

**COMPARATIVE STUDY FOR MANAGEMENT OF ORAL SUBMUCOSAL FIBROSIS  
BY USING TWO DIFFERENT DRUG REGIMENS**

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**ABSTRACT**

**Background:** Oral submucous fibrosis (OSMF) is a chronic debilitating and potentially malignant condition of the oral cavity. It is resistant and progressive affecting the entire oral cavity that sometimes causes a gradual reduction in mouth opening that may even extend up to the pharynx. Although the medical treatment is not completely systematized, optimal doses of its treatment with local injection of corticosteroids with hyaluronidase or placental extract is effective to some extent. However, a combination of oral drugs along with locally injectable drugs shows better long-term results than either agents used individually. **Materials and Methods:** A total of 60 patients diagnosed with OSMF were divided into 2 groups, group 1 patients receiving oral drugs along and group 2 were treated by administering an intralesional injection of dexamethasone 2 ml, hyaluronidase 1500 IU with 0.5 ml lignocaine HCL injected intralesionally weekly for 6 months along with the oral drugs used for group 1 patients. **Results:** Improvement in the patient's mouth opening with Definite reduction in burning sensation, painful ulceration and blanching of oral mucosa and patient followed up for an average of 6 months. **Conclusion:** Injection of hyaluronidase with dexamethasone is an effective method of managing OSMF and can possibly eliminate the morbidity associated with surgical management.

**KEYWORDS:** Dexamethasone, hyaluronidase, oral submucosal fibrosis, oral drugs.

**INTRODUCTION**

The oral submucous fibrosis (OSMF) as defined by Pindborg and Sirsat as an insidious chronic fibrotic disease that involves the oral mucosa and occasionally the pharynx and upper third of oesophagus. OSMF is characterized by a juxtraepithelial inflammatory reaction followed by fibroelastic changes in the submucosa and epithelial atrophy, that leads to stiffness of the oral mucosa causing trismus and inability to eat.<sup>[1]</sup> The term oral submucous fibrosis (OSF) follows from oral (meaning mouth), submucosal (meaning below the mucosa of the mouth) and fibrosis (meaning hardening and scarring).<sup>[2]</sup> OSF has a multifactorial etiology. Several factors such as chilli consumption, nutritional deficiency states, areca nut chewing, genetic susceptibility, autoimmunity & collagen disorders have been suggested to be involved in the pathogenesis of the

condition.<sup>[3]</sup> A wide range of treatment including drug management, surgical therapy, and physiotherapy have been attempted till date, with varying degrees of benefit, but none have been able to cure this disease.<sup>[4]</sup> This is mainly due to the fact that the etiology of the disease is not fully understood and the disease is progressive in nature.<sup>[5]</sup> Instead of continuing the limited available modes of therapy, the idiopathic nature of this condition indicates new avenues for its management.<sup>[6]</sup>

The aim of this comparative study was to compare the efficacy of orally administered drugs that consists of Alpha Lipoic Acid, Beta-Carotene, Elemental Copper, Elemental Selenium, Lycopene, Vitamin E, Zinc Sulphate (branded as S M Fibro) along with antioxidants and vitamins supplements and intralesional injection of Hyaluronidase 1,500 IU and 2 ml of injection

Dexamethasone along with 0.5 ml 2% lignocaine in each buccal mucosa once a week alternatively along with the oral drugs.

