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ORIGINAL RESEARCH

Prognosis of Oral Submucous Fibrosis With Two Drug Regimens: A Comparative Study

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ABSTRACT

Background: Oral Submucous Fibrosis is a potentially malignant disorder well known for its chronic and resistant nature. The conservative drug treatment that is currently available for this disorder is clearly inadequate. The main goal of the treatment of OSMF is to reduce trismus and burning sensation. The large number of treatment modalities have been tried both non-surgical and surgical approach. **Aim:** To compare the efficacy of treatment of Pindborg stage II, OSMF with and without lycopene in patient under intralesional dexamethasone and hyaluronidase therapy. **Methodology:** The present study included clinically diagnosed OSMF patient (stage II) and interincisal distance of less than 30mm. Complete case history was recorded with thorough clinical examination using specially designed case history format. The patients were randomly divided into 2 groups of 50 each. Group I received oral Lycopene capsules along with weekly intra-lesional injections of Dexamethasone (2mg/ml) & Hyaluronidase 1500 IU, Group II received, intralesional injection of dexamethasone (2mg/ml) and hyaluronidase (1500 IU). Difference between two groups was determined using student t-test and the level of significance was set at $p < 0.05$. **Results:** There was significant increase in mouth opening and reduction in burning sensation among Group I patients and the results were statistically significant. **Conclusion:** Lycopene in combination with intralesional steroids and Hyaluronidase, is highly efficacious in improving the mouth opening and reducing other symptoms in patients with Oral Submucous Fibrosis.

Keywords: Submucous, trismus, Lycopene, intralesional steroids.

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INTRODUCTION

Oral submucous fibrosis is defined as "An insidious chronic disease affecting any part of the oral cavity and sometimes the pharynx. It is always associated with juxta-epithelial inflammatory reaction followed by fibroelastic changes of the lamina propria with epithelial atrophy leading to stiffness of the oral mucosa and causing trismus and inability to speak".[1]The disease is exclusively reported in Indian population and in South East Asia. The prevalence of oral submucous fibrosis in India is up to 0.4%.[1,2]

OSMF is a well-recognized, potentially premalignant condition. Malignant transformation rate as high as 7.6% has been reported from the Indian subcontinent over a 17-year period[3]. OSMF has a multifactorial etiology. Several factor such as chilli consumption, nutritional deficiency state, arecanut chewing, genetic susceptibility, autoimmunity and collagen disorder have been suggested to be involved in the pathogenesis of the condition.[4]OSMF initially presents as burning sensation in oral cavity.

The main goal of the treatment of OSMF is to reduce trismus and burning sensation. The large number of treatment modalities have been tried both non-surgical and surgical approach. Reduction or even elimination of the habit of areca nut chewing is an important preventive measure. They should also be instructed to minimize consumption of spicy foods and maintain proper oral hygiene.[1,5]Ingestion of red tomatoes, green leafy vegetables and fresh fruits should be included in the regular diet since these deliver protection against the increased risk of cancer by rising levels of antioxidants.[1]

The non-surgical treatment modalities includes a use of antioxidants like (lycopene), iron supplements, curcumin, steroids, placental extract and fibrinolytic

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agents. However, no definitive and widely accepted treatment is currently available for this condition.[6]Antioxidants involves stimulation of the immune system or act by direct action on the tumor cells. They are antimutagenic and antimitogenic and operate by the common mechanism of breaking the free radical chain reactions. One such type of antioxidant is lycopene.[7]

Steroids are well recognized to act as immunosuppressive agents causing inhibition of inflammation found in OSMF lesions, thus reducing this fibro-collagenous condition.[1,5,8]Hyaluronidases an enzymes that catalyzes the hydrolysis of hyaluronic acid.Hyaluronidase attacks quickly on collagen from OSMF patients than on normal collagen. Hyaluronidase degrades the hyaluronic acid matrix, lowers the thickness of intracellular cemental substances as well as activating definite plasmatic mechanisms. As a result, reduce of trismus may be predictable through softening and diminishing of fibrous tissue.[9,10]

The most effective medical treatment has been the use of intralesional steroids in its various forms. The present study was conducted to compare the efficacy of treatment of Pindborg stage II,OSMF with and without lycopene in patient under intralesional dexamethasone and hyaluronidase therapy.

