### **Original Research Article**

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# Application of injection Kenacort, intradermal route in oral submucous fibrosis

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#### **ABSTRACT**

**Background:** Oral submucous fibrosis is a potentially pre-malignant disease, that results in progressive juxta-epithelial fibrosis of oral soft tissues, resulting in increased loss of tissue mobility, marked rigidity and inability to open the mouth. Actual treatment includes iron, multi vitamins, lycopene, pentoxifyline, steroid injections and human placental extracts. Currently available treatment with intradermal injection of Kenacort with hyaluronidase is effective to some extent.

**Methods:** This study was conducted at Basaveshwara Medical College and Hospital, Research Centre, Chitradurga, Karnataka, in the Otorhinolaryngology Department from February 2019 to August 2019 for 6 months duration. A total of 40 patients were included in this study. Mouth opening was recorded from baseline to 6 weeks. Cases were followed up for 6 months thereafter. Patients with positive history of chewing of betel-nuts, pan, gutkha and age from 18-50 years males and females were included in this study. Patients undergoing any surgery, allergic conditions, age more than 50 years were excluded. Mouth opening was assessed by objective type and subjective type.

**Results:** There was significant increase in mouth opening in patients after administration of intra-dermal Kenacort injection and oral lycopene. The results were statistically significant and patients responded better and p value <0.001. **Conclusions:** Management of moderate oral submucous fibrosis should include counselling of patients along with oral lycopene with intradermal injection of Kenacort with hyaluronidase, is highly efficacious and cost- effective in improving the mouth opening and reducing other symptoms in patients with OSMF, whereas advanced stages should be treated surgically.

Keywords: Pre-malignant conditions, Oral submucous fibrosis, Lycopene, Kenacort, Hyaluronidase

#### **INTRODUCTION**

Oral submucous fibrosis (OSMF) is a well-known premalignant condition which is insidious and progressive affecting the entire oral cavity, sometimes even extends to the pharynx. It is more commonly seen in Indian population. In the recent past more attention has drawn because of the morbidity and resistant nature of this condition. One such type of antioxidant is lycopene. Lycopene is a phytochemical, synthesized by plants (tomatoes) and microorganisms. It is a powerful

antioxidant and has a singlet-oxygen-quenching ability twice as high as that of beta-carotene and ten times higher than that of alpha-tocopherol 2. It is a potent anticarcinogenic and has demonstrated profound benefits in precancerous lesions like leukoplakia. Anyhow no single drug has provided complete relief of symptoms of OSMF and hence combination treatment modality has been opted in our study.<sup>1</sup>

Pindborg et al defined OSMF as, "an insidious, chronic disease affecting any part of the oral cavity and

sometimes the pharynx, although occasionally preceded by and/or associated with vesicle formation, it is always associated with juxta-epithelial inflammatory reaction followed by fibroelastic change of the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa and causing trismus and inability to eat."<sup>2</sup>

The etiopathogenesis of OSMF is complex and incompletely understood. The main agent involved in the pathogenesis of OSMF is areca nut. Areca nut is made up of alkaloid and flavonoid components. Four alkaloids namely arecoline, arecaidine, guvacine, and guvacoline have been identified in areca nut, of which arecoline is the most potent agent and plays a major role in the pathogenesis of OSMF by causing an abnormal increase in collagen production.<sup>3</sup>

The most commonly involved site is buccal mucosa, followed by palate, retromolar region, faucial pillars and pharynx and in some cases can even involve the pharynx, larynx, or the esophagus. It causes a stiffening of the oral mucosa due to a fibrotic change in the mucosa and its connective tissue which then restricts the mouth opening. It has been linked with an increased risk of malignancy and thus is considered as a pre-malignant condition. The disease has a variety of presentations ranging from, excessive salivation, burning sensation, lacking gustatory sensation and limitation of mouth opening leading to difficulty in chewing, swallowing, articulation and poor oral hygiene and its complications.<sup>4</sup>

OSMF has a multifactorial etiology. Several factors such as nutritional deficiency states, areca nut chewing, genetic susceptibility, autoimmunity & collagen disorders have been suggested to be involved in the pathogenesis of the condition.<sup>5</sup>

The aim of the study was to evaluate whether the efficacy of the current treatment modality for Oral submucous fibrosis can be improved by adding oral lycopene along with intradermal steroid injection.

