

Review Article

Oral Submucous Fibrosis: A Chronic Deliberating Disease of Oral Cavity

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ABSTRACT

Oral submucous fibrosis is chronic progressive condition of oral cavity. The condition is well recognized for its malignant potential. Usually the disease initiates with redness, blistering, and ulceration inside the mouth. It is characterized by progressive fibrosis of submucosal tissue. The pathogenesis of oral submucous fibrosis is not well understood. Betelquid chewing is the major etiopathological factor. In Pakistan, oral cancer is the second most common cancer in women and the third most common cancer in men. The incidence of oral cavity cancer in Karachi South district of Pakistan is the highest in the world. Head and neck cancer are major cancer burden in Pakistan. The incidence of oral submucous fibrosis is common in women as compared to men. While banning tobacco, betel nut, betel, Panmasala and Gutka is the key to prevention of the disease. No specific laboratory tests are available for oral submucous fibrosis. Comprehensive head and neck examinations should be part of all medical and dental examinations. The treatment of patient of oral submucous fibrosis depends on the degree of involvement. Commercially available of economical sachets of gutka, paan have strong association with this. Government should take some steps for the cessation of these products.

Key words: Oral Cancer, Precancerous Condition, Betel Nut, Pakistan

Introduction

The only way to keep your health is to eat what you don't want, drink what you don't Like, and do what you'd rather not.

Oral submucous fibrosis is chronic progressive precancerous condition of the oral cav-

ity oropharynx and rarely the larynx (1). The condition is well recognized for its malignant potential. Sometimes it is associated with vesicle formation (2). The disease initiates with redness, blistering, and ulceration inside the mouth and is replaced with fibrous tissue as it heals. It is characterized by progressive fibrosis of submucosal tissue. The pathogen-

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esis of oral submucous fibrosis is not well understood, but it is multifactorial. Betelquid chewing is the major etiological factor; it is a combination of areca nut, betel leaf, tobacco, and slaked lime (3). Arecoline is an active alkaloid found in betel nuts¹, which provides reactive oxygen radicals that stimulates fibroblast for the increase collagen production. Chewing of betel nut usually starts at an early age (approximately 7 to 8 years) and, most users become addicted to the habit. Betelnuts have higher carcinogenic potential compared with conventional quids. Betel nut have role in progression of multi stage cancer (4). Other factors include alcohol, tobacco, ingestion of chilies, deficiency of nutrients, trace elements, and vitamins, in addition to hypersensitivity to various dietary constituents and genetic and immunological predisposition (1). This has led to the development of a unique generalized fibrosis of the oral soft tissue, called Oral submucous fibrosis (Fig. 1).

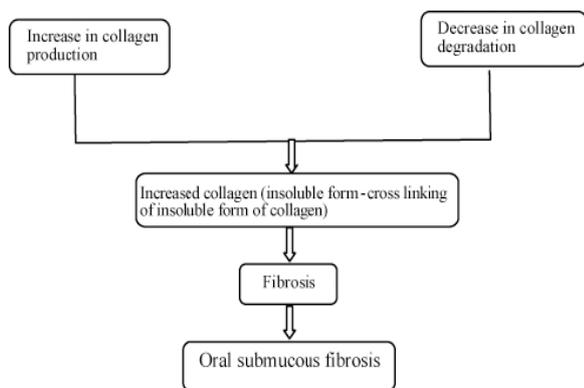


Fig. 1- Flowchart showing the development of OSF (5)

OSF is well thought inflammatory reaction of areca chewing or physical insult and the covering epithelium may exhibit precancerous changes undertaking malignant transformation (6). Oral submucous fibrosis is reported in people who never resorted to any form of areca nut habit. It is commonly

believed that pathogenic mechanism in OSF begins in the connective tissue and epithelium respond secondarily to it (2). Globally, about, 5, 75,000 new cases and 3, 20,000 deaths occur every year from oral cancer. It is necessary to establish an accurate diagnosis, to initiate optimal therapy for oral cavity lesions (7). In Pakistan Oral cancer are the second most common cancer in women and the third most common cancer in men. Areca nut devoid of tobacco is assumed of being related with oral cancer, but epidemiological studies have not evidently established its self-sufficient effect (8). Among the Karachi population the incidence of oral carcinoma is high (25per100, 000p.a) by international standards (9).

