facilitating the proliferation of malignant cells thereby promoting tumor growth, by suppressing immune surveillance, and by inhibiting apoptosis. Studies have proposed that rather than genetic changes CMI leads to epigenetic changes inhibiting DNA reparation and apoptosis Archana Gupta (2021). Thus, CMI could potentially be a promoter for OSCC rather than an initiator. The above evidence reinforces the need for evaluation of intraoral and prosthetic factors that could cause CMI in addition to the other known risk factors such as tobacco and alcohol.

Conclusion:

CMI can also be considered an effect modifier or enhancer, and hence controlling this factor in high risk population can reduce the incidence, morbidity and mortality rates of OSCC. In other words, CMI could interact with other factors, acting as a component cause of a sufficient cause and by eliminating that component cause, the effects of said sufficient cause are controlled or diminished. Although not all OSCCs are associated with cancer similar to tobacco or alcohol, defining CMI as a dependent factor could result in an undervalued interpretation of the role of CMI in carcinogenesis.

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