The objectives of the study are:

1. To clinically compare the reduction in burning sensation in study groups under treatment with time.
2. To study the improvement in mouth opening amongst the study groups under treatment with time.
3. To clinically evaluate the efficacy of intralesional injection of Dexamethasone with Hyaluronidase in treatment of OSMF patient with and without oral lycopene supplement.

MATERIAL AND METHODS

The present study was designed to be conducted on patients reporting to the outpatient Department of Oral Medicine and Radiology in Buddha Institute of Dental Sciences and Hospital, Patna during the period of January 2017 to July 2018.The study group comprises of 50 cases each of clinically diagnosed OSMF patient in stage II(according to Pindborg classification) and interincisal distance of less than 30mm (Group C and Group D, Lai. D.R. classification) & in the age range of 20-45 years.Institutional ethical committee clearance was obtained the study and patients were explained about the study in their own language and an informed written consent was taken.

Inclusion criteria

1. Patients with lesions include vertical and circular palpable fibrous bands in the buccal mucosa and around the mouth opening or lips resulting in mottled marble like appearance of the mucosa because of the vertical thick fibrous bands in association with blanched mucosa.
2. Age: 20-45 years.
3. Both sexes were included.
4. Burning sensation on eating spicy food.
5. Restricted mouth opening equal to or less then 30mm (according to classification of Lai. D.R)

Exclusion Criteria

1. Patients undergoing any surgery or any drug therapy.
2. Patients with reduced mouth opening due to any other reasons like TMJ problems, pericoronitis of lower third molars etc.
3. Coexisting lesions.
4. Patients previously treated for the OSMF.
5. Allergic conditions.
6. Patients with chronic illness,diabetes, hypertension, pregnancy, and any kind of allergy.

Methodology

Patient with clinically diagnosed oral submucous fibrosis was included and were explained about the study in own language and only those patient who have given consent were included in the study. Complete case history was recorded with thorough clinical examination using specially designed case history format.

Burning mouth sensation was assessed with the help of visual analog scale (VAS), having score ranging from 1 to 10 and measurement of the mouth opening was done with the help of Vernier caliper at every visit.The patients were randomly divided into 2 groups of 50 each. Patient in Group I received oral Lycopene capsules , one capsule/day along with weekly intralesionalinjections of Dexamethasone (2mg/ml)&Hyaluronidase 1500 IU along with 1ml of 2%(1:80,000) Lignocaine Hydrochloridein the buccal mucosa bilaterally.

Patients in Group IIreceived, intralesional injection of dexamethasone (2mg/ml) and hyaluronidase (1500 IU) along with 1ml of 2%(1:80,000) Lignocaine Hydrochloride in the buccal mucosa bilaterally (without any oral supplements) weekly upto 12 weeks. Cases were followed up till 3 months.

First, fibrous bands were palpated at the various sites of the oral mucosa and 26 gauge needles will be used to inject thedrug submucosally at fibrotic sites bilaterally. Burning mouth sensation was assessed with the help of visual analog scale (VAS), having score ranging from 1 to 10 and measurement of the mouth opening was done with the help of Vernier caliper and at every visit.

Statistical analysis

Statistical analysis was done using Mean and Standard Deviation were estimated for each study group. Mean values were compared between different study groups by using student t test on Graph pad prism software,

