International Journal of Advances in Scientific Research
ISSN: 2395-3616 (Online)
Journal DOI: 10.7439/ijasr **Research Article**

A prospective study of evaluation of methods to decrease the morbidity in oral submucous fibrosis

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Abstract

Aim: To evaluate the effect of antioxidants, intralesional steroids and laser in decreasing morbidity in patients of oral submucous fibrosis

Introduction*:* Oral submucous fibrosis (OSMF) is a chronic disorder characterized by progressive fibrosis of the lining mucosa of the upper digestive tract involving the oral cavity, oropharynx, and rarely the upper third of the esophagus, resulting in intolerance to spicy foods, burning sensation in the mouth, limitation of mouth opening and tongue mobility, xerostomia, dysphagia and hoarseness. OSMF has been reported to occur commonly in conjunction with premalignant diseases such as leukoplakia and lichen planus and therefore aprecursor to oral cavity cancer in many cases.

Materials and Methods: This prospective study included 60 patients with OSMF attending the Ear Nose & Throat Clinic of Dhiraj Hospital, Piparia. Patients of OSMF were evaluated as per Performa and for proper treatment planning were broadly classified into 4 groups based on classification suggested by Sinha *et al*.

Conclusion: Lycopene, an antioxidant has significant response in early cases of OSMF in decreasing the burning pain in oral cavity in OSMF. Inj. triamcinolone and Inj. hyaluronidase, given submucosally havesignificant response in early cases of OSMF to improve cheek flexibility.CO_2 laser have significant results in achieving satisfactory mouth opening in OSMF but notcheek flexibility.

Keywords: Oral submucous fibrosis, lycopene, laser, triamcinolone

1. Introduction

Sushrutha, a renowned Indian physician had recognized OSMF as a mouth and throat malady and labeled it as Vidhari[1]. This condition was described first in the modern era by Schwartz[2]; to which he ascribed the descriptive term "atrophiaidiopathi-catropica mucosae oris.'' Later in 1953, Joshi[3] re-designated the condition as oral submucous fibrosis.

Oral submucous fibrosis (OSMF) is a chronic disorder characterized by progressive fibrosis of the lining mucosa of the upper digestive tract involving the oral cavity, oropharynx, and rarely the upper third of the esophagus, resulting in intolerance to spicy foods, burning sensation in the mouth, limitation of mouth opening and tongue mobility, xerostomia, dysphagia and hoarseness. OSMF has been reported to occur commonly in conjunction with premalignant diseases such as leukoplakia and lichen planus and therefore a precursor to oral cavity cancer in many cases. OSMF is predominantly seen in people in south Asian countries. It has now become an Indian epidemic with an estimated 2.5 million people being affected with this disease S.C. Cox et.al (1996).[4] It is now widely prevalent in all age groups and across all socioeconomic strata as a result of the increased popularity of the habit of chewing pan masala.

Conservative treatment in form of especially antioxidants in early stages is very helpful in relieving symptoms and haltering the progression of the disease.[5] Intralesional injection of steroids is helpful to relieve local pain and inflammation and patient can do mouth opening exercises better.[5] Sharp dissection is the most common and longest established method for lysis of fibrotic bands in the treatment of OSMF. Excessive bleeding obscuring the surgical field, considerable wound contraction, recurrence of symptoms-trismus are some of the disadvantages of this technique. Hence use of laser for lysis of fibrotic bands which has a distinct advantage over cold steel with regard to the above considerations.[6]

1.1 Aims and Objectives

The Aim of this study is to evaluate the methods to decrease the morbidity in oral submucous fibrosis. The objectives are:

i. To evaluate the results of antioxidants in decreasing the burning pain in oral cavity in OSMF especially on eating spicy foods.
ii. To evaluate the results of intralesional injection of steroids in early cases of OSMF to improve trismus.
iii. To evaluate the results of laser in achieving satisfactory mouth opening in advanced OSMF and comparison with the results of cold steel in literature with regard to three factors namely - post-operative pain and discomfort, duration of healing and recurrence rate.

