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Original Research Article

Clinical Picture of Oral Submucous Fibrosis and the Effect of Local Triamcinolone Therapy

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Abstract:

Aim: Evaluation of habits, duration, causative factors and effect of intralesional Triamcinolone in oral sub mucosal fibrosis.

Materials & Methods: Design- Prospective observational study, **Setting-** Tertiary health care hospital, **Subjects-** Cases of Oral submucous fibrosis with restricted mouth opening attending ENT OPD who were willing to be a part of the study.

Methods: Diagnosis of OSMF was made on clinical features. Written and informed consent from all patients and in case of minors from their parents/guardians was taken. Detailed history was taken with special importance to the habituations and dietary habits. Detailed examination of oral cavity, oropharynx, nose and ear was done and disease staged. Treatment with Triamcinolone Acetate, injected submucosally in the dosage of 1 ml (40 mg) locally biweekly at sites of fibrosis was given. After 12 weeks, response to treatment was evaluated objectively by measuring the increase in inter–incisor teeth distance and subjectively on the basis of improvement in symptoms.

Results: Mean age was 27.48 years. Males were 2.5 times more commonly affected than females. Most (56%) of the patients used Gutkha. Following treatment, 26 % showed an increase in mouth opening of greater than 11mm. highly significant improvement in the inter incisor mouth opening was seen following with submucosal injection of triamcinolone. There was statistically significant negative correlation between increase in mouth opening, duration of the habituation and frequency of addiction of the patients.

Conclusion: There is both subjective and objective improvement in OSMF after treatment with intralesional steroid injection treatment.

Keywords: Fibrosis, Triamcinolone, Trismus, Tobacco, Oral.

Introduction

Oral Submucous fibrosis is a grave disease affecting the oral mucosa, making patients' life miserable owing to symptoms, namely intolerance to spicy food, recurrent ulceration, progressive difficulty in opening the mouth and it has been proven to be a premalignant condition. OSMF was defined as, "an insidious, chronic disease affecting any part of the oral cavity and sometimes the pharynx by Pindborg J. J. And Sirsat S. M in 1966.[1] Fibrosis is always associated with a juxta-epithelial inflammatory reaction followed by fibro elastic change of the lamina propria with epithelial atrophy resulting in stiffness of the oral mucosa causing trismus and inability to eat".[2] Schwartz (1952) described it as "Atrophica idiopathic (Tropica) mucosae Oris".[3] Other names include "Idiopathic scleroderma of the mouth'', "Idiopathic palatal fibrosis'', "sclerosing stomatitis" "Juxta-epithelial fibrosis".[4]

In these times of rampant growth in industrialization and civilization, human beings are subjected to considerable stress and tension and fall prey habits such as smoking, pan, tobacco and betel nut chewing.

They may give a false sense of elation but have detrimental effects on human body apart from being addictive.

Etiology of the disease is not exactly known

Many treatment modalities have been used ranging from gold, arsenic trioxide, large doses of iodine, liver and placental extracts, hyaluronidase, dexamethasone as medical line of treatment to surgical methods such as partial thickness skin grafts, placental grafts and buccal fat pad grafts. [5]

Recent research has shown promising results with locally injectable hyaluronidase and dexamethasone and systemically administered antioxidants.

Therefore, present study was done to evaluate the various habits, duration, causative factors in OSMF and the effect of the intralesional triamcinolone in OSMF.

Aims and Objectives:

1. To study the clinical profile of oral submucous fibrosis (OSMF).
2. To find out the causative factors in Oral Submucous Fibrosis (OSMF).
3. To study the effect of local Injection Triamcinolone Acetate in the treatment of oral sub mucous fibrosis (OSMF).

Methods

Study Design: Prospective observational study.

Study Setting: This study was carried out in the department of ENT, of a Tertiary Health Care hospital during the period of 2years.

Subjects: All cases of oral submucous fibrosis with restricted mouth opening attending ENT OPD who were willing to be a part of the study.

Method of Study: Diagnosis of OSMF was made on clinical features.

