STUDY BASED ON DIAGNOSIS AND EVALUATION OF PATIENTS AFFECTED BY ORAL SUBMUCOUS FIBROSIS (OSMF) FROM BIHAR REGIONS

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Article Info: Received 11 October 2019; Accepted 30 November. 2019

DOI: <https://doi.org/10.32553/ijmbs.v3i11.975>

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Conflict of interest: No conflict of interest.

Abstract

OSMF (Oral Submucous Fibrosis) is a widely recognized precancerous condition which is also looked upon as a potentially malignant disorder of and is characterized by a reduction in mouth opening, having palpable circumoral fibrous bands either on one side or bilaterally along with the sensation of “burning mouth”. The condition is defined as “an insidious, chronic disease affecting any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by and/or associated with vesicle formation, it is always associated with juxta-epithelial inflammatory reaction followed by fibroelastic change of the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa causing trismus and inability to eat”. The increased consumption of commercially prepared arecanut preparations (Gutkha, Pan masala) specially in the younger generation has led to such high incidence of this disease in certain areas of India. Based on above reported findings the present study was planned for Study of Cases of Oral Submucous Fibrosis (OSMF) from Bihar Region.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study. Total 30 cases of the patients suffering from oral submucous fibrosis were enrolled in the present study.

In conclusion, the result of present study provides information on the prevalence of oral mucosal lesion in our population. It is important that preventive efforts be carried out by the concerned authorities and public health professionals in establishing tobacco cessation clinics and tobacco education in such masses (especially the young generation) along with a long standing and a close knit motivation program that enables our future generations to come to avoid the menace of tobacco and its subsequent health effects.

Keywords: Oral Submucous Fibrosis, OSMF, Oral Cancer, Bihar region, etc.

Introduction

Oral submucous fibrosis (OSMF) is a chronic, progressive disease that alters the fibroelasticity of the oral submucosa, prevalent in India and Southeast Asia but rare elsewhere, and characterized by burning and pain in the oral cavity, loss of gustatory sensation, the presence of blanched fibrous bands and stiffening of the oral mucosa and oro-pharynx (leading to trismus and a progressive reduction in mouth opening) and an increased risk of developing oral squamous cell carcinoma (3-19%). It is usually associated with the chewing of the areca nut (an ingredient in betel quid) but the exact etiology is unknown and there is currently no effective treatment.

Per Jens J Pindborg and SatyavatiSirsat (1966) (Pathological definition)- ‘An insidious chronic disease affecting any part

of the oral cavity and sometimes the pharynx. Although occasionally preceded by and/or associated with vesicle formation, it is always associated with a juxta-epithelial inflammatory reaction followed by a fibro-elastic change of the lamina propria, with epithelial atrophy leading to stiffness.’[1]

Per Chandramani More and Naman Rao (2019) (Clinical definition)- ‘A debilitating, progressive, irreversible collagen metabolic disorder induced by chronic chewing of areca nut and its commercial preparations; affecting the oral mucosa and occasionally the pharynx and esophagus; leading to mucosal stiffness and functional morbidity; and has a potential risk of malignant transformation.’[2]

“Exposure to areca nut (Arecacatechu) containing products with or without tobacco (ANCP/T) is currently believed to

lead to OSF in individuals with genetic immunologic or nutritional predisposition to the disease." [3]

This hypersensitivity reaction results in a juxta-epithelial inflammation that leads to increased fibroblastic activity and decreased breakdown of fibers. The fibroblasts are phenotypically modified, and the fibers they form are more stable, produce thicker bundles that progressively become less elastic. Once the original loosely arranged fibrous tissue is replaced by the ongoing fibrosis, the movability of the oral tissues is reduced, there is loss of flexibility and reduced opening of the mouth. These collagen fibers are non degradable and the phagocytic activity is minimized. According to a recent cross sectional study the time taken for return of salivary pH to baseline levels after chewing areca nut containing mixtures is significantly longer in habitual users with OSF when compared to unaffected users. [3]

A neural network-based oral precancer stage detection method has been proposed. [4] This new technique uses wavelet coefficients from transmission electron microscopy images of subepithelial fibrillar collagen in healthy oral submucosa and in oral submucous fibrosis tissues. These wavelet coefficients are used to choose the feature vector, which, in turn, can be used to train an artificial neural network. This trained network is able to classify normal and oral precancer stages (less advanced and advanced) after obtaining the image as an input. This technology is not readily available but could theoretically be used as an adjunct to hematoxylin and eosin histologic evaluations.

