Abstract
Oral submucous fibrosis (OSMF) is a crippling disorder which is confined almost exclusively to the Indian subcontinent. The available epidemiological data showed clear cut geographical and ethnic predisposition, which suggested that certain customs/ habits prevalent among the population groups in the south-east asia might be etiological factors. Despite its association with a significantly increased risk of cancer, the etiology is still not clear. More research is needed to elucidate the problem.

Key Words: Oral submucous fibrosis, Review

Introduction
Submucous fibrosis is an insidious chronic disease affecting any part of oral cavity and sometimes the pharynx. Occasionally it is preceded by and/or associated with vesicle formation and is always associated with juxtaepithelial inflammatory reaction followed by progressive hyalinization of lamina propria. The latter sub epithelial and submucosal fibrosis leads to stiffness of oral mucosa and deeper tissues with progressive limitation in opening of the mouth and protrusion of the tongue, thus causing difficulty in eating, swallowing and phonation. Epithelial atrophy is marked in advanced stage of disease.

In 1956, Paymaster described the development of a slow-growing squamous cell carcinoma in one-third of his patients with submucous fibrosis at the Tata Memorial Hospital in Bombay. In contrast to this, Sirsat & Khanolkar remarked that this observation was not borne out by their experience.

Geographical Distribution And Prevalence
A community-based epidemiological survey in three areas of India (north and south) recorded the following prevalence's of OSMF: 0.36% in Emakulam, Kerala, and 0.04% in Srikakulam district of Andhra Pradesh (both in the south), and 0.16% in Bhavnagar, Gujarat (in the north). An epidemiological assessment of the prevalence of OSMF among Indian villagers based on baseline data recorded a prevalence of 0.2% (n = 10 071) in Gujarat, 0.4% (n = 10 287) in Kerala, 0.04% (n = 10 169) in Andhra Pradesh, and <0.07% (n = 20 388) in Bihar. The prevalence among 101 761 villagers in the state of Maharashtra (central India) was 0.03%.

Diagnosis
Various investigators have correlated the salient clinical and histological features of this condition. The onset is insidious over a 2 to 5-year period. The prodromal symptoms include a burning sensation in the mouth when consuming spicy food, appearance of blisters especially in the palate, ulcerations or recurrent generalized inflammation of the oral mucosa, excessive salivation, defective gustatory sensation, and dryness of the mouth. There are periods of exacerbation manifested by the appearance of small vesicles in the cheek and palate. The intervals between such exacerbations vary from three months to one year. Focal vascular dilatations manifest clinically as petechiae in the early stages of the disease. This may be part of a vascular response due to hypersensitivity of the mucosa towards some external irritant like chilli or areca nut. Petechiae were observed in about 22% of OSMF cases, mostly on the tongue followed by the labial and buccal mucosa with no sign of blood dyscrasias or systemic disorders; histologically they revealed a slightly atrophic epithelium with numerous dilated and blood-filled capillaries juxta-epithelially.

As the disease progresses, the oral mucosa become blanched and slightly opaque, and white fibrous bands appear. The buccal mucosa and lips may be...
affected at an early stage although it was thought that the palate and the faucial pillars are the areas involved first. The oral mucosa is involved symmetrically and the fibrous bands in the buccal mucosa run in a vertical direction. The density of the fibrous deposit varies from a slight whitish area on the soft palate causing no symptoms to a dense fibrosis causing fixation and shortening or even deviation of the uvula and soft palate. The fibrous tissue in the faucial pillars varies from a slight submucosal accumulation in both pillars to a dense fibrosis extending deep into the pillars with strangulation of the tonsils. It is this dense fibrosis involving the tissues around the pterygomandibular raphe that causes varying degrees of trismus.\textsuperscript{13}

The exact site and extent of the fibrosis and its role in the causation of trismus are determined by several factors. For example, the anatomical and physiological integrity of the underlying musculature is vital for the degree of mouth opening. Based on electron microscopical observations El Labben et al.\textsuperscript{14} reported muscle degeneration in OSMF, the extent of which may significantly affect the already existing trismus in these patients. Equally important is the involvement of the pterygomandibular raphe, a site commonly reported to accentuate the extent of trismus. Another factor is the duration of the disease in the affected individuals, which depends on the subjective evaluation of signs and symptoms. Current views of a protracted and insidious onset of the disease and its very slow progression make any sort of objective diagnostic criterion difficult, at least in the earlier stages.

A factor which seems to be overlooked by many investigators while recording the extent of mouth opening is the acuteness of oral symptoms (persistent/recurrent stomatitis and glossitis) at the time of recording. Most investigators agree that in OSMF the patient experiences a protracted period of stomatitis and/or glossitis with remissions and exacerbations, which must be taken into consideration, together with the age of the patient and the extent and site of fibrosis, when recording the extent of trismus. Sometimes the fibrosis spreads to the pharynx and down to the pyriform fossae. Upon palpation, a circular band can be felt around the entire rima oris, and these changes are quite marked in the lower lip.\textsuperscript{15} All observers have noted impairment of tongue movement in patients with advanced OSMF, but only some have registered an atrophy of the tongue papillae. With progressing fibrosis, patients complain of stiffening of certain areas of the mucosa leading to difficulty in opening the mouth, inability to whistle or blow out a candle, and difficulty in swallowing. When the fibrosis involves the pharynx, the patient may experience referred pain in the ear. Millard\textsuperscript{16} mentioned a nasal voice as one of the later signs in some patients.

