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ORIGINAL ARTICLE

A COMPARATIVE STUDY BETWEEN MANAGEMENT OF ORAL SUBMUCOUS FIBROSIS

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ABSTRACT: BACKGROUND: Oral Submucous Fibrosis is a potentially premalignant disorder well known for its chronic and resistant nature. Currently available treatment with local injection of corticosteroids with Hyaluronidase is effective to some extent. The aim of the study was to evaluate whether the efficacy of the current treatment modality for submucous fibrosis can be improved by adding either oral lycopene or oral anti-oxidants along with local injection of steroids. **METHODS:** This study was conducted from July 2012 to August 2014 A total of 38 patients were included under this study with either grade 3 or 4 submucous fibrosis they were randomly divided in to 2 groups consisting 19 patients each Group 1 were given oral lycopene of dose 16mg/day along with once weekly intralesional injection of steroids and Hyaluronidase. Group 2 were given only once weekly intralesional injection of steroids and Hyaluronidase. Mouth opening recorded from baseline to 6 weeks. Cases were followed up for 6 months thereafter. **RESULTS:** There was significant increase in mouth opening in both the groups. The results were statistically significant between Group 1 and Group 2. Group 1 patients responded better than the other group and P value <0.001. **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 fibrosis, Lycopene, Antioxidants, Steroids, Hyaluronidase.

INTRODUCTION: Oral submucous fibrosis (OSF) 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.(1)

A variety of etiologic factors including capsaicin, betel nut alkaloids, hypersensitivity, autoimmunity, genetic predisposition and chronic iron and vitamin B-complex deficiency have been suggested by various authors, the most common of which is chewing areca nut.

Excessive use of areca nut may cause fibrosis due to increased synthesis of collagen and induce the production of free radicals and reactive oxygen species, which are responsible for high rate of oxidation/peroxidation of polyunsaturated fatty acids which affect essential constituents of cell membrane and might be involved in tumour genesis.[2] Areca nut chewing habit is very common in India, people even follow it as a culture in our society.(3) especially among elderly females.

The ingredients of areca nut induce excessive reactive oxygen species which damages the cell structures, including lipids and membranes, proteins and nucleic acids. Moreover vitamin deficiency, iron deficiency anaemia, and malnutrition can derange the repair of the inflamed oral mucosa, leading to defective healing and the resulting atrophic oral mucosa is more susceptible to the effects

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of areca nut. Here comes the role of Antioxidant vitamins that stabilize and deactivate the free radicals before they attack cells.

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.[4] Anyhow no single drug has provided complete relief of symptoms of OSF and hence combination treatment modality has been opted in our study.

MATERIALS AND METHODS: Totally 38 patients with signs and symptoms of OSF were recruited for the study from an ENT department of a tertiary care centre situated in a rural area, South India.

Informed consent was obtained from all patients Inclusion Criteria was:

- History of the habit of chewing areca nut or any of its commercial products.
- Restricted mouth opening with or without palpable vertical fibrous bands on the buccal mucosa with stiffness and blanching and without tongue involvement – Grade III and IV (Chandra et al[5]).

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 given to the patients, dental opinion given regarding improving oral hygiene and also patients were motivated to stop the habit.

The patients were then randomly divided into two groups (1&2) consisting of 19 cases each.

Group 1 patients were given oral Lycopene capsules 16 mg , one capsule/day along with once weekly Intralesional injections of Triamcinolone (Kenacort) 40mg/ml, 1ml & Hyaluronidase 1500 IU mixed with 2% lignocaine. Group 2 patients were given once weekly intralesional Injections of Triamcinolone (Kenacort) 40mg/ml, 1ml & Hyaluronidase 1500 IU mixed with 2% Lignocaine. Patients were evaluated every week during the treatment period of 6 weeks.

Mouth opening

Mouth opening was assessed by measuring the inter incisal distance from the upper right central incisor to the lower right central incisor using centimetre scale. If either of the teeth were missing, their left side counterpart was used for measurement. Moth 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 month follow-up period.

