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Impact of tobacco on oral health: A review article

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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. Despite the fact that different forms of tobacco (cigarettes, cigars, pipes, dipping and chewing tobacco or inhaled) are used in order to reduce pulmonary and cardiac complications, tobacco has a negative influence on human health. Tobacco smoking increases the death rate of smokers by 30-80%. Based on the mentioned, we can determine the causal relationship between smoking and the development of oral cancer, leukoplakia and chronic impact on oral organs, i.e. lips during constant tobacco use. 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.

Keywords: carcinoma, leukoplakia, tobacco, treatment

Introduction

One of the most important risk factors for premature death globally is tobacco. In world, there are more than 1.3 billion smokers worldwide [1]. According to World Health Organization (WHO) nearly 6.4 million deaths occurs because of tobacco and hundreds of billions of dollars of economic damage worldwide each year [2]. By 2030 tobacco will kill more than 8 million people worldwide each year if the current trend continues, most of which will occur in developing countries with lower incomes 1[3]. Even after knowing that tobacco harms health, most people still accept smoking as their daily routine, unaware that more than 60 toxic chemicals including carcinogens and cancer-promoting substances in tobacco can invade the body's various systems [4, 5]. Each cigarette is made of many ingredients, and some tobacco companies may use certain flavor additives to make their tobacco products more attractive, which may also be harmful to health [6]. Original components not only cause harm, but the intermediate metabolites play an unavoidable role in the process during smoking.

Discussion

Oral squamous cell carcinoma (OSCC) is a pathological type of oral cancer, accounting for over 90% of oral cancers [1]. Oral cancer ranks eighth among the most common causes of cancer-related deaths worldwide [7]. Oral and oropharyngeal cancers are reported to account for approximately 220000 new cases per year (5% of all cancers) worldwide [8]. According to the recent epidemiology of OSCC, the incidence in lower/middle income countries or developing countries tends to be higher than that of developed countries [9]. The data show that the risk factors that attribute to OSCC are age, sex, race, gender, tobacco, alcohol, betel nut, diet and nutrition [10]. Among them the most common is tobacco. It is widely accepted that tobacco is one the most important carcinogenic factors of OSCC, and its carcinogenic pathways may be multifaceted. The purpose of this review is to summarize the possible mechanisms of tobacco that promote the development of OSCC, on the basis of relevant research, so as to provide directions and ideas for future related research [1].

In the present article, we will give brief outline of various pre malignant lesions and conditions caused by tobacco and also about the Oral squamous cell carcinoma.

Effect of tobacco on oral cavity

Effect of Tobacco in prevalence of Periodontal Disease [11, 12]

Pindborg in 1947 was one of the 1st investigators who studied the relationship of periodontal disease and smoking he stated that the nicotine causes the contraction of the capillaries and have an irritating effect on gingiva.

Gingivitis: Tobacco smoking causes decrease in the gingival inflammation, smokers have lesser bleeding during bleeding on probing because there is decrease in the level of oxygen saturation and nicotine which is the main the main constituent of tobacco has vasoconstrictive action on the gingival tissues.

Periodontitis: Tobacco smoking causes increase in the prevalence of periodontitis causing the destruction of the cells, in tobacco smoking we often see there is clinical

attachment loss along with the bone loss that can be horizontal or vertical, there are more periodontal pockets seen in tobacco patients in comparison to non-tobacco smoker patient with the periodontal disease. Deeper periodontal pockets is also visible in case of tobacco patients

Acute Necrotizing Ulcerative Gingivitis: Smoking is one of the predisposing factors of a cute necrotizing ulcerative Gingivitus

Effect of Tobacco on Implant [11, 13]

Tobacco leads to failure of all the periodontal surgical or non-surgical procedures. The risk of failure of implant is very high among the smokers. The failure rate of implant osseointegration is considerably higher among smokers, and maintenance of oral hygiene around the implants and the risk of peri-implantitis are adversely affected by smoking. Smoking has been a contributing factor to implant failure between the time of implant placement and second-stage surgery, with a failure rate among smokers twice that of non-smokers. Although the survival rate of immediate implantation is higher than non-immediate ones, smokers with an immediate implantation have a significantly higher rate of complications compared to non-smokers. Study by Bruyn and Collaert shows that patients with the smoking habits have high maxillary implant failure, so this can be concluded that the maxillary alveolar bone is compromised leading to the implant failure.

