

Comparative Study between Intralesional Steroid Injection and Oral Lycopene in the Treatment of Oral Submucous Fibrosis

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Abstract

Introduction: Oral submucous fibrosis (OSMF) is a premalignant condition with rising incidence due to increase in addictive habits like arecanut and tobacco chewing. Various treatment modalities have been tried including steroid injections though new interest in use of natural plant pigments like lycopene has occurred.

Aim: The aim was to compare the efficacy of intralesional steroid injection with oral lycopene in the treatment of OSMF.

Methodology: A randomized prospective study of 75 patients of OSMF who were divided into three groups of 25 each. Group A patients received weekly intralesional triamcinolone (40 mg/ml) injections, Group B received oral lycopene 6 mg daily, and Group C received both weekly steroid injection and oral lycopene for 2 months respectively. Mouth opening as inter-incisor distance (mm) and burning sensation in the mouth using visual analog scale were recorded weekly.

Results: Mouth opening values for the patients showed a mean increase of 6.56 mm, 3.04 mm and 7.56 mm in Groups A, B and C, respectively. Lycopene showed an early reduction in the burning sensation with a mean score of 4.8 in group B by the 1st week itself which was highly significant ($P < 0.001$).

Conclusion: Lycopene can be used as a first-line drug in the management of OSMF or even as an adjuvant with steroids giving excellent results.

Key words: Lycopene, Mouth opening, Oral submucous fibrosis, Steroid, Triamcinolone

INTRODUCTION

Oral submucous fibrosis (OSMF) is a chronic, debilitating, premalignant condition affecting all ages and both sexes in the Indian subcontinent. Although thought to be multifactorial, various risk factors like areca nut chewing, chilli consumption, nutritional deficiency states, genetic susceptibility and collagen disorders have been suggested. It is a chronic condition characterised by mucosal rigidity of varying intensity due to fibro-elastic transformation of juxta-epithelial layer. Predominantly Type I collagen with

variable amounts of other types of collagen constitute fibrosis.¹ It occurs when the synthesis of new collagen by myofibroblasts exceeds the rate at which it is degraded, such that the total amount of collagen increases over time.² This leads to restricted mouth opening and burning sensation of the oral mucosa aggravated by spicy food. However, a more serious complication is the risk of developing oral malignancy that may be as high as 3-7.6%. Most important aspect of treatment is cessation of habit of chewing betel quid, areca nut, other local irritants, spicy and hot food, alcohol intake and smoking. Various modalities of treatment ranging from conservative treatment to surgical procedures have been attempted. Intra-lesional injections of steroids has been used in its treatment since quite long as a drug of choice.

Other medical therapy include injection of placental extract, hyaluronidase, trypsin, collagenase, intralesional interferon- γ , oral zinc and pentoxiphylline. But there has

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been new interest in use of natural pigments in plants like lycopene, found to reverse the pathogenesis of OSMF.³

Carotenoids have been known to decrease the incidence of oral premalignant lesions and cancer.⁴ Lycopene is a carotenoid in tomatoes (0.9-4.2 mg per 100 g) having high singlet oxygen quenching property.⁵ It has several potent anti-carcinogenic and anti-oxidant properties and has demonstrated profound benefits in precancerous lesions such as leukoplakia and OSMF. It has also shown benefits in cancers of the prostate, pancreas and oesophagus.⁶

Lycopene has been found to inhibit hepatic fibrosis in rats as well as human fibroblast *in vitro*, and hence tried in treatment of OSMF.

MATERIALS AND METHODS

This was a clinical prospective study conducted between July 2011 and July 2013 in otorhinolaryngology department of Jagadguru Jayadeva Murugarajendra medical college. 75 consecutive patients of clinical OSMF aged between 18 years and 55 years were inducted into the study. Detailed history including symptoms, habits of areca nut chew, gutkha, pan masala, smoking, alcohol intake was taken. General and ENT examination were performed. Patients with systemic diseases, active oral infections and mouth opening grades 3 and above according to clinical staging by Ranganathan *et al.* were excluded.

All patients were properly explained about the study and their written consent was taken. The study was cleared by the hospital ethical board. The cases were randomly divided into three groups subsequently. Group A patients received intra-lesional triamcinolone injections (40 mg/ml) once weekly, Group B patients received 6 mg oral lycopene daily in divided doses and Group C received weekly steroid injections along with daily oral lycopene tablets combined for a total duration of 2 months each. The main parameters assessed were improvements in mouth opening as inter-incisor distance in mm and burning sensation by visual analog scale (VAS) from 1 to 10. The two parameters were recorded weekly for 2 months. One-way ANOVA followed by *post hoc* Tukey's test for group-wise comparisons were used.