1.2 Review of literature

Epidemiology

OSMF is predominantly seen in people in south Asian countries such as India, Bangladesh, Bhutan, Pakistan and Sri Lanka. Cases have occasionally been reported in Europeans; it also occurs in people from Taiwan, China, Nepal, Thailand and Vietnam.[7]

Oral submucous fibrosis is now widely prevalent in all age groups and across all socioeconomic strata in India condition as a result of the increased popularity of the habit of chewing pan masala and is no longer believed to be a disease traditionally associated with poor nutrition and low socio-economic class.[7] Pan masala is a mixture of spices including, betel nuts, catechu, menthol, cardamom, tobacco, lime and others. The betel nut has psychotropic properties and is often eaten at the end of the meal to help digest food and as a breath mint.[8]

Aetiology

Various reasons have been put forth as the predisposing factors, some of which are betel nut alkaloids, capsaicin, immunological disorders (autoantibodies)[9], genetic predisposition and perhaps malnutrition.[3] Arecoline is the main betelnut alkaloid causing fibrosis and trismus. It has been suggested that due to high copper content arecoline upregulates lysyl oxidase activity and stimulates fibroblastic activation and collagen synthesis and also decreases its breakdown.[10] The use of chillies (Capsicum annum and Capsicum frutescence) has been thought to cause a local hypersensitivity reaction in genetically predisposed individuals.[7] Capsaicin, which is vanillylamide of 8-methyl- 6-nonenic acid, is the active ingredient of chillies and is thought to irritate the oral mucosa and their continued use causes chronic inflammation which leads to fibrosis [11].

Nutritional deficiency in OSMF could be precipitated by the effect of defective nutrition due to impaired food intake in advanced cases and may be the effect, rather than the cause of the disease (Vitamin and iron deficiency together with malnourished state of the host leads to derangement in the inflammatory reparative response of the lamina propria with resultant defective healing and ultimate scarification)[1].

The role of free radicals in the various oxidation processes in the body has led to the identification of antioxidants in inhibiting and reversing the disease process of OSMF. The mode of action of antioxidants may involve the stimulation of the immune system. They are antimutagenic and antimitogenic and operate by the common mechanism of breaking the free radical chain reactions. Lycopene is a bright red carotenoid pigment and exhibits the highest physical quenching rate constant with singlet oxygen.[12]

Khanna *et al* in 1995 showed that intralesional injection of triamcinolone in early cases of OSMF improved the symptoms of burning pain and mouth opening while advanced cases required a surgical option. The CO_2 laser is the most appropriate surgical laser for use in surgically treating oral soft tissue pathology. The laser radiation used for therapeutic purposes has mainly a thermal action that results from the absorption by tissues of radiant energy and its conversion at the impact site into heat. All biologic tissues can absorb this kind of radiation. Although laser absorption is influenced by pigmentation of the tissues, this is not so with CO_2 laser, whose absorption is related to the water content of the target tissue and recognizes all tissues as black. The overall benefits of laser surgery include a relatively bloodless operative field and thus excellent visibility, reduced need for local anaesthesia, less chances of bacterial infection, reduced mechanical tissue trauma, fewer sutures, quicker healing, and reduced postoperative oedema, scarring and tissue shrinkage. At the same time, the possible complications in laser surgery can be excessive or collateral tissue damage due to misdirected usage. The quicker and uneventful healing after laser therapy adds to patient satisfaction.[6]

2. Materials and Methods

Prospective interventional study was conducted on 60 patients in Department of Otorhinolarygology, Dhiraj Hospital.

Inclusion Criteria: All cases of OSMF clinically as defined by Pindborg,[1] patient's willingness for discontinuation of habit and addiction to the use of any oral mucosal irritants which may be the cause of OSMF and patient's motivation to continue antioxidants and regularly do mouth opening exercises on a long term basis.

Exclusion Criteria: Coexistent Carcinomatous pathology in oral cavity and neck and patients with coexistent temporomandibular joint disorders.

Patients of OSMF were evaluated and were broadly classified into 4 groups based on classification suggested by Sinha *et al*.[14]

A) Complain of burning pain but no trismus: Antioxidant - Lycopene 4 mg soft gel per orally in two divided doses of 2 mg each, daily for a period of 3 months.

B) Complain of burning pain with few fibrous bands but no trismus: periodic intralesional injection of 1 cc of triamcinolone acetonide (10 mg/ml) and hyaluronidase (1500 IU) at an interval of 2 weeks for 6 months with mouth opening exercises.

C) Trismus ≥ 2 Finger breadth: CO_2 laser was used for lysis of fibrotic bands. All patients were operated under local anaesthesia (2% xylocaine with adrenaline) after written informed consent. Post-operative care included observation for three hours, betadine and diluted hydrogen peroxide gargles, antibiotics for a period of one week, cold diet for a period of 3 days and mouth opening exercises.

D) Trismus < 2 Finger breadth: CO_2 laser for lysis of fibrous bands in conjunction with flaps for closure of defects with or without temporal myotomy and coronoidectomy under General Anaesthesia.

Group C and D patients were specifically evaluated for Eustachian tube function,clinically by assessing movement of soft palate and objectively by impedance audiometry.