Effect of Smoking on the Microbiology of the Mouth [14]

With the recent studies and practical content available it is clear that in non-smokers the plaque accumulation is as same as the patients who smokes regularly. Smokers generally have alteration in the plaque morphology causing the shallow pockets by the several bacterial pathogens. The most common bacterial pathogen is *Bacteroides forsythus*, Smokers are more likely to haborbacteroides for sythus 2.3 times the non-smokers. Other bacterial pathogens which are seen in the Smokers are *Peptostreptococcus* micros, *Fusobacterium nucleatum,* and Campylobacter rectus in the absenceof Actinobacillusactinomycetemcomitans and Porph yromonasgingivalis. In addition to this, these bacterial pathogens are most commonly seen in the maxilla as compared to the mandible.

Effect of Smoking on the physiology of the periodontium [11]

Clinical signs of inflammation is less in the non-smokers compared to the patients who smokes regularly. Although there is no significant change or differences are observed in the healthy gingiva. Chronic hypoxia is induced by smoking causes the greater severity of the periodontal Diseases in the periodontal patients. Nicotine which is the main component of cigarette causes the fibronectin production and increase in the type 1 collagen production. Nicotine may take part in the transcription process leading to the activation of the collagenase gene either directly or by inducing cytokines by the help of fibroblast.

Pre malignant lesion

According to WHO, a pre-malignant lesion is defined as the morphologically altered tissue in which cancer is more likely to occur than in it's normal counterpart [15].

Pre malignant condition

It is defined as generalized state or condition associated with significantly increased risk for cancer development [15].

Pre-cancerous lesion induced by tobacco [12]

- Leukoplakia
- Erythroplakia
- Tobacco pouch keratosis
- Palatal changes associated with reverse smoking
- Leukokeratosis nicotina palatini

Palatal changes associated with reverse smoking [16]

In some south East Asian & American countries even in some district of Andhra Pradesh of India practice reverse smoking pattern, in which the lit end of the cigarette is placed in the oral cavity. This habit creates a hit generated severe alteration of the palatal mucosa, which can transform easily in to cancer. The palatal changes includes: Keratosis, Patches, Red area, Ulcerated area and Non- pigmented area

Histopathological Diagnosis: The epithelium shows acanthosis & hyperkeratosis. Epithelium of minor salivary gland often shows squamous cell metaplasia & hyperplasia.

Management

It is generally a reversible lesion, & resolves within two weeks after cessation of habit. If the palatal lesion do not resolve after one month of cessation of smoking habit than biopsy should be advised.

Tobacco pouch keratosis [17]

It is a alteration of oral mucosa induced by tobacco in a smokeless form, mainly by chewing& snuffing.

Clinical Diagnosis: The main changes include hyperkeratosis, granular-patch, even well-developed folds & fissures & greyishness of oral mucosa seen in the buccal or labial vestibule.

Histopathological changes: Mild to moderate grade dysplastic features can be seen

Treatment: Most of this type of lesion is reversible, which subsides within five to six months after cessation of habit.