In Pakistan and south Asian subcontinent, the most popular chewing products are paan, chalia, gutka, niswar and tambaku. Betel quid (paan) is composed of betel leaf, betel nut and slaked lime (often tobacco) is added, where as betel nut (chalia) is the seed of betel palm, gutka is the preparation of crushed areca nut, niswar is type of dipping tobacco made from fresh tobacco leaves calcium oxide and wood ash (10). The incidence of oral cavity cancer in Karachi South district of Pakistan is the highest in the world. In Pakistan, a recent study among the adolescence and adults of Karachi squatter settlement reported that 40% of the population was using at least one chewable product of betel, areca, and tobacco on a daily basis. It gives a feeling of euphoria and well-being. Head and neck cancer are major cancer burden in Pakistan. Use of paan, chalia, gutka, niswar and tambaku is acceptable in Pakistan and considered a normal culture practice. The incidence of oral submucous fibrosis is common in women as compared to men (11). Studies suggest that different socioeconomic group prefer different items. For instance, studies conducted in Karachi shows higher

consumption of betel quid among boys than girls did. Differential chewing habits of paan and tambaku among males and females have also been reported (9). Oral cancer is one of the most common cancers and constitutes a major health problem in the world, and the leading cause of the death (12). The duration of betel quid chewing before the development of oral submucous fibrosis varies from a few months to many years; Involvement on just one side of the mouth has been reported when the betel quid is habitually held in one specific site (13). Prevalence of use of chewable products is high in Pakistan with particularly high use of certain substances related with socio-demographic profiles. Industrially prepared products, chaalia and gutka, are gaining popularity among youth. Policies and focused interventions can be developed taking into consideration the preferred use of products among different sociodemographic groups (14).

Patients with early lesion have better chances to cure and less treatment thesaurus, ease of access to the mouth, most patients present with highly developed tumor, when treatment is more complicated, more expensive and less successful compared to early detection. Early revealing of oral lesions and early neoplastic changes may be best and most cost effective means to improve survival and quality of life for oral cancer patients from all socioeconomic communities (13). In some south Asian countries, areca nut and betel quid (paan) chewing is a routine daily practice and an important component of social life and culture identity (15).

Betel quid chewing is very common in Pakistan. Its chronic use has a high prevalence of developing oral cancer. Peoples are not aware that areca nut chewing can cause oral cancer and cessation of its use will lessen the development of oral cancer. People who ever chewed areca nut risk of OSF increases

up to 11 folds. A higher relative risk of oral cancer for betel quid chewing with tobacco was notably higher than that for betel quid chewing without tobacco (16). Betel nut is the fourth most common substance of abuse in the world and is chewed by 600 million people worldwide (17).

Small striking and economical sachet of betel quid have become widely available, are insistently advertised and marketed, and are inspired by all age groups. Government is aware of the health risk and there are no restriction placed on the sale of these products. The shopkeepers continue selling these products because it has become multimillion industries. Chewing betel quid without tobacco is an independent risk factor for developing oral cancer. When betel quid with tobacco is consumed with alcohol and smoking the relative risk increases 11 folds. Betel quid chewing affects oral and periodontal health with higher oral hygiene index score, increase periodontal pocket depth, and bleeding (4). Areca nuts contain alkaloid that induce euphoria and raise a person's heart rate and skin temperature. Some chewers say a cheekful of betel aids digestion. Studies have also linked betel chewing with increased risk for several other medical conditions, including heart diseases, diabetes, and asthma (18).

Many of the literature-based studies reveal that areca nut (AN) extract may demonstrate mutagenic and genotoxic effects, in addition to inducing preneoplastic as well as neoplastic lesions in experimental animals (19). An extensively more chromosomal aberrations, sister chromatid exchange, and genomic damage occurs among areca nut users, than among non- users (8).

While OSMF is predominantly a disease of the oral cavity, fibrosis is also known to extend into the pharynx via the pillars and down to the pyriform fossa. It appears logical

that the esophagus should also be involved because at least some of the material, which is chewed or kept in the mouth, will go down the esophagus, leading to irritation of the esophageal mucosa, which is similar to that of the oral cavity. While banning tobacco, betel nut, betel, Panmasala and Gutka is the key to prevention of the disease, this may not be possible in the developing countries because of the lack of political will (20). The esophageal abnormalities were frequently seen in patients who had addicted Pan masala, Gutka, betel nut, tobacco or a combination of some or all of these, for > 5 years compared to those consuming them for a shorter period of time). Oral submucous fibrosis is not a disease restricted to the oral cavity; the esophagus may also be involved (17).

