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Review Article

SAY NO TO TOBACCO - NICOTINE AND ITS EFFECT ON ORAL MUCOSA -A REVIEW

Dr. Biju baby joseph

MDS (Oral Medicine and Radiology), ACDSR Affiliated to KUHS

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ABSTRACT

Nicotine absorbed by the skin and also by the digestive, respiratory and excretory systems is one of the most known toxins found in tobacco. The intake of nicotine contained in tobacco products has a particularly negative effect on the oral cavity. Nicotine changes the oral cavity microflora, increasing the amount of harmful bacteria and pathogenic fungi.

INTRODUCTION

Tobacco has been known to man for many thousands of years, but its use in Europe started after the discovery of America by Christopher Columbus in 1492. First brought to Spain by monk Roman Pano, tobacco gained in popularity in the sixteenth century. After the successful treatment of the migraine headaches suffered by the French queen Catherine de Medici by diplomat Jean Nicot, it began to be known as nicotiana . Hence the English name 'nicotine' used for the tobacco's best-known active alkaloid, first extracted in 1828. The consumption of tobacco products causes of various diseases. According to the World Health Organization (WHO), tobacco kills half of its users, about 7 million a year, of which 6 million are active smokers and 1 million are passive. It is estimated that 1 billion people in the world population smoke tobacco.1

The mouth is a window to the body's health. It can show signs of nutritional deficiencies or general infection. Oral health is an integral component of general health and well–being for all ages.[2]

The oral mucosa plays an important role in the body, due to its multiple functions. The normal structure and the functions of the oral mucosa can be affected temporarily or permanently as a result of inflammation with or without infections, physical aggression, chemical trauma, iatrogenic or other causes. The oral mucosa is involved in signalling and protecting against aero-digestive diseases and at the same time can be an indicator and evaluator of substances that are introduced into the body voluntarily or involuntarily. The oral mucosa has the ability to absorb substances such as drugs, alcohol, nicotine, etc.[3]

The oral cavity is lined with a mucous membrane (oral mucosa), which is made up of a stratified squamous epithelium that is nonkeratinized and an underlying connective tissue layer called the lamina propria. Mucus produced by the primary and numerous smaller salivary glands keep the skin wet. Oral cavity is lined by both keratinized and nonkeratinized mucosa, which acts as a physical barrier and has many functions such as protective, secretory and sensor.[4,5]

The oral cavity lined by a layered squamous epithelium functions to ensure the formation of a primary structural barrier between the external and internal environment, as well as protection against mechanical damage or penetration of toxic substances, microbes, viruses and other pathogens, but still possessing a certain reduced absorption capacity. The oral mucosa is subjected to various mechanical, traumatic factors, pressure, thermal, chemical, infectious, irritants of various categories, etc. All of these led to a local adaptation as a part of the defence processes. The epithelium is permanently renewed from the deeper layers and are frequently replaced by cell division, around each 14 to 21 days. This mucosal renewal a process whose control is insufficiently known, a hypotheses tries to explain this control is based on a negative feedback mechanism.[6,7,8,9]

*Corresponding author: **Dr. Biju baby joseph**

MDS (Oral Medicine and Radiology), ACDSR Affiliated to KUHS

Nicotine

Tobacco in smoking or else wise is the leading cause of cancer. Nicotine is well known to have serious systemic side effects in addition to being highly addictive. It adversely affects the heart, reproductive system, lung, kidney etc. Nicotine imparts its deleterious effect on multiple organ system as read through various literatures. Nicotine, a strong alkaloid, in its pure form isa clear liquid with a characteristic odour. It turns brown on exposure to air. It is water soluble and separates preferentially from organic solvents. It is an aminecomposed of pyridine and pyrrolidine rings. Nicotine once ingested, is absorbed and metabolized by the liver.

Nicotine acts via 3 major mechanisms, producing physiological and pathological effects on a variety of organ systems :

- Ganglionic transmission.
- Nicotinic acetylcholine receptors (nAChRs) on chromaffin cells via catecholamines.
- Central nervous system (CNS) stimulation of nAChRs

Nicotine on direct application in humans causes irritation and burning sensation in the mouth and throat, increased salivation, nausea, abdominal pain, vomiting and diarrhoea. Nicotine is one of the most toxic of all poisons and has a rapid onset of action. Apart from local actions, the target organs are the peripheral and central nervous systems.[10]

Oral mucosa defence feature.