Currently, oral biopsy for hematoxylin and eosin provides the most definitive diagnosis and is crucial because of the association of oral submucous fibrosis with oral cancer. Some authorities have reported benefit with immunohistochemical techniques such as Masson trichrome staining when pathology involved muscle. [5] Alteration of cytokeratin expression, as is seen in leukoplakia and oral cancer, has also been noted in oral submucous fibrosis. Increased intensity of staining for pancytokeratin and high molecular weight cytokeratin, aberrant expression of cytokeratin 8, and decreased expression of cytokeratins 5 and 14 suggest their potential as surrogate markers for malignant transformation. [6]

Histologic findings vary according to the stage of the disease. [7] Fine fibrillar collagen, marked edema, large fibroblasts, dilated and congested blood vessels, and inflammatory infiltrates (primarily polymorphonuclear leukocytes and eosinophils) are found. Early hyalinization is characterized by thickened collagen bundles, moderate numbers of fibroblasts, and inflammatory cells (primarily lymphocytes, eosinophils, and plasma cells). [8]

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. [8]

Oral submucous fibrosis is generally characterized by diffuse hyalinization of the subepithelial stroma with pigment incontinence from the overlying epithelial melanin. [9] Other histologic findings include an atrophic epithelium and intercellular edema, with or without hyperkeratosis, parakeratosis, or orthokeratosis; epithelial dysplasia (25% of patients who underwent biopsy); squamous cell carcinoma histologically identical to typical squamous cell carcinomas; chronic inflammation and fibrosis in the minor salivary glands in the area of quid placement; and atrophy of the underlying muscle. Ultra structural changes in oral submucous fibrosis include an increase in collagen type I; however, fibrils retain the normal structure. [10]

In addition to the above clinical staging, in 1995 Khanna and Andrade [11] developed the following group classification system for the surgical management of trismus:

Group I: This is the earliest stage and is not associated with mouth opening limitations. It refers to patients with an interincisal distance of greater than 35 mm.

Group II: This refers to patients with an interincisal distance of 26-35 mm.

Group III: These are moderately advanced cases. This stage refers to patients 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.

The treatment of patients with oral submucous fibrosis depends on the degree of clinical involvement. 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. Moderate-to-severe oral submucous fibrosis is irreversible. Medical treatment is symptomatic and predominantly aimed at improving mouth movements. Treatment strategies are described below. The role of these treatments is still evolving. The US Food and Drug Administration has not yet approved these drugs for the treatment of oral submucous fibrosis.

In patients with moderate oral submucous fibrosis, weekly submucosal intralesional injections or topical application of steroids may help prevent further damage.

The rationale for using placental extract in patients with oral submucous fibrosis derives from its proposed anti-

inflammatory effect, [12] hence, preventing or inhibiting mucosal damage. Cessation of areca nut chewing and submucosal administration of aqueous extract of healthy human placental extract (Placentrex) has shown marked improvement of the condition.

The use of topical hyaluronidase has been shown to improve symptoms more quickly than steroids alone. Hyaluronidase can also be added to intralesional steroid preparations. The combination of steroids and topical hyaluronidase shows better long-term results than either agent used alone. [13]

This plays a role in the treatment of patients with oral submucous fibrosis because of its immunoregulatory effect. IFN-gamma is a known antifibrotic cytokine. IFN-gamma, through its effect of altering collagen synthesis, appears to be a key factor to the treatment of patients with oral submucous fibrosis, and intralesional injections of the cytokine may have a significant therapeutic effect on oral submucous fibrosis. [14]

OSMF (Oral Submucous Fibrosis) is a widely recognized precancerous condition which is also looked upon as a potentially malignant disorder of and is characterized by a reduction in mouth opening, having palpable circumoral fibrous bands either on one side or bilaterally along with the sensation of "burning mouth". The condition is defined as "an insidious, chronic disease affecting any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by and/or associated with vesicle formation, it is always associated with juxta-epithelial inflammatory reaction followed by fibroelastic change of the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa causing trismus and inability to eat". The increased consumption of commercially prepared arecanut preparations (Gutkha, Pan masala) specially in the younger generation has led to such high incidence of this disease in certain areas of India. Based on above reported findings the present study was planned for Study of Cases of Oral Submucous Fibrosis (OSMF) from Bihar Region.