The following criteria were used for clinical diagnosis

- Presence of burning sensation.
- Blanching of the oral mucosa.
- Restricted mouth opening.
- Palpable fibrous bands.
- Blanching is further defined as a persistent, white, marble-like appearance of the oral mucosa that may be localized, diffuse or reticular.[6]

Written and informed consent from all patients and in case of minor from their parents/guardians were taken before including them into the study.

Inclusion Criteria

1. All patients of oral submucous fibrosis (OSMF) with mouth opening restricted.
2. Age ≥ 10 years.

Exclusion Criteria

1. Patients with no mouth opening.
2. Patients with oral or oropharyngeal cancers.
3. All patients suffering from diseases in which steroids are contraindicated.

Method of Examination

Detail history of all the study participants was taken with habituations and dietary habits.

Then a detailed examination of oral cavity, oropharynx, nose and ear was done.

After thorough clinical examination, patients were staged into various stages according to the following criteria

Clinical Staging

Stage I - Early OSMF

- Mild blanching
- Normal mouth opening [35 to 45 mm]
- Burning sensation only on taking spicy or hot food

Stage II - Moderate OSMF

- Moderate to severe blanching
- Mouth opening reduced by 33%
- Burning sensation even in the absence of stimuli.
- Palpable bands felt.

Stage III - Severe OSMF

- Severe burning sensation.
- Mouth opening reduced by 66%.
- Ulcerative lesions may appear on the cheek.
- Thick palpable bands.

Figure 1: Injecting Triamcinolne in sub-mucosal plane

Figure 2: Inter-incisal teeth distance measured with Vernier Caliper

Treatment Protocol

After clinical examination, patients were advised to stay away from their habits and to take a high protein diet. They were subjected to treatment with local injection Triamcinolone Acetate. The Triamcinolone was injected submucosally in the dosage of 1 ml (40 mg) locally biweekly at sites of fibrosis with an insulin syringe. Treatment was given for 12 weeks, the response to treatment was evaluated objectively by measuring the increase in inter –incisor teeth distance with the help of vernier caliper and subjectively on the basis of improvement in symptoms Patients were followed up after 1 month, 3 months, 6 months and 1 year.

Results

The results of study are as follows: Age of patients varied from 10 years to 55 years, the youngest being a 10 year old boy. Maximum number of cases 23 (46%) were in the age group of 21 - 30 years, followed by 14(28%) in the 31 - 40 age group and 9(18%) patients in 11 - 20 years. Mean age was 27.48 years with a standard deviation of 8.61 indicating wide range of distribution.

Females followed the same age distribution as that of males with a mean of 26.97 years in males and 28.78 years in females. Out of 50 cases, 36 (72%) were males and 14 (28%) were females with a male: female ratio of 2.57:1.

Males were 2.5 t times more commonly affected than females. (Table no.1)

Table 1: age and sex distribution of patients

Age in Years	No. of patients		
	Male	Female	Total
1-10	01	0	01(2%)
11-20	08	01	09(18%)
21-30	15	08	23(46%)
31-40	09	05	14(28%)
41-50	02	0	02(4%)
51-60	01	0	01(2%)
Total	**36(72%)**	**14(28%)**	**50(100%)**

Most commonly used Areca nut products were Gutkha, commercially available as packets or prepared manually by mixing Areca nut, Tobacco and Lime. 28 patients (56%) were using this preparation and 11 (22%) patients were using supari containing areca nut only, 10 (20%) patients used betel quid which is a traditional preparation with pan, tobacco, areca nut, and lime. 1 (2%) patient had no chewing habits. (Table no.2)

Table 2: Chewing Habits

Sr. no.	Chewing habits	No. of cases
1	Gutkha	28(56%)
2	Supari	11(22%)
3	Betel Quid	10(20%)
4	No Habituations	01(2%)
Total		**50(100%)**

Trismus was present in all patients. Mouth opening was 26-30 mm in 1 patient (02 %). 21-25 mm in 20 patients (40%), 16-20 mm in 18 patients (36%).11-15 mm in 09 patients (18 %) and <10 mm in 2 patients (4 %) as shown.

After the clinical diagnosis, patients were treated with biweekly sub mucous injections of triamcinolone acetate 1ml (40mg). Patients were followed up weekly.