The oral mucosa possesses also a capacity for self-defense, intrinsically, Saliva has a role in local resistance, the strongest being immunoglobulins with antibody functions (IgA, IgG, IgM), essentially contributing to the health of the mucosa. The keratinization process itself, imparts to certain extend to defence mecahnsism.[6,11]

The permeability of the oral mucosa is evidenced by the bidirectional transport of substances and is also highly dependent on lipid solubility. However the function of filtration and reabsorption is reduced in the oral cavity but it exists and in some cases can take on major proportions.[12]

The oral mucosa develops a range of roles, including protecting underlying tissues from mechanical, chemical, and biological stimuli, secretion of vital chemicals, and a sensory function that allows temperature, touch, pain, and taste perception. 4

The oral mucosa offers preliminary protection against trauma, potential pathogens, and carcinogenic agents, foreign agents etc. Oral mucosal changes are of different types and can be seen clinically as normal variations and oral mucosal lesions. Any abnormal alteration in colour, surface aspect, swelling or loss of integrity of the oral mucosal surface due to any foreign agents can be attributed to various kinds of oral pathologies either curable like infections, benign or malignant ones. Various Infections , bacterial, fungal or viral, systemic diseases and consumption of tobacco and related products are the main cause for oral mucosal lesions. Tobacco use is one of the most important risk factors for the development of oral mucosal lesions including oral pre-cancer and cancer. Oral Potentially Malignant Disorders refers to all epithelial lesions or conditions with an increased risk for malignant transformation. Oral Potentially Malignant Disorders include oral leukoplakia, erythroplakia, erythroleukoplakia, oral submucous fibrosis, palatal lesions in reverse smokers, erosive lichen planus, oral lichenoid reactions, actinic cheilitis of the lower lip and hereditary conditions, such as dyskeratosis congenita and epidermolysis bullosa. Most of the oral potentially malignant disorders are asymptomatic in the early stages , and could be detected in routine clinical examination. Correct diagnosis and timely treatment strategy of these may help prevent malignant transformation in oral lesions. Prolonged exposure of oral mucosa to tobacco products can induce changes which could be a protective mechanism of the oral cavity or attributed to the carcinoma itself. Carcinoma related to tobacco usage accounts for nearly half of all malignancies in men and quarter of all cancers in women. Divyadarshani etal in their study recorded much valuable comments after study conducted in op based subjects .Firstly they emphasized on the greater prevalence of oral mucosal lesions calls for ample awareness and knowledge about the diagnosis and management of these lesions. They also found that the prevalence of oral mucosal lesions was relatively higher in older individuals when compared to younger age groups. They also suggested that all the dental practitioners should be updated periodically on oral lesions which will enhance their diagnostic ability.[13]

Understanding the prevalence of oral mucosal lesions may facilitate the prevention, appropriate diagnosis, and prompt treatment of the disease. Knowing the prevalence of oral mucosal lesions in a particular region helps better evaluate, diagnose, and, thus, manage these lesions. Gupta etal revealed in their study that there is a strong region based difference in oral mucosal lesions . This could be attributed to the very different geographical location. They concluded that there is a wide variation in the prevalence of oral mucosal lesions worldwide, and the prevalence is specific to a particular region only.[13]

Tobacco use in both the smoking and non-smoking forms are common in India. Commonly seen tobacco associated lesions were Palatal erythema, Tobacco pouch keratosis, Leukoplakia, Smoker's palate and Palatal changes associated with reverse smoking. Paul etal found that oral leukoplakia was the most common seen lesions in their study. There was minimal alteration of tissues in their study subjects, substantiated by the histopathological report which can be considered as low-risk.[14]

Tobacco smoking has many deleterious effects on the oral mucosa. Tobacco smoking increases the number of aneuploid nuclei in the oral epithelium and causes oral malignant and premalignant lesions. In a study conducted by Motameyal etal showed more frequent cases of oral leukoplakia in comparison with many other studies done by other authors, which showed different frequencies in same cases were in all cases was smoking subjects.[15]

