Journal of Advanced Medical and Dental Sciences Research
@Society of Scientific Research and Studies
Journal home page: www.jamdsr.com doi: 10.21276/jamdsr ICV 2018= 82.06 UGC approved journal no. 63854
(e) ISSN Online: 2321-9599; (p) ISSN Print: 2348-6805

Original Research

Efficacy of Lycopene in combination with vitamin E in management of OSMF

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***ABSTRACT*:**
Background: Oral Submucous Fibrosis (OSMF) is a chronic progressive debilitating disease of the oral mucosa involving the oropharynx. OSMF is predominantly seen in people of South and Southeast Asia – India, Bangladesh, Sri Lanka, Pakistan, Taiwan, Southern China, etc., where chewing of betel quid, areca nut or its flavored formulations is frequently practiced.Lycopene has some beneficial effects in the treatment of certain diseases of oral cavity including oral cancer and precancerous lesions; lycopene does not have the pro-vitamin A activityand its various benefits on human health. **Aim of the study:** To assess the efficacy of Lycopene in combination with vitamin E in management of OSMF. **Materials and methods:** The study was conducted in the Department of Dentistry of Shridevi Institute of Medical science and research hospital, Tumakuru, Karnataka. A total of 50 patients, who were confirmed histologically and diagnostically wit OSMF were included in the study. An informed written consent was obtained from each patient after explaining them the procedure and aim of the study.The patients were randomly grouped into two groups, Group A and Group B. Patients in Group A were treated with Lycopene 8 mg, whereas, patients in Group B were treated with Lycopene 8 mg + Vit. E (400 IU).At follow-up visits, patients were assessed for inter-incisal distance in mm and burning sensation by visual analog scale from 1 to 10. **Results:** A total of 50 patients with OSMF were included in the study.The mean mouth opening after the completion of treatment in Group A was 5.12$\pm$1.65 mm and in Group B was 6.87$\pm$2.01 mm. The results on comparing were found to be statistically significant. ($p<0.05$) In group A, burning sensation was still present after the treatment in 3 patients and was absent in 22 patients. In group B, burning sensation was still present after the treatment in one patient and was absent in 24 patients. The results on comparison were found to be statistically significant. **Conclusion**: From the results of the present study, we conclude that Lycopene 8 mg with Vitamin E is highly effective treatment for OSMF patients.
Key words: Lycopene, OSMF, Premalignant, Vitamin E.

Received: 10 May, 2019 Revised: 28 May 2019 Accepted: 29 May 2019

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This article may be cited as: K. Kumar V , LN Akshatha, Kumaraswamy S, H G Suhas, Topajiche SS. Efficacy of Lycopene in combination with vitamin E in management of OSMF. J Adv Med Dent Scie Res 2019;7(6): 6-9.

INTRODUCTION:

Oral Submucous Fibrosis (OSMF) is a chronic progressive debilitating disease of the oral mucosa involving the oropharynx. OSMF is predominantly seen in people of South and Southeast Asia – India, Bangladesh, Sri Lanka, Pakistan, Taiwan, Southern China, etc., where chewing of betel quid, areca nut or its flavored formulations is frequently practiced.[1] The rapid increase in the prevalence of this disease is due to an upsurge in the popularity of commercially available areca nut and tobacco preparations – gutkha, pan masala, flavored areca nut, mawa, etc., in Asian countries.[2] It causes significant morbidity, in terms of loss of mouth function as tissues become rigid and mouth opening becomes difficult, and mortality because of

transformation into squamous cell carcinoma. The classical features of this disease is blanching and stiffness of the oral mucosa, trismus, burning sensation in the mouth and hypomobility of the soft palate and tongue with loss of gustatory sensation.[3] Lycopene has some beneficial effects in the treatment of certain diseases of oral cavity including oral cancer and precancerous lesions; lycopene does not have the pro-vitamin A activity[4] and its various benefits on human health can be explained based on its properties of:

- AO activity
- Inhibition of cancer cell proliferation
- Interference with growth factor stimulation
- Inducing phase II enzymes
- Regulation of transcription and
- Restoration of gap junctions

Its mode of action may involve stimulation of the immune system or a direct action on the tumor cells. Lycopene has been shown to inhibit hepatic fibrogenesis in liver endothelial cell rats and it may also exert a similar inhibition on the abnormal fibroblasts in OSMF.[5] Lycopene also up-regulates the lymphocyte resistance to stress and suppresses the inflammatory response.[6] Hence, the present study was planned to assess the efficacy of Lycopene in combination with vitamin E in management of OSMF.

MATERIALS AND METHODS:

The study was conducted in the Department of Dentistry of Shridevi Institute of Medical science and research hospital, Tumakuru, Karnataka. The ethical clearance for study protocol was obtained from ethical committee of the institution. A total of 50 patients, who were confirmed histologically and diagnostically wit OSMF were included in the study. An informed written consent was obtained from each patient after explaining them the procedure and aim of the study. At each visit, patients were assessed for tobacco chewing and smoking habits and were encouraged to stop them. The patients were randomly grouped into two groups, Group A and Group B. Patients in Group A were treated with Lycopene 8 mg, whereas, patients in Group B were treated with Lycopene 8 mg + Vit. E (400 IU). The treatment commenced for a period of 3 months during which patients were called for follow up visits every 15 days. Also, patients were further followed up for 2 months. At follow-up visits, patients were assessed for inter-incisal distance in mm and burning sensation by visual analog scale from 1 to 10. The records for each visit were tabulated and subject to further evaluation.

The statistical analysis of the data was done using SPSS version 11.0 for windows. Chi-square and Student's t-test were used for checking the significance of the data. A p-value of 0.05 and lesser was defined to be statistical significant.