Methodology:

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study. Total 30 cases of the patients suffered from the oral submucous fibrosis were enrolled in the present study.

Patients were divided into four groups according to severity, following the criteria from a study done by Ranganathan et al. [15] The criteria taken was mouth opening as follows.

Grade I: Only symptoms, with no demonstrable restriction in mouth opening

Grade II: Limited mouth opening. 20 mm and above

Grade III: Mouth opening less than 20 mm.

Grade IV: OSMF advanced with limited mouth opening. Precancerous or cancerous changes seen throughout the mucosa.

Following was the inclusion and exclusion criteria for the present study.

Inclusion Criteria: Patients suffering from oral submucous fibrosis.

Exclusion Criteria: 1. Patients with any systemic disease. 2. Patients having any malignant oral lesions. 3. Patient in whom an intra oral examination is not possible due to inadequate mouth opening.

Results & Discussion:

Cox SC, Walker DM (1996) [19] indicated worldwide estimate of 2.5 million people affected with OSMF with most of the cases concentrated on the Indian subcontinent, especially southern India. A sharp increase in the incidence of OSMF was noted after commercially available products came onto the market, and the incidence continues to increase. OSMF also occurs in other parts of Asia and the Pacific Islands. P. C. Gupta et al (1998) [17] reported prevalence of OSF in Bhavnagar district during 1967 was 0.16%. The use of areca nut-containing products and tobacco was assessed through an interviewer administered questionnaire. The diagnostic criteria for OSMF were the presence of palpable fibrous bands. A total of 11262 men and 10590 women aged 15 years and older were interviewed for their tobacco habits. Among 5018 men who reported the use of tobacco or areca nut, 164 were diagnosed as suffering from OSMF. All but four cases were diagnosed among 1786 current areca nut users (age-adjusted relative risk: 60.6). Areca nut was used mostly in mawa, a mixture of tobacco, lime and areca nut, and 10.9% of mawa users had OSMF (age-adjusted relative risk: 75.6). The disease as well as areca nut use was concentrated (about 85 %) in the lower (<35 years) age group. An increase in the prevalence of OSMF, especially in the lower age groups, directly attributable to the use of areca nut products was observed.

Ranganathan K et al (2004) [18] have claimed that, the number of cases of OSMF has raised rapidly in India from an estimated 250,000 cases in 1980 to 2 million cases in 1993. Choubey KK et al (2006) [19] did an etiological and epidemiological study of oral submucous fibrosis (OSMF) in Patna, Bihar. Total 157 cases of OSMF and 135 control subjects were selected for the study in the period of 2002-2004. It was observed that Male: Female ratio was 2.7: 1. The youngest case of OSMF was 11 year old and the oldest one was 54 years of age. Maximum numbers of cases were belonging to 21-40 years of age and they belonged to low or middle socioeconomic class.

V. K. Hazarey et al. (2007) [20] did a study to ascertain the gender specificity for different habits and severity of

OSMF. A hospital-based cross-sectional study on various habit patterns associated with OSMF was performed in Nagpur over a 5-year period. A total of 1000 OSMF cases was evaluated. The male-to-female ratio of OSF was 4.9:1. Occurrence of OSMF was at a significant younger age group (30 years) among men when compared with women. There was a marked difference in literacy, socioeconomic status, and areca nut chewing habits, symptoms and disease severity in women when compared with men in the central Indian population.

Anuna Laila Mathew et al. (2008) [21] evaluated the prevalence of oral mucosal lesions in Manipal, Karnataka State, India. A total of 1190 patients were interviewed and clinically examined for oral mucosal lesions. The result showed the presence of one or more mucosal lesions in (41.2%) of the population. Out of that, oral submucous fibrosis was 2.01%. Mucosal lesions like tobacco-related lesions (leukoplakia, smoker's palate, oral submucous fibrosis, and oral malignancies) were more prevalent among men than among women.