Erythroplakia [18, 19]

This lesion is rare as compared to leukoplakia, but it's potential to malignant transformation is very much higher. Although the etiological cause of thus lesion is unknown but the incidents seems to be very much higher non-smokers & alcohol consumers Erythroplakia appears as bright red velvety or granular red patch which is painless varies in size & raised & may be circumscribed sometimes. Clinical features: It is generally seen 6th-7th decade of life (mostly) with equivalent sex predilection. Clinically there are two forms of erythroplakia Homogeneous and Homogenious erythroplakia interaspersed with patches of leukoplakia, speckled erythroplakia Area involved: Floor of the mouth, retromolar area**,** mandibular alveolar area and mucobuccal fold. The speckled type of erythroplakia has more malignant potential than the homogenous type. Histopathological changes The epithelium shows less keratin production & is atrophic, but it may be hyperplastic as well. The lack of keratin & progressive atrophy allows the underline microvasculature to show through, thus the lesion appears reddish. The connective tissue shows chronic inflammation.

Toluidine Blue Test: Erythroplakia can be differentiated from malignant changes by using this taste, that is 1% toluidine blue solution, the malignant cells retain more of this dye.

Management

- Removal of the cause is always the initial way of management.
- Erythroplakia is very closely associated with carcinoma *in-situ*, dysplastic changes, so it is always advised to take an incisional biopsy.
- A conservative surgical treatment of mucosal stripping, without causing much damage to the deeper connective tissue is preferred.
- Laser ablation and cryosurgery is also preferred.
- Regular follow up are advised after every 3 months for atleast 4 years.

Leukoplakia [19, 20]

It is defined as a white patch or plague which cannot be scrapped of easily & cannot be characterized clinically or pathologically as any other disease Pathophysiology

Mucosa is irritated by various mechanical, chemical or galvanic stimuli & To adopt these changes from stimulus the mucosa undergoes hyper keratinization

Age & etiology: Mostly 3rd & 5th decade of life**.** Smoking is a main etiological factor.

Phases of Leukoplakia

Phase 1: Thin grey white plaque

Phase 2: Homogenous thick smooth or fissured

Phase 3: Nodular, granular, verruciform

Phase 4: Non homogeneous

Clinical types

A. Homogeneous: Uniform white plaque present on buccal mucosa (Have low malignant potential)
B. Non homogeneous: It may be verruciform or speckled,that is combination of leukoplakia &erythroplakia. This speckled leukoplakia consist of nodules or flakes on erythematious base. It has highest malignant potential. Homogenous type is usually asymptomatic & non-homogenous forms are associated with localized pain & discomfort
C. Proliferative verrucous leukoplakia:It is the most aggressive form of oral leukoplakia with highest malignant potential. 1/3 of PVL are seen in heavy smokers
D. Verrucous hyperplasia Grading:

Mild, Moderate and Severe (Based on the biopsy) Staging: On the basis of size and presence or absence of Dysplachanges

4 stages are present

L 1: Size of leukoplakia <2cm, L 2: Size of leukoplakia 2-4cm and L 3: Size of leukoplakia >4cm

L X: Size of not specified

P: Pathology

P 0: No epithelial dysplasia

P 1: Distinct epithelial epithelial dysplasia

P X: Dysplasia not specified

OLEP STAGING

STAGE 1: L 1 P 0

STAGE 2: L 2 P 0

STAGE 3: L 3 P 0 or L 1 L 2 P 1

STAGE 4: L 3 P 1

Histopathological Diagnosis: Hyperparakeratosis or Hyper orthokeratosis of the oral epithelium. Acanthosis of the oral mucosa followed by dysplastic changes in the epithelium. Liquefaction degeneration followed by basal cell hyperplasia.

Malignant potential: The chances of leukoplakia to convert into malignant lesion is.3 to 10%. Females have more tendency then males. Noduler form of leukoplalia have more chances of malignant transformation and lesion around the tongue and lips have slightly higher rates.

Treatment

- Removal of the cause is the main form of management of the lesion done by cessation of tobacco in any form
- Combination of Vitamin E and Vitamin E are given or simply Vitamin A analogue like 13- cis retinoic acid at the dose of 1.5 to 2 mg/kg of body weight of pt.
- Antioxidant like Beta carotene supplement are also given.
- In cases of candidal leukoplakia NYSTATIN therapy is given.
- Panthenol oral spray and lingual tablet are used against glossodynia and glossitis.
- In extreme condition Cryosurgery, Laser surgery and conventional ablative surgery are done.