#### **METHODS**

The study was conducted after obtaining Institutional Ethical Committee Clearance.

A total of 40 patients with signs and symptoms of OSMF were recruited for the study from Otorhinolaryngology department of Basaveshwara Medical College and Hospital, Research Centre, Chitradurga, Karnataka, from February 2019 to August 2019 for 6 months duration.

Informed consent was obtained from all the patients before recruiting for the study.

Inclusion criteria were patients with history of the habit of chewing areca nut (betel nut) or any of its commercial products; age from 18-50 years males and females.

Exclusion criteria were patients undergoing any surgery, allergic conditions, age more than 50 years.

According to Ranganathan et al, the grades of OSMF are grade 1 as only symptoms, with no demonstrable restriction in mouth opening; grade 2 as limited mouth opening 20 mm and above; grade 3 as mouth opening <20 mm; grade 4 as OSMF advanced with limited mouth opening, pre-cancerous or cancerous changes seen throughout the mucosa.<sup>6</sup>

Patients were explained about the premalignant potential of OSF and were counselled to stop the habit of using areca nut in all its form. Complete oral prophylaxis was given to the patients, dental opinion given regarding improving oral hygiene and also patients were motivated to stop the habit.



Figure 1: Fibrous bands over buccal mucosa.



Figure 2: Restricted mouth opening.



Figure 3: Measuring scale.

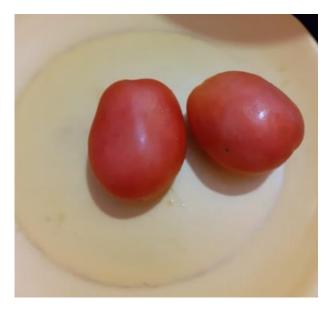


Figure 4: Tomatoes.

All the 40 patients were given oral Lycopene capsules 16 mg, one capsule or day along with once weekly intralesional injections of triamcinolone (Kenacort) 40 mg/ml, 1 ml and hyaluronidase 1500 IU by using insulin syringe, to the site, where fibrosis was present. Patients were evaluated every week during the treatment period of 6 weeks.

Mouth opening was assessed by measuring the interincisal distance from the upper right central incisor to the lower right central incisor using calipers or centimeter scale as an objective type and by using patient's own three fingers, inserting inside his/her mouth vertically is a subjective type. If either of the teeth were missing, their left side counterpart was used for measurement. Mouth opening was recorded at baseline before the start of the treatment and subsequently at the end of every week for 6 weeks during treatment period. It was also recorded post treatment at 6 months follow-up period.

The statistical analysis was used student-t test in this study.

#### **RESULTS**

Patients fall within the age range of 30 and 50 years with maximum number of patients in the age (Table 1). Mean age was 16 years.

Out of 40 patients 28 (70%) were male patients and 12 (30%) were female patients (Table 2).

According to their residence, we have considered both rural (n=32, 80%) and urban (n=8, 20%) areas patients (Table 3).

Inter-incisal distance was assessed and the improvement was calculated. P value is <0.001 highly significant (improvement is significant) by using student-t test (Table 4).

**Table 1: Gender distribution (n=40).** 

Sex distribution	No of patients	Percentage (%)
Males	28	70
Females	12	30
Total	40	100

Table 2: Age distribution (n=40).

Age distribution (in years)	No of patients	Percentage (%)
18-<30	10	25
30-40	18	45
41-50	12	30

Table 3: Patients residing place (n=40).

Residence	No of patients	Percentage (%)
Rural	32	80
Urban	8	20

Table 4: Inter-incisal distance improvement.

Inter- incisal	At base line (mean±SD)	At 6 months (mean±SD)	P value
distance	3.1±1 mm	4.5±2 mm	< 0.001

By using Student-t test. Improvement is significant.