#### PATIENTS AND METHODS

This study was conducted in at our institution, between 2015 and 2017. The patients for the study were selected from those who visited our department. A formal ethical clearance to conduct this study was given by the Ethical Committee of the institute. An informed consent was obtained from the patients before including them in the study. A detailed case history of the patient with emphasis on their habits (chewing betel nut, tobacco products, chilly consumption etc.) and a thorough clinical examination was recorded on a designed proforma. A clinical diagnosis of OSF was made based on the World Health Organization (WHO) criteria and the patients were graded clinically according to Gupta Dinesh Chandra S. *et al.*<sup>[7]</sup> The diagnosis was confirmed histopathologically by a punch biopsy of the lesion. 60 patients in the age group of 15 years to 60 years, thus diagnosed as having OSF, were included in the study and were divided randomly into two groups for the purpose of study. Group 1-Patients were administered orally tablet that consists of Alpha Lipoic Acid, Beta-Carotene, Elemental Copper, Elemental Selenium, Lycopene, Vitamin E, Zinc Sulphate (branded as S M Fibro) along with antioxidants and vitamins supplements. Group 2-Patients were administered intralesional injection of Hyaluronidase 1,500 IU and 2 ml of injection Dexamethasone along with 0.5 ml 2% lignocaine in each buccal mucosa once a week along with the drugs in group 1. Patients in both the groups were asked to discontinue all betel nut chewing habits during the entire study period. Both groups were treated for 6 months. Patients were asked to observe for any local allergic symptoms as itching, redness or ulcerations at the site of injection or if any constitutional symptoms developed and to report the same immediately. Treatment was

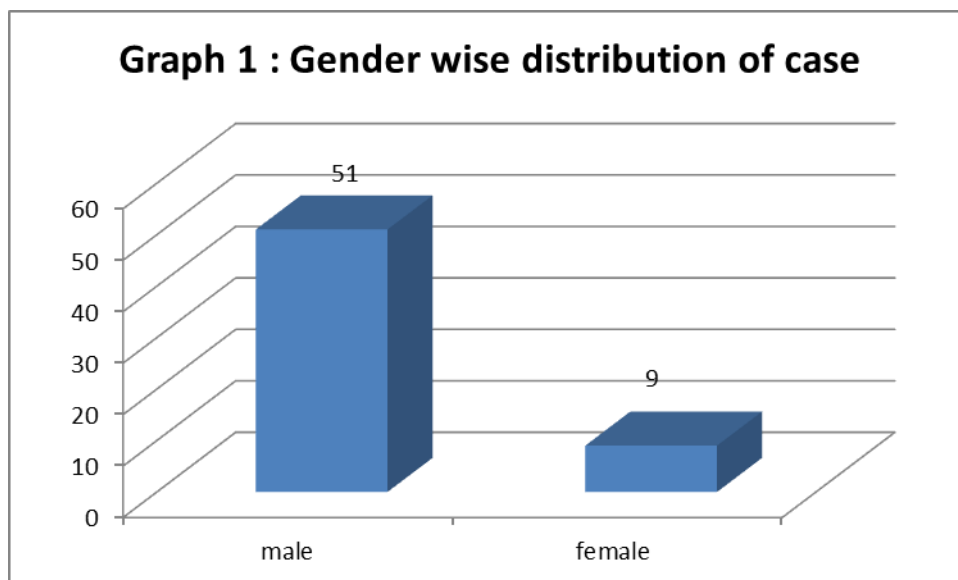
discontinued in such patients. During the subsequent visits the patient's response to the treatment procedures was recorded with emphasis on ascertaining the amelioration of specific symptoms like burning sensation, trismus, and intolerance to hot and spicy foods. Clinical examination of the oral mucosa, site of lesion, margins, extension, color and surface texture and presence of fibrotic bands was recorded. The interincisal opening of the mouth was recorded during each visit.

