

## ORIGINAL RESEARCH

### Management of oral Submucous Fibrosis with oral lycopene and injection Kenacort, Hyaluronidase intradermally

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#### ABSTRACT

**Background:** Oral submucous fibrosis (OSMF) is an oral precancerous condition characterized by inflammation and progressive fibrosis of the submucosal tissues resulting in marked rigidity and trismus. OSMF is still challenging for clinicians due to elusive pathogenesis and less well-defined classification systems. However current treatment strategy with oral lycopene and intralesional injection of kenacort and hyaluronidase is effective to some extent.

**Methods:** A total of 30 patients diagnosed with OSMF were treated in SMGS hospital, GMC jammu for a span of 9 months. They were treated with oral lycopene and intralesional injection of kenacort and hyaluronidase weekly for 6 weeks.

**Results:** There was significant improvement in opening of mouth and definite reduction in burning sensation, painful ulceration and blanching of buccal mucosa.

**Conclusion:** Management of OSMF includes counseling 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 receding other symptoms in patients with OSMF, whereas advanced stages should be treated surgically.

#### INTRODUCTION

The oral submucous fibrosis (OSMF) as defined by Pindborg and Sirsat as an insidious chronic fibrotic disease that involves the oral mucosa and occasionally the pharynx and upper third of oesophagus. 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<sup>2</sup>. 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> The etiological factors are excessive consumption of spicy food, nutritional deficiencies like chronic iron and vitamin B complex deficiency, areca nut chewing habits.<sup>2</sup> The symptoms and subjective signs observed are burning sensation exacerbated by spicy or acidic foods, pain often referred to temporal region, increased or decreased salivation,

reduced mouth opening, difficulty with mastication, difficulty with phonation and deglutition, vesiculation or ulceration of oral mucosa. 3(figure1)



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>4</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 oesophagus. It causes a stiffening of the oral mucosa due to 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>5</sup>

#### **HYALURONIDASE IN OSMF**

Hyaluronidase by breaking down hyaluronic acid (the ground substance in connective tissue) lowers the viscosity of intercellular cement substance. Better results were observed with respect to trismus and fibrosis.<sup>6</sup>

#### **DEXAMETHASONE IN OSMF**

Acts as an immune suppressive agent due to its antagonistic activity on the soluble factors released by the sensitized lymphocytes succeeding the activation by non specific antigens.<sup>7</sup>. It additionally muzzles the inflammatory reaction.

#### **LYCOPENE**

An effective anti-oxidant from tomato extract has been proved to be the most potent radical scavenger in various in-vivo and in-vitro studies.

## MATERIALS AND METHODS

The study was conducted on 30 patients with OSMF who attended as outpatients in the Department of ENT of GMC Jammu for a span of 9 months. Informed consent was obtained from all the patients. This study was carried out after obtaining the patient's consent and with the approval of the ethical committee of the institute. Clinical diagnosis of OSMF was based on symptoms of burning sensation in the mouth on consumption of spicy or hot food, dryness of mouth, presence of vesicles, oral ulcers in the mouth and restriction of mouth opening. Patients who were medically compromised and those received previous treatments were not included in the study. Out of 30 patients, the number of male patients were 20 and female subjects were 10. The patients were informed about the condition and its outcome and instructed to discontinue the use of areca nut with tobacco. Their personal history regarding frequency, duration of use of areca nut and symptoms like burning sensation and mouth opening were recorded. 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 20mm and above; grade 3 as mouth opening <20mm; grade 4 as OSMF advanced with limited mouth opening, pre-cancerous or cancerous changes seen throughout the mucosa.<sup>8</sup>

Mouth opening was assessed by measuring the inter-incisal 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 as a subjective type. Mouth opening was recorded at baseline before the start of the treatment and subsequently at the end of every week for 6 weeks during the treatment period. Intraorally, the findings like blanching of oral mucosa, presence of vesicles and ulcers, palpable bands, limitation of tongue movement were observed.

All the 30 patients were given oral Lycopene capsules 16mg, one capsule per day along with once weekly intralesional injections of 1 ml of triamcinolone (kennacort) 40mg/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. Fig2 shows intralesional injection of kannacort and hyalase



## 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 30 patients 18 (70%) were male patients and 12 (30%) were female patients (Table 2). Area wise we divided into rural (n=22, 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=30).**

Sex distribution	No of patients	Percentage (%)
Males	18	70
Females	12	30
Total	30	100

**Table 2: Age distribution (n=30).**

Age distribution (in years)	No of patients	Percentage(%)
18-30	7	25
31-40	14	45
41-50	9	30

**Table 3: Area wise (n=30).**

Residence	No of patients	Percentage (%)
Rural	22	80
Urban	8	20

**Table 4: Inter-incisal distance improvement.**

Inter-incisal distance	At base line (mean+_SD)	At 6 months (mean+_SD)	P value
	3.1+_1mm	4.5+_2mm	<0.001

By using Student-t test. Improvement is significant.

## DISCUSSION

OSMF is a precancerous condition and reports suggest that it is present since the time of Sushruta<sup>9</sup> reported by Schwartz in 1962 and by Joshi in 1953; who described its singleton among the Indians. Many trials have been conducted but as such no definitive treatment is currently available.<sup>10</sup> However, improvement can be obtained passably by intralesional injection of cortisone and hyaluronidase.<sup>11</sup>

Kumar et al suggests that severe case of OSMF are poor responders to lycopene.

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.<sup>12</sup> 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.<sup>12</sup>

In our study, we found that lycopene when combined with intra-lesional steroids offer more benefit than when used alone. Our study was supported by Chole 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, greater improvement in mouth opening when lycopene was combined with intralesional steroids and hyaluronidase used together with a significant p value of<0.001.<sup>13</sup>

With the exception of the individual's habit, the systemic conditions like iron deficiency and vitamin B complex deficiency subsists.<sup>14</sup> study of Borle and Borle postulated that treatment

following intralesional injections of various drugs leads to aggravated fibrosis and pronounced trismus.<sup>15</sup> The resultant worsening of this condition with submucosal injections are attributed to repeated needle stick injury<sup>16</sup> to the soft tissues at multiple sites, clinical irritation from drugs being injected, and to the progressive nature of the disease. The same outcome has been observed with some surgical methods employed to treat OSMF.

Nasolabial technique flap has versatility with single stinging 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 20mm. The primary action of CST is through immune modulation. CST suppress inflammation, decelerate fibrosis and up regulate immune mediated fibrinolytic pathways.

Excision of fibrous bands is also managed by CO<sub>2</sub> and KTP laser<sup>17</sup> a potassium-titanyl-phosphate that doubles the frequency of pulsed neodymium-yttrium-aluminium garnet laser energy to 532 nanometer wavelength.<sup>18,19</sup>

## CONCLUSION

It is important to make early diagnosis by periodic screening and biopsies of oral mucosa and management of high-risk oral premalignant lesions and prevention of cancer.

Management of moderate OSMF (Oral submucous fibrosis) includes oral lycopene with intradermal injection of kenacort and hyalase once weekly for 6 weeks. For advanced stages surgery is the better option.

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