**Clinical and functional staging\textsuperscript{17}**

**Clinical stage**

1. Faucial bands only
2. Faucial and buccal bands
3. Faucial, buccal, and labial bands

**Functional stage**

A. Mouth opening \( \geq 20 \) mm
B. Mouth opening 11-19 mm
C. Mouth opening \( \leq 10 \) mm

**Precancerous Nature Of The Condition:**

The precancerous nature of OSMF was first postulated by Paymaster\textsuperscript{5}, who described the development of a slow-growing squamous cell carcinoma in one third of OSMF cases seen in the Tata memorial Hospital, Bombay. The frequency of malignant change in patients with OSMF ranges from 3% to 6%.

**Treatment**

Usually drug treatment was used when patients were at an early stage, and surgical treatment was preferred in patients at an advanced stage or when a lesion was circumscribed. However, the high recurrence rate of restricted mouth opening, complications after surgical procedures, and the limited indications meant that surgical treatment cannot be considered popular among patients. After several decades of clinical trials, some drugs proved to be partially effective for relieving patients of the symptoms and signs of OSF.

**Steroids**

Steroids, and especially glucocorticoids, were first used in the treatment of OSF, and were extensively used in the past several decades because of their anti-inflammatory property. Several glucocorticoids were used, such as short-acting drugs (hydrocortisone), intermediate-acting drugs (triamcinolone), and long-acting drugs (betamethasone and dexamethasone). Glucocorticoids exert their anti-inflammatory activity by inhibiting the generation of inflammatory factors and increasing the apoptosis of inflammatory cells. They partially relieved patients of their symptoms at an early stage of OSF, as confirmed in many studies. They were less useful in reversing the abnormal deposition of fibrotic tissues and recovering the suppleness of the mucosa, and thus this treatment was always associated with a high incidence of relapse.\textsuperscript{18-19}
Enzymes

According to several studies, a prominent characteristic of OSF is its abundant and abnormal accumulation of collagen fibres in the lamina propria and submucosa of the oral mucosa, including muscle fibres and salivary glands. Collagenase is a lysosomal enzyme, capable of degrading phosphate esters, proteins, polysaccharides, glycosides, and sulphate esters. In a controlled clinical trial, Lin and Lin 20 found that intralesional injections of collagenase resulted not only in significant improvement in mouth opening, but also in a striking reduction of hypersensitivity to spices, sour, cold, and heat. Further study found that hyaluronidase could ameliorate the symptoms and signs of OSF by depolymerising hyaluronic acid, which is the ground substance in connective tissue, lowering the viscosity of the intercellular cement substance, and decreasing collagen formation. 21

Antioxidants

Gupta et al 22 found that after 6 weeks of treatment with tablets containing mostly _-carotene and vitamin E, patients showed an effective increase in mouth opening and tongue protrusion. Moreover, the decrease in mean malondialdehyde level (a marker of free radical damage) and the increase in levels of carotene after treatment were found to be statistically significant (P .01 and P .001, respectively), and these factors may play an important role in treatment. Kumar et al 23 studied the effects of lycopene soft gels in the treatment of OSF by RCT. Their results indicated that lycopene was more efficacious in improving mouth opening in patients and reducing associated symptoms than was placebo treatment (P .001). They attributed this curative effect to an inhibition of abnormal fibroblasts, up-regulation of lymphocyte resistance to stress, and a suppression of the inflammatory response.

Vitamins And Minerals

Vitamins and microelements are essential in the normal metabolism of organisms. Some studies regarded deficiencies in vitamins and minerals as a prominent characteristic of OSF. 24 Numerous studies used vitamins as a standard or adjunct therapy, and vitamins partially accelerated ulcer healing and relieved symptoms such as burning sensations and intolerance of spicy food. 25 Generally, in the long run, no satisfactory results were achieved through treatment with vitamins alone.

Conclusion

Several therapeutic and surgical methods have been tried in the treatment of submucous fibrosis. Following therapy the oral mucosa should regain and retain its normalcy, and there should be a reduction in the risk for oral cancer. However, no such definitive and widely accepted treatment is currently available for this condition. Some temporary relief from the symptoms and improvement in the oral opening with medicinal treatment such as local injections of cortisone, enzymes and placentrex, has been observed. In view of the lack of availability of curative treatment, and the precancerous nature of this disease, it is essential to follow-up the patients regularly. Furthermore, they must be educated to discontinue the use of areca nut and tobacco in any form, with the aim of preventing further progress of the disease and perhaps reducing the risk of oral cancer.

References