In a study conducted by sella etal found that significant clinical changes were found including halitosis and dry mouth among other hard tissue changes among subjects. This was a stratified, cross-sectional study, to show the effect of tobacco heat caused changes in oral mucosa . Cigarette smoking has detrimental effects on oral health and has been associated with an increased risk of oral diseases, such as premalignant and malignant lesions. The inhaled constituents induce inflammatory and structural changes in the oral epithelium and cause histopathological

alternations. Cigarette smoke can affect the quantity and quality of saliva, In another two study quoted by this author showed significant reduction or changes in saliva output . Rad et al. found a significant difference between the symptoms of dry mouth in smokers and nonsmokers, indicating that long-term tobacco use significantly reduces saliva output.[16]

Nicotine, the main ingredient of tobacco, promotes oral carcinogenesis via regulating Prx1. Tobacco can induce reactive oxygen species (ROS) production extensively in cells, which is a major risk factor for oral leukoplakia (OLK) development. Peroxiredoxin 1 (Prx1) is a key antioxidant protein, upregulated in a variety of malignant tumours. The main addictive component of tobacco, nicotine affects tumorigenesis by regulation of cell survival, apoptosis, proliferation, metastasis, angiogenesis, and immunosurveillance. Cell proliferation is a vital indicator for understanding the mechanisms of function of certain genes, proteins, and pathways involved in cell survival and death. The cytoskeleton may induce cell proliferation through modulating cell hardness, and mechanical forces in cells can influence the cytoskeleton assembly, which in turn affects cell proliferation. An Activated gene named CFL1 participates in some essential biological processes of malignant tumors including proliferation, apoptosis, invasion, and chemo-resistance. CFL1 could be a marker for the treatment of tobacco related lesions of oral mucosa .Nicotine present in tobacco increased expression of CFL1. A study showed that nicotine upregulated a gene named CFL1 and downregulated PPP2R1A both depending on Prx1 and thus promoted the development of OLK. CFL1 or PPP2R1A could be a marker for the treatment of tobacco related oral leukoplakia.[17]

Nicotine exerts a negative effect at the cellular level by modifying metabolism, and disturbs the interactions between tissues, which strongly promotes the formation of cancer-like changes. Smoking tobacco and the consumption of other tobacco products have adverse systemic effects and affect the condition of the directly exposed oral cavity and nasopharynx. This action is associated with thermal and chemical injury from exposure to tobacco smoke..

Nicotine addiction causes a variety of problems , its metabolites modify proteins and nucleic acids in cells, which leads to the development of oral cancer. Nicotine influences the formation of cancerous changes by protecting cancer cells against apoptosis and creating an immunosuppressive environment . Inhibiting the body's immune response involves compromising immune cell chemotaxis and reducing antibody production.[18]

Nicotine affects proliferation, binding and chemotaxis of periodontal ligament cells negatively. Smoking makes binding of some pathogen microorganisms to the epithelium easier. The initiation and the advancement of the periodontal diseases are commonly related to smoking as it can increase the rate of the buildup of the calculus, which can extend the rate of the plaque deposition accelerating the gingival recession and deep pocket formations. The causal link between smoking and oral cancer can be attributed to the significant rate of oral epithelial dysplasia that can follow the heavy rate of smoking and which can contribute to the carcinoma in situ. Although the majority of oral mucosal lesions are innocent and require conservative treatments, some oral lesion can potentially progress into malignancy.[18,19]

The ability of binding to the epithelium is important for colonization of bacteria in the oropharyngeal mucous membranes and stops the destruction of the bacteria The consumption of tobacco is closely associated not only with the development of oral cancer, but also with the course of disease evolving a poor prognosis. Smoking can lead to precancerous lesions and oral cancers related to p53 mutations.[20]

Occurrence of tobacco associated oral mucosal lesions varies with the form of tobacco usage. A study conducted by Neven Kumar etal found at the common lesions that were in conventional smoking group are leukoplakia, and erythroplakia. Tobacco smoke disrupts the functioning of nearly every human organ system, causing most deaths through cancer, heart disease, and noncancer respiratory diseases. Health risks extend not only to the person using tobacco but to people involuntarily exposed to smoke.[21- 28]

The evaluation of carcinogenic risks of smokeless tobacco by the International Agency on Research for Cancer (IARC) has confirmed that smoke lesstobacco is carcinogenic to human and the main target organ being the oral cavity . This study was done in an epidemiological survey mode.