Patients were followed up after taking Triamcinolone therapy and mouth opening were measured at regular interval. This table shows mouth opening of the patients at the end of 1 Year follow up. (Table no.3)

Table 3: Pre-Treatment and Post Treatment Mouth Opening of Patients

Sr. No.	Pretreatment mouth opening (mm)	No. of cases	Post treatment mouth opening(mm)	No. of cases
1	26-30	01(02%)	36-40	03(06%)
2	21-25	20(40%)	31-35	19(38%)
3	16-20	18(36%)	26-30	12(24%)
4	11-15	09(18%)	21-25	05(10%)
5	<10	02(4%)	16-20	07(14%)
6			11-15	04(08%)
7			<10	0
	Total	**50(100%)**	**Total**	**50 (100%)**

Out of 50 patients treated,13 (26 %) patients showed an increase in mouth opening of greater than 11mm,24 (48%) showed an increase of 6 - 10 mm and the rest 12 patients showed an increase of less than 5mm. 1 patient showed no improvement, i.e. no increase in mouth opening.(Table no.4)

Table 4: Increase in mouth opening

Sr. No.	Increase in mouth opening (mm)	No. of patients
1	Nil	01(2%)
2	<5	12(24%)
3	6-10	24(48%)
4	11-15	13(26%)
Total		**50(100%)**

Highly significant improvement in the interincisor mouth opening was seen following treatment in study group with submucosal injection of triamcinolone. (Table no.5)

Table 5: Mean interincisal mouth opening in millimeters in patients **treated with inj. Triamcinolone**

	Mean	D	Df	P-value
Pretreatment, mean interincisor mouth opening in mm (n=50)	19.42 ± 4.35	8.04±3.25	49	P=1.14 E-22 i.e. P < 0.001 Very High significant
Post treatment mean interincisor mouth opening in mm (n=50)	27.46±7.13			

There was significant correlation between initial mouth opening and the increase in mouth opening following treatment. There was statistically significant negative correlation between increase in mouth opening and the duration of the habituation of the patients. There was highly significant negative correlation between frequency of addiction and increase in mouth opening. (Table no.6)

Table 6: Correlation between increase in mouth opening and initial mouth opening, duration of habituation and Frequency of Habituation

Correlation between increase in mouth opening and	R	Df	P-value
Initial mouth opening	0.74	49	P=3.34 E-10 i.e. P<0.001 Very High significant
Duration of habituation	-0.28	49	P=0.04203 i.e. P < 0.05 Statistically Significant
frequency of habituation	-0.42	49	P=0.002171 i.e. P < 0.01 Highly significant

Discussion

Oral submucous fibrosis is a chronic, crippling condition resulting in significant health and social problems, which may interfere with adequate nutritional intake, dental hygiene, speech and regular inspection of the oral cavity for cancer.[7]

The presence of palpable fibrous bands is a requisite criterion.[8] Clinical features are burning sensation in the mouth, excessive salivation, defective gustatory sensation, mild hearing impairment due to occlusion of the Eustachian tube and limitation of mouth opening leading to difficulty in chewing, swallowing, articulation and

poor oral hygiene. Previous studies have shown that areca quid chewing habit (with/without tobacco) is causal to triggering changes that lead to OSMF in susceptible individuals.[9] Reports have shown that the prevalence of OSMF in South East Asia ranges from 0.04% to 24.4%.[7] Recent epidemiological data indicate that, the number of cases has rapidly increased in India from an estimated 250,000 cases in 1980 to 5 million cases in 2002. Carcinogenic potential of the disease is often underestimated and because it is common and follows a chronic course, clinicians and patients tend to take it casually. OSMF is a precancerous condition with malignant transformation rates as high as 7.6%.[7] OSMF is also commonly coexistent with oral cancer lesions, which coupled with the co morbidity rate is more than 40%.

Symptomatology

All the patients 50 (100%) in the present study had a common complaint of trismus (difficulty in Opening the mouth) and burning sensation in the mouth. Some of the other less common complaints were retrosternal burning pain, pain in throat, change of taste, difficulty in swallowing etc. Main symptoms in the cases studied by Desa (1957)[10] were recurrent stomatitis, trismus, inability to blow the cheeks and inability to protrude the tongue. George (1958)[11] in his study reported that the main symptoms of the patients were burning sensation on taking pungent articles in food and difficulty in opening the Mouth. Ammer N.T. and Shukla R.K.[12] studied 52 OSMF patients and observed that all patients of OSMF had trismus and burning sensation of mouth, which is consistent with the present study.

