

## Original Article



# Study On Outcome of Different Combination of Dexamethasone, Hyaluronidase and Placental Extract for Treatment of Oral Submucous Fibrosis

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### Abstract

**Background:** Oral submucous fibrosis is a chronic debilitating disease of the oral cavity characterized by inflammation and progressive fibrosis of the submucosal tissues. It is a precancerous condition of the oral mucosa characterized by excessive production of collagen leading to inelasticity of the oral mucosa and atrophic changes of the epithelium. 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. **Objectives:** To evaluate the efficacy of Intralesional 'Dexamethasone Plus Hyaluronidase plus Placental extract in comparison to intralesional injections of 'Dexamethasone plus Hyaluronidase in the management of OSMF patients. **Materials and Methods:** Thirty patients with OSMF were randomly divided equally into two groups. Fifteen patients in 'Dexamethasone plus Hyaluronidase(Group-I)' group received biweekly intralesional injections of Dexamethasone (4mg/ml) plus Hyaluronidase 1500 IU in buccal mucosa for a period of 12 weeks. Other Fifteen patients in'Dexamethasone plus Hyaluronidase plus placental extract (Group-II)' group received biweekly intralesional injections of Dexamethasone (4mg/ml) plus Hyaluronidase 1500 IU plus placental extract in buccal mucosa for a period of 12 weeks. Parameters taken in the study were burning sensation, and mouth opening. Descriptive statistics, paired t test and unpaired t test were used for statistical analysis. **Results:** The pre- and post-treatment Differences were found to be statistically not significant for both the groups ( $p < 0.001$ ) and for both the treatment outcomes. **Conclusion:** In the present study, the efficacy of Intralesional 'Dexamethasone Plus Hyaluronidase plus Placental extract' showed no superiority over intralesional injections of 'Dexamethasone plus Hyaluronidase' in the management of OSMF patients.

**Key words:** Anti-fibrotic, Mouth Opening, oral Submucous Fibrosis (OSMF).

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### Introduction

Oral Submucous Fibrosis (OSMF) is a debilitating but preventable oral disease.<sup>1</sup> Oral submucous fibrosis is a chronic insidious disease and a well recognized pre-malignant condition of the oral cavity characterized by inflammation and a progressive fibrosis of the lamina propria and deeper connective tissues. Although occasionally preceded by vesicle formation, it is always associated with juxta-epithelial inflammatory reaction followed by a fibroelastic change of lamina propria with epithelial atrophy leading to stiffness of oral mucosa, causing trismus.<sup>2</sup> The condition is seen predominantly in residents of Asia with more prevalence in

India. OSMF has also been found in Nepal, China, Thailand and South Vietnam.<sup>3</sup> OSMF has a multifactorial etiology. Chilli consumption, nutritional deficiency states, areca nut chewing, genetic susceptibility, autoimmunity & collagen disorders have been suggested to be involved in the pathogenesis of this condition.<sup>4</sup> The main etiological agent causing the disease is confirmed as arecoline in arecanut.<sup>5</sup> It is considered as a disorder of collagen metabolism and is characterized by increased production and decreased degradation of collagen fibers.<sup>6</sup> This leads to inelasticity of the oral mucosa and atrophic changes of the epithelium.<sup>7</sup> Thick inelastic rope like fibrous bands appear vertically in the

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buccal mucosa, along the contours of the faucial pillars and around the entire circle of lips thus leading to trismus.<sup>8</sup> The fibrosis also leads to difficulty in mastication, speech and swallowing, pain in the throat and the ears, burning sensation on taking spicy food, excessive salivation.<sup>9</sup> The most common sign of oral submucous fibrosis is the presence of palpable bands in the oral mucosa, especially in the buccal mucosa. Other features of this condition are diffuse blanching of the mucosa, hyperpigmented areas adjacent to zones with loss of pigment, loss of tongue papillae, a leathery consistency of the mucosa etc. The risk of the development of oral squamous cell carcinoma (SCC) is observed.