Other effects of tobacco on mouth [21]

Smoke from of tobacco mainly leads to development of deep brown strains on the surface of the tooth, even discoloration of dental prosthesis & restoration. In smokers pigmentation is seen in the oral mucosa which is known as Smokers melanosis. Even hairy tongue & some coatings are also seen on surface of the tongue. In smokers it is observed that there is a increase risk of development of oral candidiasis & it can be treated by antifungal drugs

Tobacco induced cancerous lesion [1]

Squamous Cell Carcinoma: It is the most common malignancy occuring in the oral cavity at any sites, most common sites are; Lip, Tongue, Floor of the mouth, Gingiva, Palate and Maxillary Sinus

Etiology & Prevalence

Mainly oral cancers occur due to the use of tobacco either in smoke form or in smokeless form. Mostly, it is seen that tobacco along with alcohol induced the oral cancer more as compared to use of tobacco alone. Deficiency of vitamin C & vitamin A and along with use of tobacco can also lead to oral cancer. Chronic trauma of the oral mucosa due to presence of any sharp tooth. Person consuming tobacco & having infection of human papilloma virus also develop oral cancer. Mostly males have a higher chances of developing oral cancers as compared to females.

Clinical appearance

Ulcers with indurated margins are seen in clinically

Metastasis

Most of the oral cancers spreads through lymphatic route & rarely through the blood. The measure lymphnodes which are involved are; Submaxillary, Superficial & deep cervical lymph node. Occasionally the oral cancer also involves: Submental, Pre-auricular, Post-auricular and Supra-clavicular

[A] Carcinoma of lip [22]

Lip cancer is mostly seen in pipe smokers. Mostly lower lips are involved & sometimes lip commissures are also involved

Clinical appearance & spread
Lip cancers begin on the vermilion border of lip of one side of mid line. It begins as small induration or ulceration, soon gets transformed in to a crater like defect or can give rise to an exophytic mass. Ipsilateral metastasis is seen involving submental & submaxillary lymphnode. Somtimes even contralateral metastasis is also seen.

[B] Carcinoma of tongue [22]
Carcinoma of tongue constitutes 25 – 50% of all oral cancer.
Clinical appearance & spread
The lesion appears as painless ulcers, it begins as superficial indurated ulcer with raised borders which can develop in to fungating or exophytic mass. The cancer may infiltrate the deep layer of tongue causing fixation. Most commonly the cancer of tongue occurs in lateral border followed by ventral surface & rarely involviong the dorsum. If the cancer occurs on the base of the tongue it remains asymptomatic. Sometimes the patient shows disphagia & sore throat.

[C] Carcinoma of floor of mouth [22]
It constitute about 15% of intra-oral cancer. Smoking Specially pipe smoking or cigar are the main etiological factor. Clinical appearance & spread The lesion is indurated ulcer which may be painful or painless, seen on one side of mid line. The lesion occurs in anterior area of mouth & can extend in to lingual mucosa of mandible & tongue. The carcinoma of floor of the mouth extends into sub-maxillary & sub-lingual glands. Due to involvement of tongue there is a hindered movement of tongue resulting in slurry speech.

[D] Carcinoma of buccal mucosa [22]
Carcinoma of buccal mucosa occurs in those person having habit of chewing betel nut or tobacco for years.
Clinical appearance & spread
The lesion is seen along or inferior to a line situating opposite to occlusion plane. Anteriorly, the lesion extends from lip commissure to the third molar region posteriorly. Ulcerative lesion with marked induration & sometimes verrucous & or exophytic growth are the classical clinical appearance. The lesion may also infiltrate in to deeper tissue. Mostly sub-maxillary lymphnodes are involved.