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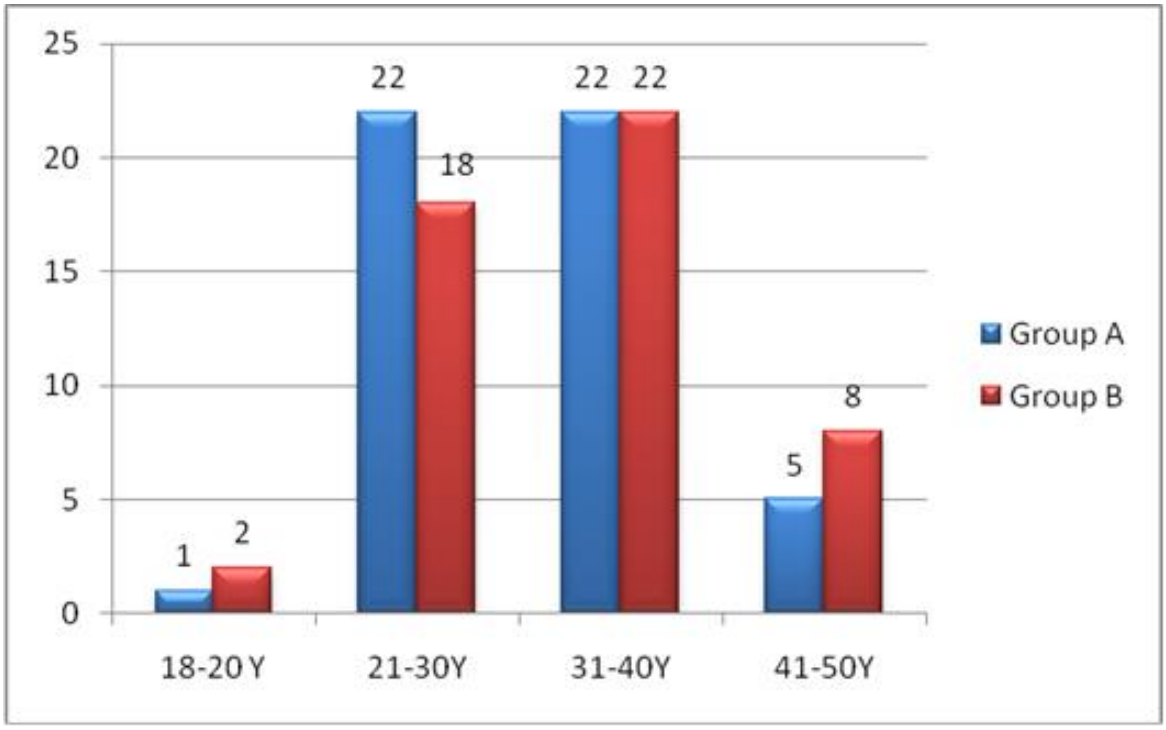
version 5. In the present study, $p < 0.05$ was considered as the level of significance.

RESULTS

Group A and Group B equally contains 43 male patients and 7 female patients.All the patients fall within the age range of 18 to 50 years with maximum number of patients in the age group of 31 to 40 years, both group A and group B have 22 patients in this age group(Graph 1).



Graph 1: Age distribution among the study subjects

Table 1, graph 2 shows that patients in Group A (receiving oral Lycopene capsules, one capsule/day along with weekly intralesional injections of Dexamethasone &Hyaluronidase shows better treatment than after 12 week on burning sensation than Group B (receiving, intralesional injection of dexamethasone and hyaluronidase, without any oral supplement) with statistically significant difference as p=0.039.

Table 1: Efficacy of intralesional injection of Dexamethasone with Hyaluronidase in treatment of OSMF patient with and without oral lycopene supplement

Group	VAS Scale Of Burning Sensation (Baseline) Mean±SD	VAS Scale Of Burning Sensation (After 12 Weeks) Mean ± SD	Percent reduction in burning sensation	P Value
Group A	6.6±0.89	1.4±0.75	52 %	0.039
Group B	5.8±1.2	2±0.54	38 %	