Chewing betel nuts is an important and popular cultural activity in many Asian countries. It is often chewed at ceremonies and gatherings and preparation techniques vary from region to region. Increase mouth ulcer and gum deterioration caused by betel chewing, when betel quid chewing done regularly it causes harmful effect on health including oral cancer and damage to gums. The international agency for research on cancer (IARC) regards betel quid to be a known human carcinogen. In countries and Communities where betel is consumed extensively, there are vastly higher levels of oral cancer. In Asian countries where it is consumed oral cancer form up to 50%, malignant cancer (21). Betel quid is chewed for many reasons including for its stimulants effect, to satisfy hunger, to sweeten the breath and as a social and cultural practice (22). Lee chiehfang said, "If you chew betel nut, smoke, or drink, you must take time out to check the condition of your mouth. The probability of betel nut chewers and smokers getting mouth cancers compared to the rest of the population are 28 and 18 times higher, respectively. Those who do both are 89 times

more likely to get mouth cancer whilst those who smoke, drink and chew betel nut are 123 times more likely to get mouth cancer (23). Tobacco smoking habits are strongly associated with oral mucosal lesion but no association with OSF has been reported so far. OSF was reported higher in patients with chewing areca nut (24). Caners of the oral cavity, excluding salivary cancer categories C00- 06, ranks in the world in both sexes. In Karachi the malignancy, rank second in both genders (25).

History

The condition was prevalent in the days of Sushruta (600 BC), a great practitioner of ancient medicine labeled this condition as 'Vidhari'. Vidari had features of progressive narrowing of mouth, discoloration of oral mucosa and pain on taking food. After the lapse of many years, Schwatz (1952) was the first person to bring this condition to limelight. He described this condition as 'Atrophia idiopathic mucosa oris'. The most susceptible sites of oral submucous fibrosis are; buccal mucosa, soft palate, lip mucosa, anterior pillar of the fauces. Rarely does it affect the membrane lining of the pharyngeal box, vocal cords, upper part of the esophagus. It is also capable of involving eustachian tube. Clinically it shows marked rigidity, atrophy of muscle fiber, inability to open the mouth, burning sensation of oral cavity, excessive salivation, recurrent oral ulceration, loss of gustatory sensation, hearing loss due to stenosis of Eustachian tube, nasal tonality to the voice, reduced mobility of soft palate, intolerance to eating hot and spicy food, impaired mouth movement (1).

Oral submucous fibrosis is clinically divided into 3 stages: Stage 1: Stomatitis; Stage 2: Fibrosis a- Early lesions, blanching of the oral mucosa, b- Older lesions, vertical and circular palpable fibrous bands in and, around the

mouth or lips, resulting in a mottled, marble-like appearance, of the buccal mucosa and Stage 3: Sequelae of oral submucous fibrosis leukoplakia, speech, and hearing deficits.

Khanna and Andrade (11) in 1995 developed a group classification system for the surgical management of trismus. Group I: Earliest stage without mouth opening limitations with an interincisal distance of greater than 35mm Group II: Patients with an interincisal distance of 26-35 mm. Group III: Moderately advanced cases with an interincisal distance of 15-26 mm. Fibrotic bands are visible at the soft palate, and pterygomandibular raphe and anterior pillars of fauces are present. Group IVA: Trismus is severe, with an interincisal distance of less than 15 mm and extensive fibrosis of all the oral mucosa. Group IVB: Disease is most advanced, with premalignant and malignant changes throughout the mucosa (26).

Histopathological Findings

The main histopathological characteristics of OSF is the deposition of collagen in subepithelial connective tissue, reduced degradation of collagen alpha 1 trimmer synthesized by the OSF fibroblast may induce alteration of the ratio of alpha1(I) to alpha2 (I) chains. Collagenase activity is found to be lower in OSF patients than normal oral mucosa. Less vascularized collagenous connective tissue, minimal to moderate degree of chronic inflammatory infiltration.1 Fibroelastic transformation of the juxtraepithelial connective tissue so it is also termed as Juxtraepithelial fibrosis. Chewing habits are the major risk factor of OSF, especially affecting the younger generation. However, no significant correlation found between trismus and hisopathological grading (4). OSF exhibit disturbance in homeostasis in fibrous tissue and altered in epithelial component Histologic findings vary according to the

stage of the disease.