Local examination

All the patients in the study group had trismus. The 50 cases had an average interincisor mouth opening of 19.42 mm though it ranged from 9mm-26mm before treatment. Desa [10] in his study found that trismus was present in 35 out of 64 cases. Most patients in the present series presented themselves for medical aid when the disease was rather advanced. Other workers also reported trismus to be most common finding in cases of oral sub mucous fibrosis. Patients presented with well-established stage of fibrosis in all cases i.e. 100% there was blanching of buccal mucosa with areas of fibrosis and also over the mucosa of soft palate.

There was blanching in other areas like anterior faucial pillars in 36 patients (72%), uvula in 39 cases (78%), tongue in 6 cases (12%) and lips in 3 cases (6%). Sites commonly involved, according to Wahi et al. (1966),[13] were palate (51.3%), buccal mucosa (44.2%), tongue (2.7%), lip and gingival (0.9%). Blanching of oral mucosa has been described as a leading finding by all other investigators. In some cases, hard bands of fibrosis were also felt over anterior pillars and the pterygomandibular raphe. Uvula was fibrosed to a small bud like mass in 39 cases (78%). Blanching of oral mucosa with areas of fibrosis is diagnostic of submucous fibrosis as fibrosis as described by all other previous investigators. Cross-sectional study of OSMF in central India and the effect of local Triamcinolone therapy by Ammer N.T. and Shukla R.K.[12] Showed that all the patients had trismus and a burning sensation. The 50 cases before treatment had an average inter incisor mouth opening of 19.4 mm and it ranged from 9mm to 25 mm.

Effect of triamcinolone therapy

Patients were followed up and mouth opening was noted by measuring inter incisor teeth distance with the help of a vernier caliper. Efficacy of the Triamcinolone therapy in bringing about clinical improvement was thus assessed objectively by measuring the inter incisor teeth distance (mouth opening).

Various studies show effects of local Injections in OSMF Patients

Gupta Deepak and Sharma S.C.[14] Treated OSMF patients by dividing them into 8 groups. All groups received biweekly submucosal injections of different drugs for 10 weeks.

- Group 1 – Inj. Dexamethasone 4 mg
- Group 2 – Inj. Hyaluronidase 1500 IU
- Group 3 – Inj. Chymotrypsin
- Group 4 – Inj. Placental Extract 2 ml
- Group 5 – Inj. Dexamethasone and Inj. Hyaluronidase.
- Group 6 – Inj. Dexamethasone and Chymotrypsin
- Group 7 – Inj. Dexamethasone, Hyaluronidase and Chmotrypsin.
- Group 8 – Inj. Dexamethasone and Placental extract.

Better results were obtained by giving local injections of Dexamethasone, Hyaluronidase and chymotrypsin. Khanna J.K. and Andrade N.N. [15] studied 100 OSMF cases over 6 years by dividing them into 4 categories.

- Group1 – Very early cases, received Inj. Triamcinolone Acetate.
- Group 2 – Early cases received Inj. Triamcinolone Acetate.
- Group 3 – Moderately advanced cases, Treated surgically
- Group 4a – Advanced cases, Treated surgically.
- Group 4b – Advanced cases with pre malignant and malignant changes. Treated surgically

Patients of Group 1 and Group 2 responded favorably. Kumar et. Al [15] evaluated fifty-eight patients with oral submucous fibrosis and randomly divided them into 3 groups, evaluated weekly over a 2-month period. Patients of group A (n = 21) received 16 mg of lycopene. Group B (n = 19) were given 16 mg of lycopene along with biweekly intralesional steroid injections, and those of group C (n =18) were given a placebo. Mouth opening, burning sensation, visual findings in concern with the shape of the uvula and tongue protrusion and palpatory findings in respect to presence of bands weekly were studied as parameters. Mouth-opening values for the patients showed an average increase of 3.4 mm, 4.6 mm, and 0.0 mm for patients in groups A, B, and C, respectively.