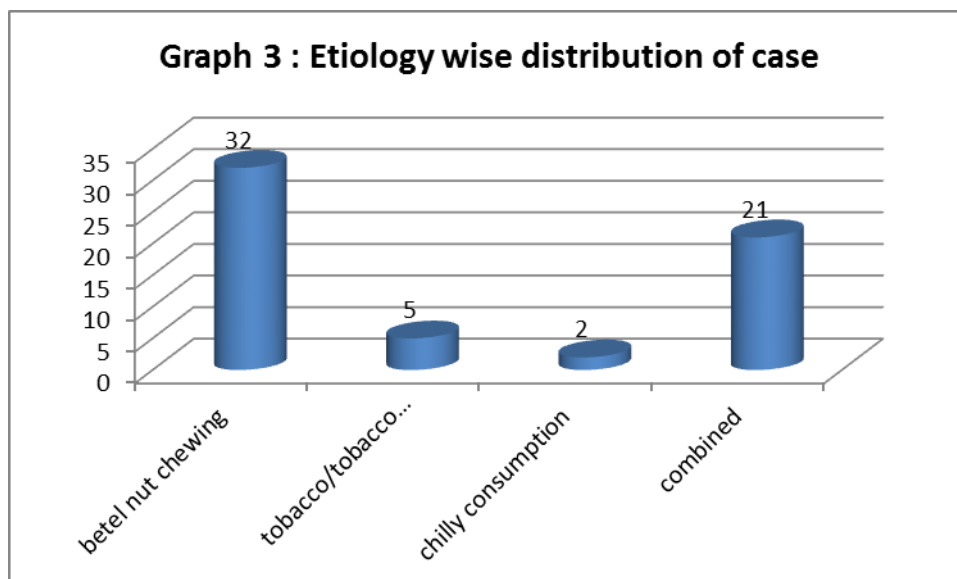
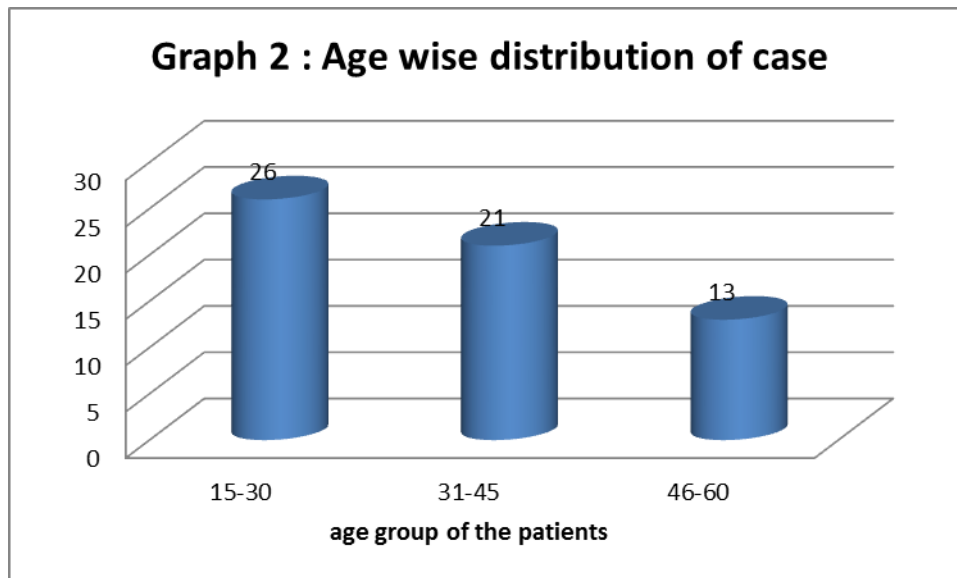
#### RESULTS

60 patients of OSMF were selected for the present study and were divided randomly into two groups with 30 patients of OSMF in each group. Out of 60 patients 51 were male and 9 were female (graph 1). The age of patients in our study ranged between 15 to 60 years with maximum number of patients between 15-30 years age group (graph 2). The most common etiology was betel nut chewing consisting of 32 cases (graph 3). The interincisal opening in our study ranged from 10mm to 34 mm (table 1).

The patients in the first group were given orally tablet that consists of Alpha Lipoic Acid, Beta-Carotene, Elemental Copper, Elemental Selenium, Lycopene, Vitamin E, Zinc Sulphate (branded as S M Fibro) along with antioxidants and vitamins supplements and the patients in the second group were given intralesional injections of 2ml of Dexamethasone 4mg/ml, 0.5 ml of Lignocaine 1:80000 and 1500 IU of Hyaluronidase along with the drugs in group 1, every week for 6months.