Post-operative follow up was done at the 2nd day, 7th day, end of 1st month and 3rd month and findings noted as per follow-up performa. Post-op pain and discomfort following laser surgery was assessed by a VAS scale on continues basis. Healing of the post laser lesion was assessed after one month with complete healing being denoted as complete mucosalisation with no slough/granulation.

3. Results and observation

60 patients were equally divided into 3 groups (A,B & C), 40 were male and 20 female. Most of the patients, 26 (43.3%) were in the age group of 20-30 years followed by 23 (38.3%) between 30-40 years, 9 (15%) between 40-50 and 2 (3.4%) between 50-60. 38 patients (63.3%) patients had frequency of tobacco chewing 6-10 times per day followed by 14 (23.3%) of > 10 times per day and 8 (13.3%) having 1-5 times per day. Most of the patients 23 (38.3%) had history of addiction since 5-10 years followed by 21 (35%) of ≤ 5 years and 16 (26.7%) of > 10 years.

All 60 patients presented with complain of burning sensation in oral cavity. 20 patients presented with complain of decrease mouth opening, 33 presented with complain of reduced cheek flexibility, 24 presented with complain of recurrent oral ulcers and 18 patients presented with complain of difficulty on mastication.

Oral cavity findings depicted in table 1. Most common site for fibrotic bands was buccal mucosa followed by RMT. In Group A and B after 3 months of treatment there was only 1 patient in Group A and 2 patients in Group B complaining of burning sensation. In Group B and Group C, pre-treatment there were 13 and 20 patients respectively with reduced cheek flexibility. After 3 months of post treatment there was only 1 patient in Group B and 9 patients in Group C who had reduced cheek flexibility.

Table 1: Oral Cavity Findings

Signs	Lycopene (Group A)	Inj. Trimcinolone and Hyaluroninidase (Group B)	CO_2 Laser (Group C)
Trismus with interincisional mouth opening	0	-	-
10 – 20 mm		0	16 (80%)
20 - 30 mm		11 (55%)	4 (20%)
30 – 40 mm		9 (45%)	0
Palatal erosions/vesicles	10 (50%)	9 (45.0%)	5 (25.0%)
Blanching of Oral Mucosa	20 (100%)	13 (65.0%)	20 (100%)
Loss of Elasticity of Buccal Mucosa	0 (0%)	13 (65.0%)	20 (100%)

Table 2: Evaluation of post-operative results in Group C

Group C	Pre op	Day 2	Day 7	1 Month	3 Months	6 Months
Trismus with Interincisional mouth opening						
10 – 20 mm	16 (80%)	2 (10%)	2 (10%)	2 (10%)	2 (10%)	2 (10%)
20 – 30 mm	4 (20%)	0	3	5	7 (35%)	7 (35%)
30 – 40 mm	0	18(90%)	15(75%)	13(65%)	11 (55%)	11 (55%)
Healing Complete	--	--	--	20 (100%)	--	--
Mean Post-op. Pain & Discomfort Acc. to VAS scale	--	7.35	5.55	1.9	0	0

Table 3.0: Persistent reduced cheek flexibility at 3 months after intervention co-related with duration of habit

CF 3 months	Duration of addiction			Total
	≤ 5 yrs	5-10 yrs	>10 yrs	
Group – B	1	0	0	1
Group – C	0	2 (22%)	7 (78%)	9

4. Discussion

Oral sub mucous fibrosis (OSMF) is a high risk precancerous condition of the oral cavity and oropharynx characterized by changes in the connective tissue fibers of the lamina propria and deeper parts leading to stiffness of the mucosa and restricted mouth opening.

Desa (1954)[15] reported maximum incidence in the second and third decade, the average age being 40.5 years. In our study, maximum incidence is seen in the age group of 20 to 30 years, approximately 43.3%.

An equal distribution of cases among the males and females was noted by Joshi (1953)[3], Desa (1957)[15] and Pindborg and Sirsat (1962)[16]. In our study, out of 60 patients 40 (66.7%) patients were male and 20 (33.3%) were females.

The most common initial symptom is a burning sensation in the mouth often experienced when the patient is eating spicy food. Others include blisters (especially on the palate), ulcerations or recurrent stomatitis, excessive salivation, defective gustatory sensation and dryness of mouth. In our study, all patients presented with complain of burning sensation in oral cavity. There were 24 patients (40%) who had recurrent oral ulcers and vesicles. No patient in our study complained of defective gustatory sensation, dryness or excessive salivation.

The onset of the condition is insidious over 2 to 5 years duration. In our study, all 20 patients (Group C) presented with complain of trismus with 18 of them (30%) presenting with complain of difficulty in mastication.