Very early stage Fine fibrillar collagen, marked edema, large fibroblasts, dilated and congested blood vessels, and inflammatory infiltrates (primarily polymorphonuclear leukocytes and eosinophils) are found.

Early stage Early hyalinization is characterized by thickened collagen bundles, moderate numbers of fibroblasts, and inflammatory cells (primarily lymphocytes, eosinophils, and plasma cells).

Moderately advanced and advanced stages

Dense bundles and sheets of collagen, thick bands of subepithelial hyalinization extending into the submucosal tissues (replacing fat or fibrovascular tissue), decreased vascularity, no edema, and inflammatory cells (lymphocytes and plasma cells) are found, diffused hyalinization (14).

Diagnosis

The onset is between 2 to 5 years (2). An adequate incision biopsy taken from an area representative of the lesion can provide over 98% diagnostic accuracy as to whether the lesion is malignant or not, when routine pathological techniques are used. Comprehensive head and neck examinations should be part of all medical and dental examinations. Primary care physicians are well suited to providing head and neck examinations and to screening for the presence of suspicious lesions. A neck mass or mouth lesion combined with regional pain might suggest a malignant or premalignant process. Most cancers are in advanced stages at diagnosis, and treatment does not improve survival rates. Early recognition and diagnosis of cancer might improve patient survival and reduce treatment-related morbidity (7).

Laboratory Studies

No specific laboratory tests are available for

oral submucous fibrosis, and abnormalities may be related to secondary nutritional deficiencies. Some oral submucous fibrosis studies have reported the laboratory findings in including decreased hemoglobin, iron, protein and vitamin B complex levels and increased erythrocyte sedimentation rate.

Management

The treatment of patient of oral submucous fibrosis depends on the degree of involvement. Biopsy detected neoplastic or dysplastic changes. If the disease is detected at a very early stage, cessation of the habit is sufficient. Most patients with oral submucous fibrosis present with moderate to severe disease Oral cytology becoming increasingly important in the early diagnosis of oral cancer. The cytological study of oral cavity is simple and rapid, non-aggressive and relatively painless.

Medical Treatment:

Medical treatment includes, steroids, placental extracts, hyaluronidase, pentoxifiline, IFN-gamma, and lycopene. Medical treatment is symptomatic and predominantly aimed at improving mouth Movements (4,13, 27).

Physiotherapy This includes measures such as forceful mouth opening and heat therapy. Heat has been commonly used and the results have been described as satisfactory (28).

Surgical Modalities

Surgical treatment is indicated in patients with severe trismus (3). Surgical modalities that have been used include the following: Simple excision of fibrous band; Split thickness skin grafting; Nasolabial flaps; and Lingual pedicle flaps. Physical therapy included muscle stretching for the mouth may be helpful in preventing further limitation of mouth movement.

Complications

Complications include white lesion on oral

mucosa, dysphonia, gum pathology, tongue abnormality, stomatitis and dysphagia.

Future Perspectives

Upto the 1980s available data showed oral submucous fibrosis as a comparatively rare disease, occurring potentially among older individuals, mostly betel quid chewers. By 1990s, the situation had changed, the population prevalence of oral submucous fibrosis had increased manifold and it had become mostly occurring among young individuals.

Steps should be taken to curb the demand include increasing tax on all betel quid product, control smuggling, closure of all advertising avenues and creation of infrastructure for enforcement of law. As well as there is a need for improved primary prevention of these habits in different community groups as well as targeted initiatives for groups or individuals at risk. Future research should aim to provide evidence for people to make informed decisions about whether these treatments are effective and should explore treatment plans, which include patient education, aimed at cessation of the chewing habit (5).

Conclusion

From the above discussion, we came to know that oral submucous fibrosis is potentially precancerous condition of oral cavity that has a potential to transform into malignant condition. Commercially available chewing products like gutka, paan has strong association with OSF. Termination of these habits will reduce the incidence

When a lot of remedies are suggested for a disease, which means it can't be cured."

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