Various treatment modalities have been tried to treat patients suffering from this disease.<sup>10</sup> Medical interventions include dietary supplementation with vitamins, antioxidants, corticosteroid therapy, proteolytic agents such as hyaluronidase and placental extracts and anticytokines.<sup>11</sup> Surgical intervention is sometimes needed. Severe trismus and refractory cases are treated by surgical excision of fibrous bands.<sup>2</sup> The main goal of the treatment of OSMF is to reduce trismus and burning sensation. One of the important therapeutic modalities is intralesional injection therapy. The most commonly used intralesional agents are placental extract, corticosteroids and hyaluronidase. The mechanism of action and therapeutic efficacy vary from one drug to another and their combinations used.<sup>12</sup> Steroids have anti-inflammatory action which helps to provide symptomatic relief. It also has antifibrotic activity and prevents fibrosis by decreasing fibroblastic proliferation and deposition of collagen.<sup>13</sup> Hyaluronidase causes breakage and dissolution of fibrous bands thus providing relief from the condition.<sup>14</sup> It acts by breaking down hyaluronic acid.

## Materials and Method

This was an interventional study. The study was conducted in different dental clinic and Dental unit of Rajshahi Medical College, Rajshahi during the last Two years time. This study is intended to compare the efficacy of Intralesional 'Dexamethasone Plus Hyaluronidase plus Placental extract in comparison to intralesional injections of 'Dexamethasone plus Hyaluronidase in the management of OSMF patients. Prior to conducting the study, the subjects were explained the need for the study and a written consent was taken from them. Patients who were not taking any medications for OSMF previously were only included in the study. Patients with known systemic diseases such as bleeding and clotting disorders, cardiac disorders, diabetes mellitus, renal or hepatic disorders, collagen diseases like scleroderma, thromboembolic disorders were excluded from the study. Also Patients not willing to participate in study or not ready to quit the use of quid were excluded from study. Patients having clinical or histological evidence of malignant change, extension of the disease either onto the pharynx or floor of mouth were also excluded. Patients having history of recent myocardial infarction, uncontrolled hypertension, diabetes, peptic ulcer, tuberculosis, and cirrhotic liver disease were all excluded as steroids can

potentially worsen the aforementioned conditions. A detailed case history of the patient with emphasis on their habits (chewing betel nut, pan parag, guthkha etc.) was taken. Clinical examination conducted and was recorded on a standard proforma. VAS scale was used to record the severity of burning sensation in the patients, with the severity of symptoms extending from a numerical 0 (no pain or discomfort) to 10 (severe most pain /discomfort). Patients' maximum mouth opening was measured by measuring the distance between the centre of incisal edges of maxillary central incisors and mandibular central incisor at maximum opened mouth position.<sup>18</sup> A clinical diagnosis of OSMF was made and the patients were graded clinically according to the classification of Ranganathan K et al.<sup>27</sup> The subjects were counseled to quit the habit during the study period. Thirty patients in the age group of (50-70 years), thus diagnosed as having OSMF, were included in the study and were divided randomly into two groups for the purpose of treatment. The study was conducted to evaluate the efficacy of Intralesional 'Dexamethasone plus Hyaluronidase plus Placental extract' in comparison to intralesional injections of 'Dexamethasone plus Hyaluronidase' in the management of OSMF patients.

Thirty patients with OSMF were randomly divided equally into two groups. 15 patients in 'Dexamethasone plus Hyaluronidase' group received biweekly intralesional injections of Dexamethasone (4mg/ml) plus Hyaluronidase 1500 IU in buccal mucosa for a period of 12 weeks. Other 15 patients in 'Dexamethasone plus Hyaluronidase plus placental extract' group received biweekly intralesional injections of Dexamethasone (4mg/ml) plus Hyaluronidase 1500 IU plus placental extract in buccal mucosa for a period of 12 weeks. Parameters taken in the study were burning sensation, and mouth opening. Descriptive statistics, paired t test and unpaired t test were used for statistical analysis.