Table 1: Age & Sex of Patient

Age	No. of Cases
21 – 30 years	8
31 – 40 years	10
41 – 50 years	3
51 – 60 years	5
Above 60 years	4
Total	30
Males	24
Females	6
Total	30

Table 2: Oral Habits

Sr.No.	Habits	No. of patients
1.	Areca nut	21
2.	Gutkha chewing	19
3.	Spicy food	18

Table 3: Distribution as per Clinical Grades

Sr.No.	Mouth opening(in mm)	No. of patients
1.	>40	1
2.	31-39	2
3.	21-30	12
4.	<20	15

Table 4: Sign & Symptoms

Signs and symptoms	Grade I	Grade II	Grade III	Grade IV	Total
Burning sensation to hot and spicy food	1	2	9	11	23
Dryness of mouth	0	1	5	6	12
Presence of white fibrous bands	0	1	9	12	22
Limitations of mouth opening	1	1	2	5	9
Restricted tongue movement	0	0	3	2	5

The occurrence of OSMF was seen significantly in those having one or the other forms of areca nut. This occurrence has shown that the products which leaches out from areca nut would be responsible for the development of OSMF. [22] People having tobacco alone have never been seen to have OSMF. This was also observed in our study that there was no synergistic effect on development of OSMF in those consuming tobacco along with gutkha or in those consuming alcohol, tobacco, and gutkha simultaneously. If tobacco would have been a causative factor for OSMF then other forms of tobacco like cigarette, bidi, pipe smoking should have manifested OSMF as one of the clinical feature. In the areca nut chewers the lysyl oxidase activity is upregulated to alter fibroblast metabolism producing more collagen. This may add to the conclusion of the occurrence of OSMF due to the products leaching out from areca nut causes OSMF and not from those leaching out from tobacco. [23]

The pathogenesis of OSMF involves the mechanical as well as chemical trauma to the oral mucosa. The dry areca nut pieces present in gutkha and pan masala causes microtrauma to the oral mucosa. The traumatized mucosa undergoes chronic inflammation due to repeated microtrauma and irritation. This causes the oxidative stress and cytokines production due to chronic inflammation. The hypothesis that dense fibrosis and less vascularity of the corium, in the presence of an altered cytokine activity creates a unique environment for carcinogens from both tobacco and areca nut to act on the epithelium is widely being accepted. The alkaloid like arecoline, arrecadineguaccine, tannins, catechins, leaches out in saliva from areca nut and acts on the chronically inflamed mucosa. Increased amount of cytokines produced in oral mucosa like fibroblast growth factor, transforming growth factor and platelet-derived growth factor increases the production of collagen in the submucosal region. Also the inhibitory cytokine in collagen-production interferon-alpha is decreased in oral mucosa which leads to decreased degradation of collagen. Alkaloid leached out from areca nut acts on the fibroblast and induces the phenotypic changes, which leads to the decreased capacity of fibroblasts to degrade and remodel the collagen fibers in the submucosal region. This leads to the increased amount of collagen fibers in the submucosal region of oral cavity leading to OSMF. [24]

OSMF is considered as a premalignant condition of oral cavity. Pindborg et al., 1966, has given five criteria for relation of malignancy and OSMF like high occurrence of OSMF in oral cancer patients, incidence of squamous cell carcinoma (SCC) in OSMF cases, high occurrence of dysplasia of epithelium of oral cavity in OSMF cases, high frequency of leukoplakia along with the OSMF. [25] Pay Master 1956 was the first person to introduce the malignant potential of OSMF by showing the atypia in oral mucosal epithelium and also the presence of dysplastic changes in the oral mucosa of OSMF. Jeng has shown the

carcinogenicity of areca nut without tobacco. [26] Also IARC has declared areca nut as 'Group 1 carcinogen'. [27]

Conclusion:

In conclusion, the result of present study provides information on the prevalence of oral mucosal lesion in our population. It is important that preventive efforts be carried out by the concerned authorities and public health professionals in establishing tobacco cessation clinics and tobacco education in such masses (especially the young generation) along with a long standing and a close knit motivation program that enables our future generations to come to avoid the menace of tobacco and its subsequent health effects.

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