Diagnostic imaging features [23]
- Location: Squamous cell carcinoma, whenever cause any change in the underline bone than it is only visible on radiograph. The most common bony invasion site is posterior lingual surface of mandible. When Squamous cell carcinoma involves the attached gingiva the radiographic changes seen are quite similar to that seen in periodontal diseases.
- Radio graphical appearance: Squamous cell carcinoma may invade the underline bone from any direction & cause destruction of the bone thus giving rise to a radiolucent lesion, which is described as “cookie bite” lesion. Usually the borders are irregular & poorly defined. Sometimes pathological fractures are also seen. Sclerosis in underline bone is also seen along with erosion. Sometimes within the central area of radiolucency small islands of residual bony trabeculae are also seen. The lesion leads to increase in the width of inferior alveolar cannal & if the lesion is present in maxilla it invades the floor of nasal cavity & maxillary sinus. The dental effects include widening of periodontal ligament space & loss of lamina dura is also seen. There is a gross displacement of tooth, sometimes floating tooth appearance is also seen due to mass destruction of bone.

Histopathology [24]
SCC is graded in to three grades based on dysplastic changes.

Grade 1: [Mild Dysplasia] Hyperplasia of basal an para basal layer of lower third of epithelium. Slide cytological atypia. Mild cellular & nuclear pleomorphism.

Grade 2: [Moderate Dysplasia] Proliferation of aty[ical cells in to middle third of epithelium. More severe cytological changes. Prominent cellular & nuclear pleomorphism. Architectural changes are seen in lower half of epithelium alomg with bulbous rete pegs. Hyperkeratosis of epithelium.

Grade 3: [Severe Dysplasia] Abnormal proliferation of basal layers in to nupper third of epithelium marked change in n/c ratio. Prominent cellular & nuclear pleomorphism. Prominent architectural changes are seen. Abnormal keratinization are seen along with keratin pearl. Earliest Signs of invasion are also seen.

Grade 4: [Carcinoma *in-situ*] It is the most severe form of epithelial dysplasia in which full thickness cytological & architectural changes are seen.

Treatment [25]
Usually oral squamous cell carcinoma is treated by radi therapy, surgical excision of lesion, cryosurgery. Chemotherapy is less frequently used in the treatment of oral squamous cell carcinoma.

Radiotherapy
- External radiotherapy: Large dose of 6000-8000cGy unites are given at the rate of 200cGy unites per day.
- Interstitial radiotherapy: This therapy is mainly used in case of small cancerous lesion in which Caesium 137 or iridium wires are placed within the tumor.

Surgical treatment: In case of early carcinoma of oral cavity a wide excision is followed by split skin graft.
In case of infiltrative lesion a wide excision followed by a flap reconstruction, usully pectoralis major myocutaneous flap is used.
In case of advance carcinoma en-block resection followed by removal of lymph node is the treatment of the choice. In case of carcinoma of tongue partial glossectomy, hemiglossectomy, total glossectomy are done according to severity of the case, & reconstruction of tongue is done by nasolabial flap is done.
Commando’s Surgery: This is done when carcinoma of tongue is fixed to mandible with infiltration of floor of the mouth, hemiglossectomy with hemimandibulectomy, removal of floor of mouth & radicak dissection of neck is done in this process.

Verrucous Carcinoma [26]
The verrucous carcinoma is a warty variant of squamous cell carcinoma which is characterized by precense of well

defferentiated epithelium with exophytic growth showing minimal cellular atypia & locally destructive pushing margins. The verrucous carcinoma is mainly seen in person taking tobacco in a chew form. Clinical appearance & spread verrucous carcinoma is seen in aged patient mainly sixth-seventh decade of life, it is seen more in males. It is a exophytic growth which is having a pebbly surface & is covered by a white leukoplakic film thus it appears papillary. When this lesion occurs on alveolar ridge or gingiva, it invades the overlying soft tissue & become fixed to over line periosteum of bone & gradually cause destraction of bone. The lesion is painful sometime bleeds & patients complains difficulty in mastication. The regional lymph node are enlarged & tender.