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Habits: All the patients included under the study had the habit of chewing areca nut either in the pure form or in the form of gutkha, pan masala or mawa. The most common form of areca nut used was in its pure form with tobacco leaves and lime (60.52%). 23 out of 38 patients were using it.

The mean duration of habits was 10 yrs. The mean frequency of chews per day was 3 times.

MOUTH OPENING:

Change in mouth opening among Group 1 Patients: Standard mean of mouth opening before the commencement of treatment was about 1.5 cm and on follow up after 6 months mouth opening increased to a standard mean of 4.7cm ± 1.5mm.

Change in mouth opening among Group 2 patients

Mouth opening after 6months increased to a standard mean of 3.5cm± 1mm.

RESULTS:

Age and sex Distribution: Patients fall within the age range of 33 and 67 years with maximum number of patients in the age group 41-50 years. 11 patients in group 1 and 8 patients in group 2 are in this age group. Out of 38 patients 27 were male patients and 11 were female patients.

Intergroup comparison in mouth Opening: When improvement in mouth opening is being compared between the two groups. There is a significant change between improvement showed by group 1 and group 2 at the end of 6 months.

Improvement in Group 1 Patients after 6 months	4.7cm ± 1.5mm.
Improvement in Group 2 Patients after 6 months	3.5cm± 1mm

P-value calculated to be <0.001 highly significant.

DISCUSSION: Oral submucous fibrosis is well known for its chronic and resistant nature. The conservative drug treatment that is currently available for OSF is clearly inadequate. No single drug has provided complete relief of symptoms of OSF; 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.

The antioxidant properties of lycopene are thought to be primarily involved in its preventive effects in chronic diseases, with a singlet-oxygen-quenching ability twice as high as that of β-carotene and 10 times higher than that of α-tocopherol.

The antioxidant potential has been ranked as follows: lycopene > α-tocopherol > α-carotene > ß-cryptoxanthin > zeaxanthin = ß-carotene > lutein.[8] OSF is well known for its high rate of malignant transformation and use of combination of drugs may be of great benefit by withholding its progression to carcinoma.

In our study 71% of the patients were males. It demonstrates the male predominance of the condition. In a study conducted by Ranganathan et al which recorded a male to female ratio of 9.9:1 among OSF patients.(9) Maximum number of patients in our study fell under the age group of 41-50 years. Almost all the patients from our study are chewing areca nut in its pure form as a cultural practice (84%). Even though OSF is more prevalent in Gutkha chewers (according to Bathi et al) than its pure form long duration of its use has led to the development of OSF in the population we studied.

Kumar et al suggests that severe cases of OSF are poor responders to lycopene. So in our study, we included patients only with grade III and IV OSF. When intergroup comparisons were made with regard to mouth opening, there was significant difference between Group 1 and 2. Lycopene exerts its anti-inflammatory action by increasing the lymphocyte resistance to stress,[9] inhibition of pivotal pro-inflammatory mediators, such as the reduction of reactive oxygen species, the inhibition of synthesis and release of pro-inflammatory cytokines, changes in the expression of cyclooxygenase and lipoxygenase, modifications of eicosanoid synthesis, and modulation of signal transduction pathways, including that of the inducible nitric oxide synthase.[10]

In our study we found out that lycopene when combined with intralesional steroids offer more benefit than when used alone. Our view is also 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, the greater improvement in mouth opening when lycopene was combined with intralesional steroids and Hyaluronidase it has contributed to the synergistic effect obtained when all these three drugs were used together with a significant P value of <0.001 in the group treated with lycopene.

CONCLUSION: Our study clearly demonstrates that 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.

It can be prescribed either alone as a first-line drug in early stages of the disease or in combination with intralesional steroids in moderate stages of OSF. Oral submucous fibrosis and to demonstrate the probable mechanisms through which it exerts its action.

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