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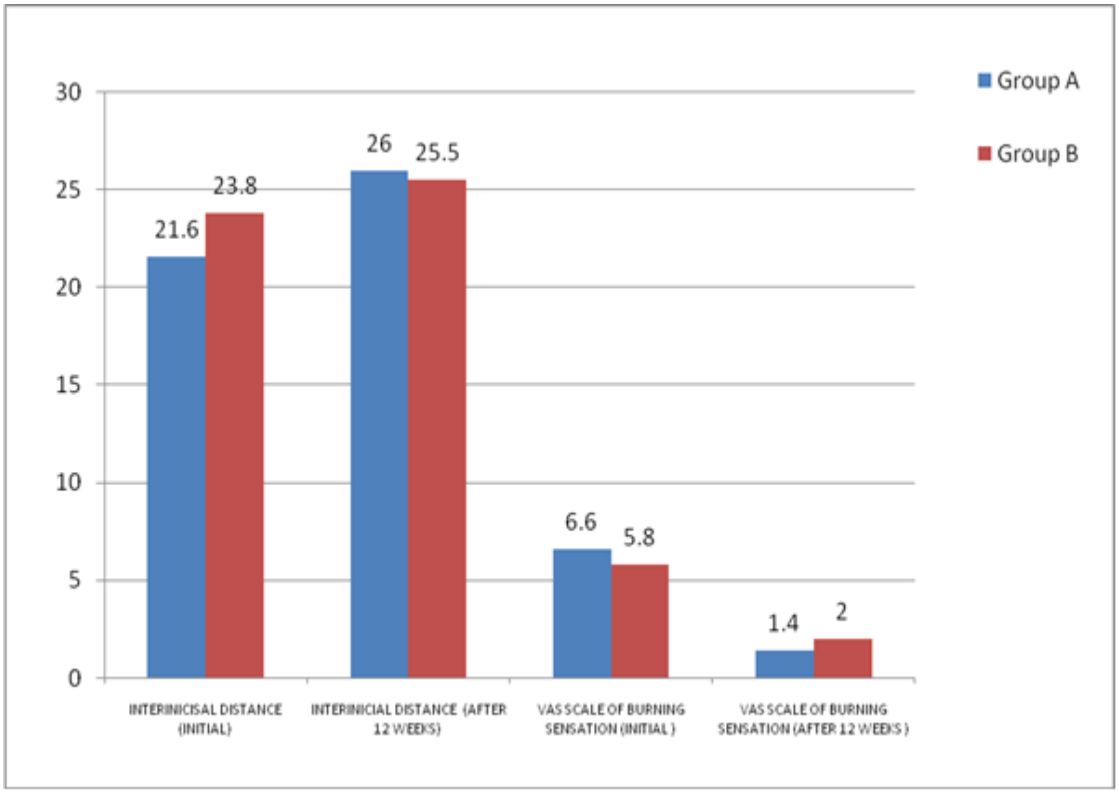

Graph 2: Efficacy of intralesional injection of Dexamethasone with Hyaluronidase in treatment of OSMF patient with and without oral lycopene supplement

Table 2 shows that patients in Group A (receiving oral Lycopene capsules, one capsule/day along with weekly intralesional injections of Dexamethasone &Hyaluronidase) shows better treatment than after 12 week observation on mouth opening than Group B (receiving, intralesional injection of dexamethasone and hyaluronidase, without any oral supplement)with statistically significant difference as p=0.039.

Table 2: Efficacy of intralesional injection of Dexamethasone with Hyaluronidase in treatment of OSMF patient with and without oral lycopene supplement

Drug Treated	Interinicisal Distance (Baseline) Mean ± SD	Interinicisal Distance (After 12 Weeks) Mean±SD	Percent increase in Mouth opening	P Value
Group A	21.6±4.2	26±4.5	44 %	P=0.041
Group B	23.8±3.3	25.5±3.6	17 %	

DISCUSSION

In the present study, maximum incidence of clinically diagnosed OSMF patients was seen in the age group of 31-40 years. This result is consistent with the study of Saran et al in 2018[11], V. Reddy et al[12]. According to Anjum Aaraet et al[4] in 2012 found maximum number of OSMF patients were found in the age group 21-30 years in their study.

In this study, prevalence of OSMF was to be more in males than females. The result is consistent with the findings of Mangal Singh, H.S. Niranjan et al in 2010[13] .

In the present study, group A shows the initial burning sensation of 6.6 which decreases to 1.4 after 12 week while the Group B shows the initial burning sensation of 5.8 which decreases to 2 after 12 week and P value was 0.041 which was statistically significant changes in burning sensation among Group A and Group B. In a study conducted by PH SHAH et al, the average decrease in burning sensation noted by VAS scale scores from baseline to 8th week was 5.13±1.13 in Group A and 4.90±1.29 in Group B. When the average VAS scores at baseline and at 8th week of treatment were compared, the differences were found to be statistically highly significant for both the groups, which was in consistent with our study.[14]Saran, et al conducted a study in year 2018 and found that the Group A patients who were treated with lycopene showed significant reduction in the burning sensation from the initial visit where mean was 65.83% ± 3.98% (VAS) after 3 months; there was complete cessation of burning sensation.[15]Similar findings were reported by Kumar et al. in 2007 who conducted a study on 89 OSMF patients where lycopene with intralesional injection was found effective in reducing the burning

