

EFFIACY OF BETAMETHASONE, PLACENTAL EXTRACT AND HYALURONIDASE IN THE TREATMENT OF OSMF: A COMPARATIVE STUDY

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ABSTRACT

INTRODUCTION: Oral submucous fibrosis, an insidious chronic precancerous condition of oral cavity, chiefly occurs in the Indian sub continent. It is characterised by excessive collagen formation and thus stiffness and inelasticity of oral mucosa. It manifests as stiffness of oral mucosa, trismus, burning sensation thus affecting the general well being of patient. Intralesional injection of drugs like betamethasone, placental extract and hyaluronidase helps to improve the condition and thus the health of the patient.

OBJECTIVE: To evaluate the efficacy of betamethasone, placental extract and hyaluronidase therapy in the treatment of oral submucous fibrosis.

MATERIALS AND METHODS: Fifteen patients with clinico-pathologically diagnosed oral submucous fibrosis were included in the study. All patients underwent hematological and clinical examination to rule out any systemic disease. Patient with TMJ disorder or restricted mouth opening due to pericoronitis and other causes were excluded. Patients were divided randomly into three groups and betamethasone, placental extract & hyaluronidase intralesional injection was given to the separate groups of the patient for a period of 8 weeks. Mouth opening and burning sensation was recorded clinically & subjectively.

RESULTS: Observed data were compared statistically using Student's Paired t test analysis for the efficacy of the drugs used and the results were tabulated. Improvement in mouth opening was observed the maximum with intralesional injection of hyaluronidase with 9.38mm in average ($t= 27.61$; $p= 0.0000$) and improvement in burning sensation was observed maximum with intralesional injection of betamethasone ($t= 12.35$; $p= 0.0002$).

CONCLUSION: Oral submucous fibrosis is a chronic precancerous condition. Though there is no definitive treatment for the condition, intralesional injection of betamethasone, placental extract and hyaluronidase may provide relief from restricted mouth opening and burning sensation thereby improving the quality of life of the affected individual.

Key words: Betamethasone; hyaluronidase; oral submucous fibrosis; placental extract

INTRODUCTION

Oral submucous fibrosis is known since ancient age. Sushruta – the ancient Indian medical text, describes a condition termed “VIDARI” under mouth and throat diseases as ‘progressive narrowing of mouth, depigmentation of oral mucosa and pain on taking food.’¹ In the modern literature, this condition was first reported by Schwartz (1952). Joshi (1953) was the first person to describe this entity in India. The prevalence of submucous fibrosis in India is up to 0.4%. It affects an estimated 2.5 million people, mostly in Indian subcontinent. Incidence of oral cancer is 7.6% with median 10 yrs follow up period. It is associated with the practice of chewing betel quid products containing areca nut such as Pan, Gutka, Mawa. This condition is prevalent between the age group of 11-60 years.²

Oral submucous fibrosis is a disease due to a chronic, insidious change in fibroelasticity, characterized by burning sensation in the oral cavity, blanching, and stiffening of the oral mucosa and oro-pharynx leading to trismus and inability to open the mouth (Fig.1). The condition starts with inflammation and ulceration inside the mouth that eventually replaced by fibrous tissue as it heals. It is a precancerous condition that is likely to cause malignancy of oral mucosa and oro-pharyngeal structures. It is an irreversible and yet avoidable collagen metabolic disorder of the mouth.



Fig.1

Most important aspect of medical treatment is cessation of habit of eating betel quid, arecanut, other local irritants, spicy and hot food, alcohol and smoking. The most common mode of medical treatment had been the use of steroids in its various forms.

In our institution a study was done to compare the efficacy of three individual drugs (Betamethasone; Hyaluronidase; Placental extract) in the treatment of oral submucous fibrosis. Clinico-pathologically diagnosed cases of oral submucous fibrosis were included in our study. Patient with TMJ disorder or restricted mouth opening due to pericoronitis and other causes were excluded from our study.

MATERIAL AND METHOD

This prospective clinical study was done on 15 cases of clinically diagnosed oral submucous fibrosis who reported to the department of oral medicine and radiology. Clinical diagnosis of oral submucous fibrosis was based on symptom of burning sensation in the mouth upon consumption of spicy or hot foods and palpable fibrous bands. Patients were randomly assigned into three groups (Gr. A, Gr. B, Gr. C). Informed consent was obtained. Detailed history with reference to oral habits like chewing paan, betel nut, tobacco etc. obtained. Routine blood examination was done. Initial mouth opening was measured by using vernier caliper in millimeters (Fig 2).