The tissues of oral cavity are always inevitably to suffer damage, because it is the first part stimulated by cigar smoke . In fact, cgarsmoke is one of the most established major risk factors for many oral diseases, including periodontal disease, dental caries, aphthous ulcers, primary Sjögren's syndrome and peri-implantitis. The complicated pathogenic impacts of CS are considered as the attribution that leads to OLK and even its malignant transformation.[29-30]

Oral mucosal lesions.[38-47]

Smoking has been associated with several oral conditions such as tooth stains, halitosis and impaired taste. It is also associated with delayed wound healing, increased tooth mobility, bone loss, and xerostomia. Moreover, an increased risk of pre-cancerous lesions and cancers of mouth, pharynx, larynx and lip has been also linked to smoking. Nevertheless, Electronic cigarettes, initially introduced as cessation tools, have gained popularity, particularly among young adults due to their increased social acceptance, despite the American Dental Association's (ADA) recommendation against using them as a tobacco substitute . Cigarette smoking and the harmful chemicals released during smoking have negative effects on oral health. Cigarettes contain a variety of harmful and potentially harmful constituents that have adverse health effects. Smoking is associated with an increased risk of developing cancer, as well as cardiovascular, respiratory, and oral diseases.

The oral tissue may be affected by heat and mechanical irritation of cigarette smoke, but the most significant pathology results from chemical irritation and molecular interactions with harmful constituents that increase inflammation and cause potentially malignant or malignant conditions. The oral mucosa responds to local irritation via morphologic changes e.g., keratinization, hyperkeratosis, atrophy, metaplasia. These changes can lead to smoker'smelanosis, nicotine stomatitis, and premalignant and malignant lesions.

Cellular changes.

Pathological evaluation of buccal mucosal smears revealed

multiple cellular changes among smokers including nuclear polymorphism, hyperchromatism, increase in nuclear-cytoplasmic ratio, prominent nucleoli and perinuclear halo.

Periodontal disease and dental implants.

Periodontal disease is a preventable disease in which tobacco use is considered the strongest modifiable risk factor. Tobacco smokers display an increased gingival microvascular density with considerable gingival inflammation, suppressed angiogenesis due to local immune suppression, and oxidative stress

leading to periodontal disease and increased risk of complications. The deleterious effects of tobacco smoking on dental implants have been extensively reported. The implant failure rate was found to be higher among smokers. A systematic review found a dose-response effect between cigarette smoking and implant failure. Negative effects of smoking might be through both systemic and local routes. The heat from smoking and its toxic by-products such as nicotine, carbon monoxide, and hydrogen cyanide may impair healing, arteriolar vasoconstriction and decreased blood flow may affect the success of surgical procedures involving implants.

Oral cancer.

Oral cancer is the eighth most common cause of cancer-related mortality in the world. Tobacco, smoked or smokeless, causes oral squamous cell carcinoma (OSCC.). Oral cancer is the eighth most common type of cancer and one-third of oral cancer-related mortality in the world is attributable to tobacco smoking Cigarettes and other combusted tobacco products are dangerous nicotine delivery devices that contain a complex mixture of tumour promoters, co-carcinogens, and various toxicants that exacerbate the effects of the carcinogens. Tobacco may cause epigenetic alteration of oral epithelial cells and inhibit multiple systemic immune functions of the host. Its toxic metabolites may also cause oxidative stress on tissues releasing reactive oxygen species that can damage, cause mutations and induce OSCC.

CONCLUSION

All types of smoking adversely affect oral health and can induce cellular changes in the oral mucosa Tobacco has detrimental effects on oral health. Tobacco users have significantly higher rates of oral cancer, oral mucosal lesions, periodontal disease, dental caries, and implant failure. Dental practice settings provide a unique opportunity in providing tobacco cessation assistance.

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