Diagnosis

- Histopathology:
- Marked epithelial proliferation
- Parakeratin plugging
- Pushing margin
- Inflametory changes in lymph node
- Toludine blue staining

It is done to know the malignant potential of the lesion

Management

- Radical surgical excision of the lesion
- Sometimes radio therapy is also treatment of choice.

Tobacco Usage Control Rules and Regulations [27]

India became a Party to the WHO Convention on tobacco control on February 27-2005.

Smoke free places

Smoking is completely banned in many public places and workplaces such as healthcare, educational and governmental facilities and on public transport. The law, however permits the establishment of smoking areas or spaces in airports, hotels having 30 or more rooms, and restaurants having seating capacity for 30 or more.

Tobacco Advertising, Promotion and Sponsorship

Advertising through most forms of mass media is prohibited. There are some restrictions on tobacco sponsorship and the publicity of such sponsorship.

Tobacco Packaging and Labelling

Health warning labels are pictorial and text; cover 85 percent of the front and back panels of the tobacco product package parallel to the top edge; and are rotated every 12 months. Misleading packaging and labelling, including terms such as “light,” and “low-tar” and other signs, is prohibited**.**

Cigarette Contents and Disclosures

The law does not grant the authority to regulate the contents of cigarettes. The law does not require that manufacturers and importers disclose to government authority’s information on the contents and emissions of their products.

Sales restriction

The law prohibits the sale of tobacco products via vending machines and within 100 yards of any educational institution. In addition, several states ban the sale of single cigarettes and gutka and other forms of smokeless tobacco. There are no restrictions on internet sales or the sale of small packets of cigarettes or other tobacco products. The sale of tobacco products is prohibited to persons under the age of 18.

E-Cigrettes

The law prohibits the production, manufacture, import, export, transport, sale, distribution, and advertising of e-cigarettes. There are no restrictions on the use of e-cigarettes.

Roadmap to Tobacco Control Legislation

The Cigarettes and Other Tobacco Products (Prohibition of Advertisement and Regulation of Trade and Commerce, Production, Supply and Distribution) Act, 2003 (COTPA) is the principal comprehensive law governing tobacco control in India. The Act was passed before India became a Party to the WHO Framework Convention on Tobacco Control. In 2004, the Ministry of Health and Family Welfare exercised the powers granted to it in Section 31 of COTPA by promulgating a first set of rules, which, with respect to smoke free and tobacco advertising issues, have been stayed by court order or superseded. With respect to general enforcement of COTPA, G.S.R. 1866(E) lists certain officers who are authorized to carry out the entry, search, and seizure provisions of the Act.

On October 15, 2014, the government introduced new larger warnings via G.S.R. 727(E) that, among other things, increased the warning size from 40 percent of one side of tobacco product packaging to 85 percent of both sides of tobacco packaging and amended the rotation scheme prescribed in G.S.R. 985(E). Although the rules announced by G.S.R. 727(E) were to have gone into effect on April 1, 2015, G.S.R. 739(E) establishes April 1, 2016 as the implementation date of the 85-percent health warnings. The government implemented new rounds of warnings on September 1, 2018 (G.S.R. 331(E)) and December 1, 2020 (G.S.R. 458(E)). Provisions prohibiting misleading descriptors and obscuring the health warnings on the package remain in G.S.R. 182(E) unaltered

Conclusion

It has been proven that the use of tobacco is associated with the development of OSCC. Periodontal diseases, dental implant failure, oral cancers, pre-cancerous diseases and leukoplakia are closely related to tobacco consumption. Advising patients to quit tobacco use is a dental professional responsibility and the dentists may play active role in nicotine replacement counselling. Close collaboration of both dentists and general physicians with smoking cessation programs is advocated in the treatment of tobacco-smoking patients.

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