Fig.2

VAS (Visual Analog Scale)

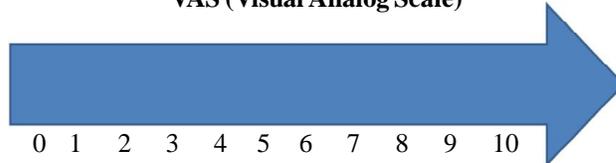


Fig.3

Burning sensation was assessed by visual analog scale (VAS) Fig.3. Fibrous bands were palpated and 26 gauge needle was used to inject the drug submucosally at multiple sites bilaterally. Group A was treated with intralesional injection of betamethasone 4mg/ml weekly; Group B with 2ml of placental extract (market preparation manufactured from 0.1gm of fresh human placenta) weekly. Group C with Hyaluronidase 1500 IU mixed with 2% lidocaine. The duration of treatment for all three groups was 8 weeks. Response to the treatment was evaluated every week. Improvement in mouth opening was measured using vernier scale and in burning sensation was measured by visual analogue scale.

RESULTS

The study group consisted of fifteen patients. Male to female ratio was 4:1. The age range was between 32-46 years with a mean age of 43.6 years. In Group A (Betamethasone) the average improvement in mouth opening was 7.34 mm with maximum reduction in burning sensation (Table A). In Group B (Placental Extract) average improvement in mouth opening was 5.86mm with marked reduction in burning sensation (Table B). In Group C (Hyaluronidase) improvement in mouth opening was 9.38mm with moderate reduction in burning sensation.

TABLE I (Betamethasone Gr.)

Patient	Age	Sex	Mouth opening(mm)			Burning sensation (VAS)		
			Initial	Final	Difference	Initial	Final	Difference
A	40	M	12.3	17.2	04.9	9	2	7
B	42	M	14.2	21.3	07.1	10	2	8
C	36	M	20.2	30.5	10.3	9	0	9
D	32	F	16.3	24.2	07.9	8	2	6
E	34	M	18.5	25	06.5	8	2	6

Average improvement in mouth opening was 7.34 mm with maximum reduction in burning sensation

TABLE II (Placentex Gr.)

Patient	Age	Sex	Mouth opening(mm)			Burning sensation (VAS)		
			Initial	Final	Difference	Initial	Final	Difference
A	45	M	25.4	29.2	4.8	10	5	5
B	43	M	18.3	25.5	7.2	10	4	6
C	39	F	23.2	28.4	5.2	9	4	5
D	36	M	20.1	26.1	6.0	8	3	5
E	37	M	15.2	21.3	6.1	8	3	5

Average improvement in mouth opening was 5.86mm with marked reduction in burning sensation

TABLE III (Hyaluronidase Gr.)

Patient	Age	Sex	Mouth opening(mm)			Burning sensation (VAS)		
			Initial	Final	Difference	Initial	Final	Difference
A	46	F	17.5	26.5	9	8	4	4
B	45	M	20.1	30.5	10.4	10	6	4
C	38	M	22.4	31.5	9.1	7	4	3
D	34	M	16.5	25.0	8.5	9	5	4
E	33	M	15.3	25.2	9.9	10	5	5

Average improvement in mouth opening was 9.38 mm with moderate reduction in burning sensation.

TABLE IVA

Paired t-test results comparing improvement in mouth opening before and after treatment

Variable	Mouth opening (mm)	Change Mean+ SD	t value	p value
	Mean+ SD			
Hyaluronidase Before After	18.36 ± 2.87 27.74 ± 3.05	9.4 ± 0.76	27.61	0.0000
Placentex Before After	20.44 ± 4.01 26.10 ± 3.09	5.7 ± 1.26	10.04	0.0006
Betamethasone Before After	16.30 ± 3.18 23.64 ± 4.90	7.3 ± 1.99	8.26	0.0012

p values are significant (at 1% level) for all

TABLE IV B

Paired t-test results comparing improvement in burning sensation before and after treatment

Variable	Burning sensation	Change Mean+ SD	t value	p value
	Mean+ SD			
Hyaluronidase Before After	8.8 ± 1.30 4.8 ± 0.84	4.2 ± 0.71	12.65	0.0002
Placentex Before After	9.0 ± 1.00 3.8 ± 0.84	5.2 ± 0.45	26.00	0.0000
Betamethasone Before After	8.8 ± 0.84 1.6 ± 0.89	7.2 ± 1.30	12.35	0.0002

p values are significant (at 1% level) for all

DISCUSSION

Oral submucous fibrosis is a high risk precancerous condition that predominantly occurs among Indians. Many therapeutic and surgical methods have been tried in the treatment of Oral Submucous Fibrosis. No definitive and widely accepted treatment is currently available. Some temporary relief from the symptoms and improvement in the oral opening with medicinal treatment such as local injections of cortisone, hyaluronidase and placental extract has been observed.