Table 2 represents % of relief of symptoms post treatment in both the groups which states that there was improvement in symptoms in patients of both the groups but patients in group 2 receiving injection along with oral drugs as in group 1 showed better response to the treatment.





**Table 1 : Distribution of cases based on interincisal opening pre treatment.**

Inter-incisal opening	No. of patients
10-14	12
15-19	14
20-24	18
25-29	11
30-34	5

**Table 2: % of relief of symptoms post treatment in both the groups.**

Symptoms	Group 1 (relief of symptoms %)	Group 2 (relief of symptoms %)
Limited mouth opening	25/30 (83.33%)	29/30 (96.66%)
Burning sensation	27/30 (90%)	30/30 (100%)
Tongue protusion	26/30 (86.66%)	29/30 (96.66%)
Cheek flexibility	23/30 (76.66%)	29/30 (96.66%)
Painful ulceration	30/30 (100%)	100/30 (100%)
Blanching of oral mucosa	24/30 (80%)	28/30 (93.33%)

## DISCUSSION

OSMF is a precancerous condition and reports suggest that it is present since the time of Sushruta 5. reported by

Schwartz in 1962 and by Joshi in 1953; who described its singleton among the Indians. Several medical and surgical approaches have been tried for the management

of OSF over the decades. The results are not predictable with some therapies and none has been consistently successful. Many trials have been conducted but as such no definitive treatment is currently available.<sup>[8]</sup>

Conservative line of treatment like topical steroids, vitamins, antioxidants, physiotherapy would give expected symptomatic relief of pain and burning sensation.<sup>[9]</sup> Treatment modalities like intralesional injections of placental extracts that acts essentially by biogenic stimulation based on tissue therapy are also encouraged.<sup>[10]</sup> Clinical trial by Haque *et al.* using gamma-interferon treatment has shown improvement in the patients mouth opening<sup>[11]</sup> (inter incisal distance) with net gain of  $8 \pm 4$  mm (42%), the range being 4-15 mm. Excision of fibrous bands is also managed by CO<sub>2</sub> and KTP laser,<sup>[12]</sup> a potassium-titanyl-phosphate that doubles the frequency of pulsed neodymium:yttrium-aluminium garnet laser energy to 532 nanometer wavelength.<sup>[13,14]</sup>

However, improvement can be obtained passably by intralesional injection of cortisone and hyaluronidase.<sup>[15]</sup> as in our study. It was observed that patients receiving oral drugs alone showed improvement in the burning sensation and painful ulceration produced by the effects of local by-products, although combination of oral drugs along with injection of dexamethasone and hyaluronidase gave better long-term results than other regimens.<sup>[16]</sup> and this was in line with the findings of our study. However, the addition of dexamethasone has its own advantages and contraindications and a slight improvement in the overall result observed in the combination group justifies the addition of dexamethasone to hyaluronidase.

Since, large amounts of the drug and its metabolites enter the liver and then the bile and, hence, should not be administered to patients with hepatic disease.<sup>[17]</sup> Follow-up blood cell count should also be performed periodically and medication stopped if the toxic effects develop. Tests to determine baseline serum urea nitrogen, creatinine levels, a complete blood cell count, and liver function test, performed prior to initiating the treatment and during follow-up of our patients also recorded values within the normal range.

## CONCLUSION

To, conclude, in the present study, the increase in mouth opening, decrease in burning sensation and improvement in cheek flexibility in puffed state in oral submucous fibrosis patients showed better results by treatment with combination of oral drugs along with injection of dexamethasone and hyaluronidase than oral drugs alone. The encouraging results should prompt a clinical trial on more number of OSMF patients to broaden the therapeutic usefulness and applications of one of our most ancient treatment agents. This baseline study gives scope for further studies with the injection of

dexametasone and hyaluronidase alone in the treatment of OSMF.

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