RESULTS

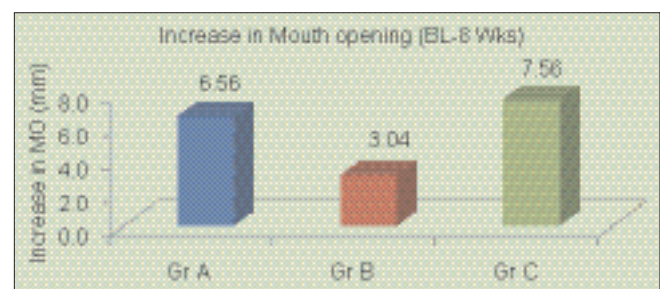
Seventy-five patients participated in our study (25 in each Group A, B and C) aging between 18 years and 55 years with a mean age of 28.6 years. In group A, 33.3% were males and 66.6% were females. In Group B, 55.5% were males and 44.4% were females and in Group C, 52% were males and 48% were females. Trismus was the most common

symptom, followed by burning sensation in the mouth on eating spicy food, dryness of mouth and ulceration. The average baseline mouth opening in Groups A, B and C were 25.84 mm, 23.76 mm and 23.08 mm, respectively. The inter-incisor distance at the end of the study was 32.4 mm, 26.8 mm and 30.64 mm in Groups A, B and C with mean increase in mouth opening of 6.56 mm, 3.04 mm and 7.56 mm respectively as shown in Table 1 and Graph 1.

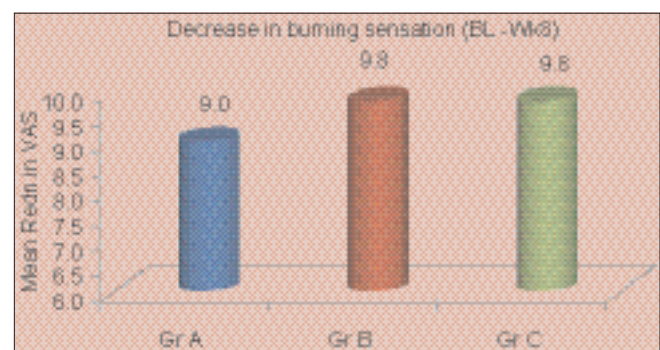
The average baseline VAS score of burning sensation in all the three groups was 10 at the beginning of the study. The score at end of study were 1, 0 and 0 in Groups A, B and C with a mean decrease in burning sensation of 9, 9.8 and 9.8 respectively over the study period as shown in Table 2 and Graph 2. Lycopene showed an early reduction in the burning sensation with a mean score of 4.8 in Group B by 1st week itself which was highly significant ($P < 0.001$). There were no local or systemic side effects due to the treatment in any of the groups.

DISCUSSION

OSMF was defined by Schwartz as 'a chronic disease affecting any part of the oral cavity and sometimes the pharynx, associated with juxta-epithelial inflammatory reaction followed by a fibro-elastic change of the lamina propria leading to stiffness of oral mucosa and causing trismus. Although various risk factors are implicated, most important factor is areca nut chewing in various forms such as gutkha, pan masala etc. The active ingredients in areca



Graph 1: Increase in mouth opening (baseline-8 week)



Graph 2: Decrease in burning sensation (baseline-week 8)

Table 1: Improvement in mouth opening (mm)

Group	Baseline	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8
A	25.84	27.04	27.76	28.84	29.68	30.36	31.6	32.4	32.4
B	23.76	23.88	24.24	24.64	25	25.52	26.04	26.52	26.8
C	23.08	24.56	25.44	26.92	27.8	28.6	29.92	30.56	30.64

Table 2: Improvement in burning sensation (VAS score)

Group	Baseline	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8
A	10	7.2	6.1	5.2	4.5	3.7	2.7	2.1	1.0
B	10	4.8	2.4	1.5	0.9	0.5	0.2	0.2	0.2
C	10	5.6	4.0	2.4	1.8	1.0	0.4	0.2	0.2

VAS: Visual analog scale

nut include arecoline, arecaidine and tannins which stimulate fibroblast proliferation and dysregulate collagen synthesis. Intra-lesional steroids benefit by immunosuppression and inhibition of fibroblast proliferation and collagen synthesis.⁷

Among the steroids, triamcinolone acetonide was selected for the study as it has better local potency, longer duration of action and lesser systemic side effects.⁸ Lycopene is a 40 carbon acyclic carotenoid containing 11 conjugated double bonds, with a molecular mass of 536. It has anti-oxidant, anti-fibroblast and anti-carcinogenic properties.⁹ In our study, there was a significant difference in improvement of mouth opening between Groups A and B, with steroid showing better improvement in mouth opening. The effect of steroid injection in improvement of mouth opening is comparable to the study by Ameer *et al.*¹⁰ However, maximum improvement in mouth opening and decrease in burning sensation was recorded in the group C where a combination of steroid and lycopene were given to the patients. A possible explanation could be increased blood perfusion due to lycopene which increased the local bioavailability of steroid in the fibrotic buccal mucosa. Definite reduction in the burning sensation and an increase in the mouth opening were noted with oral lycopene in the study by Kumar *et al.*¹¹ Bhagavan *et al.* also found encouraging results with lycopene therapy and added that long term maintenance therapy may be needed to have an impact on oral cavity cancer incidence.¹²

CONCLUSION

Combination of intra-lesional steroid injection and oral lycopene therapy has great benefits in alleviating the

symptoms of OSMF patients and can be tried out as a first-line treatment in selected patients suffering from the disease.

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