Steroids act by opposing the action of soluble factors released by sensitized lymphocytes following activation by specific antigens steroids act as immunosuppressive agents. It also prevents or suppresses inflammatory reactions thereby preventing fibrosis by decreasing fibroblastic proliferation and deposition of collagen. The initial symptomatic relief could be due to the anti inflammatory action of the steroids, which helps in clearing the juxtaepithelial inflammation⁷. Placentrex is an aqueous extract of human placenta that contains nucleotides, enzymes, vitamins, amino acids, and steroids. Its action is essentially "biogenic stimulation" which suggested that it stimulates the pituitary and the adrenal cortex, and regulates the metabolism of tissues. It also increases the vascularity of tissues. Its use is based on the method of "tissue therapy" which explains that animal and vegetable tissues, when severed from the parent body and exposed to conditions unfavourable but not mortal to their existence, undergo biological readjustment leading to development

of substances in state of their survival to ensure their vitality. Such tissues or their extracts, implanted or injected into the body after resistances to pathogenic factors, stimulate the metabolic or regenerative processes, thereby favouring recovery¹¹. Hyaluronidase causes breakage and dissolution of fibrous bands thus providing relief from the condition³. By virtue of its specific action on hyaluronic acid, which plays an important role in the formation of collagen, hyaluronidase may be responsible for the better results in patients with restricted mouth opening.

Reduction of burning sensation and improvement in mouth opening were the basis of our treatment regimen. In our institution three different drug regimen were compared for their efficacy in improving mouth opening and reducing burning sensation in patients suffering with oral submucous fibrosis. Mean age of occurrence was 43.6 years. Male to female ratio was found to be 4:1. This finding was similar to the study done by Sharan et al⁴. Oral habits of chewing arecanut, betel nut and guthka were present in 100% of cases. In accordance with the recommendation of Borle et al 0.2 ml solution was given at particular site and repeated injection was avoided to decrease mechanical insult of tissue. Patients were advised to do mouth opening exercise for 20 minutes daily⁵. When compared there was marked improvement in mouth opening and decrease in burning sensation in all three treatment group. In a single drug regimen, hyaluronidase showed quicker and better improvement in mouth opening. The finding is similar to the study conducted by Kakar et al⁶. Improvement in burning sensation was better when betamethasone used alone. Many combination drug regimens (usually with steroid) were used in the treatment of oral submucous fibrosis. But the aim of our study was to compare the efficacy of single drug regimen in the treatment of oral submucous fibrosis. Every drug regimen has different mechanism of action. Oral submucous fibrosis is a chronic disease and differs in severity and symptoms at every stage. One particular drug regimen may be more efficient than other in management of symptoms associated with particular stage of disease as observed in our study. So, different drug regimen should be used for a patient as per need. It will provide more customised treatment for a particular case. Though rare, long term intra lesional injection of steroid has side effects like osteoporosis, myopathies, peptic ulcer or central serous chorioretinopathy¹². So in cases where adequate mouth opening is achievable with the use of intra lesional injection of hyaluronidase alone use of steroid should be avoided to minimize side effects. In our study treatment with intralesional injection of placentrex provided only moderate improvement in mouth opening and reduction in burning sensation.

Results of our study suggest counselling for cessation of habit completely followed by weekly intra lesional injection of hyaluronidase with jaw dialting exercises for the patient with chief complaint of restricted mouth opening and weekly intralesional injection of betamethasone for the patient complaining of burning sensation with minimal limitation of mouth opening.

Inconsistent reporting of patients on recall visit, small sample size and no long term follow up were the limitations of our study. So the outcome of our regimen needs further standardization by multicentre evaluation.

CONCLUSION

Oral submucous fibrosis is considered as a disease of collagen metabolic disorder characterised by increased collagen production and decreased collagen degradation. Several therapeutic and surgical methods have been tried in the treatment of submucous fibrosis. However, no such definitive and widely accepted treatment is currently available for this condition. 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.

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