#### **DISCUSSION**

Kumar et al suggests that severe cases of OSMF are poor responders to lycopene. So, in our study, we included patients only with Grade 3 and 4 OSMF. Lycopene exerts its anti-inflammatory action, by increasing the lymphocyte resistance to stress, inhibition of pivotal proinflammatory mediators, like reduction of ROS, the inhibition of synthesis and release of pro-inflammatory cytokines, changes in the expression of cycloxygenase and lipoxygenase, modifications of eicosanoid synthesis and modulation of signal transduction pathways, including that of the inducible nitric oxide synthase.<sup>3</sup>

Oral submucous fibrosis is well known for its chronic and resistant nature. Currently available treatment for OSMF is clearly inadequate. No single drug has provided complete relief of symptoms of OSMF; this has led to the use of combination of drugs to treat the condition. Lycopene is a major carotenoid found in tomato which has potent anticancer activity in many types of cancer.<sup>4,5</sup>

In our study 70% of the patients were males. It demonstrates the male preponderance of the condition. In a study conducted by Ranganathan et al, which recorded a male to female ratio 28:12 among OSMF patients. In our study, male:female ratio was 4.9:1.6 Maximum number of patients in our study fell under the age group of 35 years. Almost all the patients from our study are chewing areca nut in its pure form as a cultural practice (70%). Even though OSMF is more prevalent in gutka chewers (according to Bathi et al) than its pure form long duration of its use has led to the development of OSMF in the population we studied.6

In our study, we found out that lycopene when combined with intra-lesional steroids offer more benefit than when used alone. Our study was supported by Chloe et al, but it was contradicting with the findings of Kumar et al, he suggested that lycopene is more effective when used alone. In our study, the greater improvement in mouth opening when lycopene was combined with intralesional steroids and hyaluronidase used together with a significant p value of <0.001.

Kakar et al reported that patients treated with hyaluronidase showed quicker improvement in symptoms but a combination of corticosteroids gave better and long-term results. Steroids are well-known immunosuppressive agents for suppression of fibroproductive inflammation found in OSMF. Hyaluronidase degrades the fibrous matrix promoting the lysis of fibrinous coagulum and activating specific plasmatic mechanism. Relief of symptoms like stiffness in oral cavity occurs through softening and diminishing fibrous tissue. In our study, intra lesional CST injection with injection hyaluronidase was given biweekly to make the treatment easily acceptable by the patients, for better compliance and it also becomes cost effective for them.

Nasolabial technique flap has versatility with single sitting operation. Linear closure of donor site resulting in well- camouflaged scar in the nasolabial fold. Large defects can be closed. Periodic biopsies of suspicious regions of oral mucosa are essential for early detection and management.

In many centres, intra-lesional injection of CST is being implemented as the first line therapy for patients (grade 2 and 3 OSMF) with mouth opening less than 20 mm. The primary mechanism of action of CST is through immune modulation. CST suppress inflammation, decelerate fibrosis and up regulate immune mediated fibrinolytic pathways.<sup>7-10</sup>

The mechanism of action steroids is by opposing the action of soluble factors generated by sensitized lymphocytes after activation by specific antigens. Steroids also act as an immunosuppressive agent and suppress inflammatory reactions. This prevents fibrosis by decreasing fibroblastic proliferation and collagen deposition. 11-15

Results of our study were in accordance to the study done by previous studies which also showed combination of triamcinolone acetonide and hyaluronidase better in treatment of OSMF.<sup>16-20</sup>

#### **CONCLUSION**

Management of moderate oral submucous fibrosis should include counselling of patients along with oral lycopene with intradermal injection of Kenacort with hyaluronidase, is highly efficacious and cost- effective in improving the mouth opening and reducing other symptoms in patients with OSMF, whereas advanced stages should be treated surgically.

Early diagnosis of cancer plays a lifesaving pivotal role in overall management. This can be very useful aid for "early diagnosis of cancer." This is perhaps the most important service we can provide

Periodic screening and biopsies of suspicious regions of the oral mucosa are essential for the early detection and management of High-risk oral pre-malignant lesions and prevention of cancer.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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