## Result

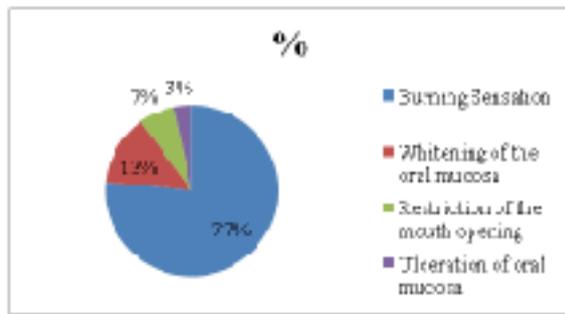
Among the thirty patients the maximum age range was 70 and lowest range was 40 (Table I). Among the studied patients was more (67%) than the male (33%) patients (Table II). Burning Sensation, Whitening of the oral mucosa, Restriction of the mouth opening, Ulceration of oral mucosa are the main presentation of Oral Submucous Fibrosis (Figure 1). The pre- and post-treatment Differences were found to be statistically not significant for both the groups ( $p < 0.001$ ) and for both the treatment outcomes.

**Table I:** Age distribution of the patients (n=30)

Variables	Years	Percentage (%)
Age	40-50	60
	50-60	30
	60-70	10

**Table II:** Sex distribution of the patients (n=30)

Variables	Number of Patients	Percentage (%)
Male	10	33
Female	20	67



**Figure 1:** Manifestations of the studied patients (n=30)

**Table III:** Outcome of the patients in Group I (Two Drugs regime) (n=15)

Variables	Improvement of the patients				Percentage (%)
	Burning Sensation	Whitening of the oral mucosa	Restriction of themouth opening	Ulceration of oral mucosa	
Follow up at 6 months	10	1	1	0	85.75
Follow up at 9 months	5	1	0	0	13.25
Follow up at 12 months	0	0	0	0	0.00
Follow up at 18 months	0	0	0	0	0.00

Outcome of two drugs regime at 6<sup>th</sup>, 9<sup>th</sup>, 12<sup>th</sup>, 18<sup>th</sup> month.

**Table IV:** Outcome of the patients in Group II (Three Drugs regime) (n=15)

Variables	Improvement of the patients				Percentage (%)
	Burning Sensation	Whitening of the oral mucosa	Restriction of the mouth opening	Ulceration of oral mucosa	
Follow up at 6 months	8	0	0	0	85.75
Follow up at 9 months	4	0	0	0	6.25
Follow up at 12 months	2	1	0	0	4.25
Follow up at 18 months	1	1	1	0	2.75

Outcome of two drugs regime at 6<sup>th</sup>, 9<sup>th</sup>, 12<sup>th</sup>, 18<sup>th</sup> month.

**Table V:** Comparison between the improvement proportions of two groups:

Follow up	Percentage of Improved Patients		P value
	Group I	Group II	
6 months	85.75	85.75	1.0 0.5252
9 months	13.25	6.25	
12 months	0	4.25	0.4275
18 months	0	2.75	0.5249

## Discussion

OSMF is a chronic debilitating condition with a high risk of malignant transformation. It is a chronic disease and differs in symptoms and severity at every stage.<sup>17</sup> Many surgical and therapeutic treatments have been tried for the cure of OSMF, but still no definitive or widely accepted treatment is currently available.<sup>7</sup> Intralesional injections of drugs like dexamethasone, triamcinolone, hyaluronidase and placental extract have shown relief from the symptoms and improvement in the mouth opening in patients with OSMF.

Various combinations of drug regimens have been used in the treatment of OSMF and each drug has a different mechanism of action.<sup>7</sup> Among the thirty patients the maximum age range was 70 and lowest range was 40. All of the patients had habit of chewing gutkha, pan, areca nut. This finding was similar to that of Aara et al., Bhatta et al Shah et al.<sup>21-23</sup> This finding emphasizes the role of areca nut as the main etiologic factor for OSMF.<sup>23</sup> In the present study, increase in mouth opening and reduction in burning sensation were considered as two basic parameters to compare the efficacy of both the regimen. Statistically significant improvement was observed both in mouth opening and burning sensation with the use of hyaluronidase+dexamethasone combination indicating the efficacy of this regimen in the treatment of OSMF. When the therapeutic efficacy of both the regimen was compared, it was not statistically significant in term of Burning Sensation, Whitening of the oral mucosa, Restriction of the mouth opening and Ulceration of oral mucosa.

## Conclusion

It was an intervention study of with small sample size, which doesn't reflect the scenario of the whole country. In the present study, the efficacy of Intralesional 'Dexamethasone Plus Hyaluronidase plus Placental extract' showed no superiority over intralesional injections of 'Dexamethasone plus Hyaluronidase' in the management of OSMF patients.

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