The results indicated that lycopene either singly or in combination with intralesional steroids is, indeed, efficacious in improving the mouth opening in patients with sub mucous fibrosis and in reducing associated symptoms. Lin HJ, Lin JC [16] included twenty seven patients with well-developed OSMF, as verified by biopsies and divided them into three groups (A, B, and C) with nine patients in each group. Patients in group A, regardless of age, received phosphate buffered saline injection as a control. Patients in group B were injected with 1 ml of Triamcinolone diacetate plus 1 ml of xylocaine and group C patients with 1 ml of collagenase (1% solution) mixed with 1 ml of xylocaine.

All patients received their injections once a week for 6 weeks. The effect of treatment was monitored weekly by measuring the extent of mouth opening, response to spicy foods, tolerance to cold and hot foods, blood circulation and stiffening of the oral mucosa by fibrous bands in the area affected. Their results revealed that collagenase treatment not only resulted in a significant improvement of oral opening, but patients also experienced a striking reduction in hypersensitivity to spices, sour, cold, and heat which helped restore eating function.

They concluded that reduced content of functional collagenase observed in OSMF mucosa of patients might be a mechanism responsible for collagen accumulation. Therefore, the intervention of OSMF by collagenase treatment at the early stage may reduce the incidence of developing oral carcinoma. Similarly, in our study, we found improvement in recurrent ulcerations, burning sensation in the oral cavity, improvement in blanching of the oral mucosa.

However, objective parameter of measurement of inter-incisor teeth distance was used as a criterion to assess the clinical improvement. Ameer N. T. and Shukla R. K.[12] studied 52 patients of OSMF who were injected Triamcinolone Acetate 1 ml (40 mg) biweekly for 12 weeks. The effect of therapy was evaluated subjectively by improvement in symptoms and objectively by increase in mouth opening. Triamcinolone Acetate had a significant effect on oral sub mucous fibrosis and its effect depends on the stage of presentation and frequency of the chewing habits and not on the duration of the habits.

In our study**,** pretreatment mean was 19.42 ± 4.35 and post treatment mean was 27.46±7.13. Paired t test was applied and p value obtained was less than 0.001 i.e. very highly significant. Hence, post treatment with Triamcinolone therapy, highly significant improvement in mouth opening i.e. interincisor teeth distance was noted. There was a highly significant positive correlation between the pretreatment inter-incisor distance and post treatment inter-incisor distance. Coefficient of correlation was calculated between these variables and P value was < 0.001 i.e. very high significant.

Hence, there was more benefit of therapy in those patients in whom the pretreatment inter-incisor distance was more (i.e. in early stage of the disease). Highly significant correlation was found between initial inter-incisor teeth distance and increase in inter-incisor teeth distance. This was consistent with study by Ameer N.T. and Shukla R.K. (2012).

We therefore infer that there is significant effect of Local Injection Triamcinolone therapy in the treatment of OSMF and its effect depends on duration of chewing habit. Statistically significant negative correlation was found between the duration of the chewing habit and the increase in mouth opening. (P = 0.04203, less than 0.05 so statistically significant). So if the duration of chewing habit is more, then the effect of Inj. Triamcinolone therapy is less. Ameer N.T. and Shukla R.K. (2012) concluded that there was no significant correlation between the duration of the chewing habit and increase in inter-incisor teeth distance after Inj. Triamcinolone therapy. Highly significant negative correlation between frequency of addiction and increase in mouth opening (R= -0.42, P=0.002171 i.e. P < 0.01) was noted. This implies that the increase in mouth opening following Triamcinolone therapy is less in patients whose frequency of chewing habit is more and vice versa. This finding is consistent with the study done by Ameer N. T. and Shukla R.K. (2012) says that there was a highly significant negative correlation (P= 0.0007) between frequency of addiction and increase in mouth opening.

Key Messages

Thus we conclude that there is both subjective and objective improvement in OSMF after treatment with intralesional steroid injection treatment. Response to treatment varies with:

1. Stage of the presentation (Early the stage, the effect of triamcinolone therapy is more)
2. Frequency of chewing habits (if frequency is more effect of triamcinolone therapy is less and vice versa)
3. Duration of the chewing habits (effect of therapy is more if duration of chewing habit is less and vice versa)

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