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sensation and the associated symptoms of OSMF.[16]Patel TL and Surjeet Singh et al conducted a study in year 2015 and found that the symptoms of burning sensation (VAS score) was decreased more in case of OSMF patients, which was consistent with our study.[16]

In the present study, Group A shows the initial mouth opening of 21.6 mm which increases to 26 mm after 12 week while the group B shows the initial mouth opening of 23.8 mm which increases to 25.5 mm after 12 week. There was statistically signigicant change in mouth opening among Group A and Group B. Canniff et al, in 1986, found that only intralesional steroids were not very useful in the management of OSMF. In another study done by Borle and Borle, in which intralesional injections of triamcinolone were combined with hyaluronidase, there was no improvement in mouth opening, which was contradicted with our study.[17]

Selvam et al conducted a study in year 2013 and found that the comparisons were made with regard to mouth opening, there was significant difference between Group A (lycopene with intralesional steroids) and C (intralesional steroids alone) as well as Group B (antioxidants with intralesional steroids) and C (intralesional steroids alone) ('p' value < 0.0001). But even though Group A (lycopene with intralesional steroids) showed greater improvement in mouth opening (34.9 ± 5.6) than Group B (antioxidants with intralesional steroids) (32.2 ± 6.7), the results of Group A and B did not differ enough to be statistically significant ('p' > 0.05) which was consistent with our study.[18] Saran et al results showed that clinical improvements in mouth opening (P < 0.001), which was in consistent with our study. Lycopene can bring about significant clinical improvements in symptoms such as mouth opening. Similar study was carried out by Sudarshan et al. in 2012 to compare the efficacy of aloe vera with antioxidants in the treatment for OSMF.[11]

In the present study patients in Group A (receiving oral Lycopene capsules, one capsule/day along with weekly intralesional injections of Dexamethasone &Hyaluronidase shows better treatment than after 12 week on burning sensationthan Group B (receiving, intralesional injection of dexamethasone and hyaluronidase, without any oral supplement). Percentage of reduction in burning sensation in Group A and Group B was 52% and 38% respectively (P=0.039) which is statistically significant. For mouth opening, percentage of increase mouth opening in Group A and Group B was 44% and 17% respectively.(P=0.041) which is statistically significant. In a study conducted by Singh D et al, patients treated with lycopene (Group I) had a reduction in burning sensation by 94.2% and Patients treated with intralesional steroid injections (Group II) had a reduction in burning sensation by 54.1%. The mean improvement in mouth opening in Group I (lycopene group) was 37.62% (12 mm) at the end of the treatment and it was very highly significant (P < 0.001)and Group II (only intralesional steroids) was 13% (3.9 mm) at the end of the treatment, which was a statistically highly significant difference from the baseline (P = 0.018) , which was in consistent with our study .

Borle and Borle is also found that treatment of OSMF with intralesional injections of hyaluronidase and corticosteroids (triamcinolone acetonide) reduced burning sensation by 86.84%. This is similar with our study.Goswami R et al in their study showed that in group A(vitamin B complex, lycopene and topical application of triamcinolone); 62% patients were relieved of burning sensation. There was 1 to 5 mm increase in interincisal distance in 5 patients only out of 40 patients. 80% of Group B(intralesional injections of triamcinolone + hyaluronidase) patients showed actual increase 62% in inter incisal distance and 92% patients showed improvement in burning sensation. These results are similar to our study.[19]

CONCLUSION

In the present study it was observed that Lycopene in combination with intralesional steroids(Dexamethasone) and Hyaluronidase is highly efficacious in improving the mouth opening and reducing burning sensation in oral submucous fibrosis patients. No side effects were reported with its usage. Further research on a larger study sample size and a longer follow up is essential to substantiate the benefits of the combination drug regimen (antioxidants , steroids and Hyaluronidase) in the treatment of OSMF.

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