The oral mucosa becomes blanched, slightly opaque and fibrous bands appear as the disease progresses. The extent of mucosal involvement varies from small, focal, pale, streaked or puckered areas to extensive diffuse, white indurated lesions involving the whole buccal mucosa and even extending to adjoining areas. In our study there was generalized oral blanching in all 20 cases (Group A) & extensive, diffuse opaque lesions in all 20 cases (Group C). 13 cases in Group B had oral blanching with puckered areas while 7 cases (11%) had focal fibrous bands without oral blanching or reduced cheek flexibility.

Over the years many treatment modalities have been used ranging from gold, arsenic trioxide, large dosage of iodine, liver extracts, placental extracts, hyaluronidase, dexamethasone as medical line of treatment to surgical methods such as partial thickness skin grafts, placental grafts, buccal fat pad grafts and lasers. Recent researches have shown promising results with locally injectable hyaluronidase and triamcinolone and systemically administered antioxidants.

In our study, 20 patients (Group A) were given lycopene 4 mg bd daily for 3 months and after 3 months 19 patients (95%) had no burning sensation in oral cavity only 1 patient had no significant response because of irregular medication.

Chaturvedi *et al*[17] treated 103 OSMF cases by intraoral, sub mucosal infiltration of hydrocortisone 1 ml and hyaluronidase 1500 units given together locally bi-weekly for 12 weeks. Improvement in painful, recurrent ulcerations, tolerance to chilies, in burning sensation, in suppleness of oral mucosa, in colour of oral mucosa, in mouth opening occurred in 53%, 74.7%, 86.4%, 69.6%, 76.6%, 74.1% cases respectively. In our study, 20 patients (Group B) were given bimonthly sub mucosal inj. triamcinolone 1 cc (10 mg/ml.) and inj. hyaluronidase (1500 IU) for 3 months with adjuvant systemic antioxidant therapy to prevent relapse. These patients were evaluated for improvement in burning sensation in oral cavity and reduced cheek flexibility. After 3 months of treatment, 18 patients had no burning sensation. Out of these 20 patients, only 13 (65%) had reduced cheek flexibility before treatment. After 3 months of treatment only 1 (5%) patient had no significant relief both in cheek flexibility and burning sensation. This patient had the shortest duration of use (2 years) of betel quid in our study; implying possibly a genetic susceptibility to OSMF.

OSMF cases treated by split thickness skin grafting resulted in gradual contracture.[18] Surgical flaps and grafts have resulted in more fibrosis & disability[3][15][20]. Hence the CO_2 laser is the most appropriate surgical tool for use in surgically treating oral soft tissue pathology.

In our study, 20 patients (Group C) were treated with CO_2 laser for excision of fibrous bands to relieve trismus. Out of theses 20 patients, 16 patients (80%) presented with interincisional mouth opening 10-20 mm (1 to 2 finger mouth opening) and only 4 patients (20%) presented with 20-30 mm

mouth opening. At 3 months post op., 11 patients (55%) had interincisional mouth opening of 30-40 mm (3 to 4 finger) & 7 patients (35%) had 20-30 mm interincisional mouth opening. Laser was not effective in 2 patients (10%) in relieving trismus and both patients were planned at a later date for bilateral coronoidectomy and temporal myotomy. However cheek flexibility did not improve completely in all 18 cases despite relief of trismus and was still significantly reduced in 9 patients (50%) at 3 months. The mean post-op. Pain according to a VAS scale from 0 to 10 was 7.3 after 48 hours; 5.55 after 1 week and 1.9 after a month. Thus all the patients had almost no pain & complete healing after one month of procedure.

In our study, the duration of addiction was highly correlated with the severity of the disease and the persistent reduced cheek flexibility post intervention. Out of 9 patients in Group C with persistent reduced cheek flexibility at 3 months, 7 patients (78%) had a positive history of long standing use for 10 or more than 10 years. One patient in Group B did not show improvement in cheek flexibility at 3 months, despite having the shortest duration of use (2 years) of betel quid in our study; implying possibly a genetic susceptibility to OSMF.

5. Conclusion

Lycopene, an antioxidant has significant response in early cases of OSMF in decreasing the burning pain in oral cavity in OSMF especially on eating spicy foods.Inj. Triamcinolone and Inj. Hyaluronidase, given submucosally have significant response in early cases of OSMF to improve cheek flexibility.CO_2 laser have significant results in achieving satisfactory mouth opening in OSMF but not cheek flexibility. Aural manifestations of OSMF due to Eustachian tube dysfunction and speech abnormality due to soft palate immobility are not evident in OSMF cases with mouth opening more than one finger breadth.

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