RESULTS:

A total of 50 patients with OSMF were included in the study. Patients were randomly grouped into Group A and B. patients in Group A received treatment with Lycopene and In Group B received treeatment with Lycopene and Vitamin E. Table 1 shows the comparison of mouth opening post-treatment between Group A and Group B. The mean mouth opening after the completion of treatment in Group A was 5.12 ± 1.65 mm and in Group B was 6.87 ± 2.01 mm. The results on comparing were found to be statistically significant. ($p<0.05$) Table 2 shows the comparison of burning sensation after the completion of treatment between both groups. In group A, burning sensation was still present after the treatment in 3 patients and was absent in 22 patients. In group B, burning sensation was still present after the treatment in one patient and was absent in 24 patients. The results on comparison were found to be statistically significant. ($p<0.05$)

Groups	Mean mouth opening (post-treatment) (mm)	p-value
Group A	5.12 ± 1.65	0.02
Group B	6.87 ± 2.01	

Table 1: Comparison of mouth opening (post-treatment) between Group A and Group B

Groups	Burning sensation (post-treatment)		p-value
	Present	Absent	
Group A	3	22	0.01
Group B	1	24	

Table 2: Comparison of burning sensation after the completion of treatment between both groups

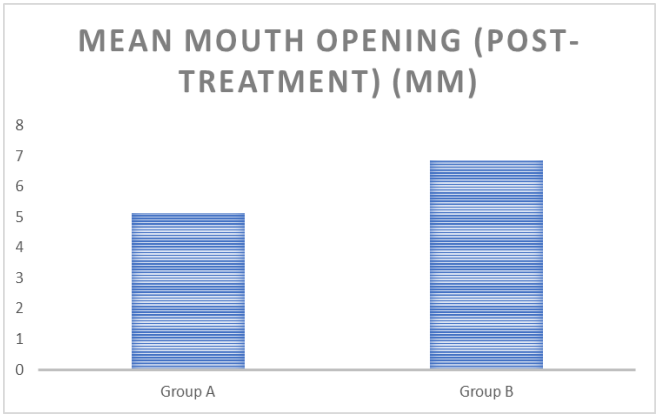

Fig 1: Comparison of mouth opening (post-treatment) between Group A and Group B

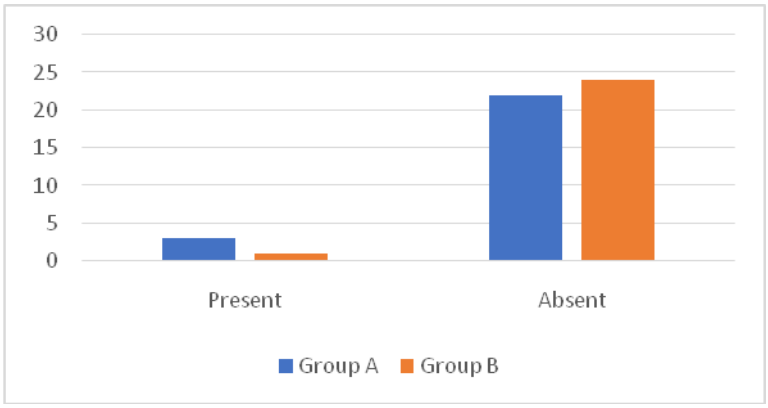

Fig 2: Burning sensation after the completion of treatment between both groups

DISCUSSION:

The present study was conducted to assess the efficacy of Lycopene with Vitamin E for the treatment of OSMF. A total of 50 patients with OSMF were included in the study and were randomly grouped into two groups. It was observed that both the groups had significant improvement in symptoms, however, patients in group B had more improvement as compared to group A. The results were found to be statistically significant. The results were compared with previous studies in literature. Johny J et al evaluated the efficacy of lycopene and lycopene−hyaluronidase combination and compared the efficacy of lycopene and lycopene−hyaluronidase combination in the treatment of OSMF. The study consisted of 45 patients with OSMF divided into three equal groups. Patients in Group A were given Lycored 16 mg daily in two equally divided doses for 3 months. Patients in Group B were given LycoRed along with hyaluronidase intralesional injection of 1500 IU twice weekly for 3 months. Patients in Group C were given placebo capsules. Patients were evaluated after 3 months. The following parameters were recorded: mouth opening, visual inspection, palpatory findings, and burning sensation. There was statistically significant change in mouth opening and burning sensation for lycopene and lycopene–hyaluronidase combination than in the placebo group in the treatment of OSMF, but the lycopene–hyaluronidase combination did not show any statistically significant change when compared with lycopene alone. They concluded that Lycopene appears to be a very promising antioxidant in the management of oral submucous fibrosis, both in clinical and symptomatic improvement. Saran G et al compared and evaluated the efficacy of lycopene and curcumin given orally in clinically diagnosed OSMF patients. Sixty patients were divided randomly into two groups Group A and Group B. After fulfilling the eligibility criteria, sixty patients were randomly allotted based on fishbowl method into thirty each. This technique eliminated the selection bias arising in the study. Group A individuals were treated with 4 mg of lycopene and Group B individuals were given 300 mg of curcumin thrice daily for 3 months. Both the groups were

assessed in terms of mouth opening and burning sensation. The statistical analysis was done using SPSS Version 16.0 statistical Analysis Software. In Group A, the initial burning sensation was 65.83 ± 3.98%, and in Group B, it was 62.33 ± 5.22% (visual analog scale). After 3 months, there was complete cessation of burning sensation in both the groups. Burning sensation between the groups was statistically nonsignificant. In Group A, mean mouth opening at baseline (1st visit) observed was 3.17 ± 0.08 cm which improved to 3.52 ± 0.07 cm after 3 months of the treatment period. In Group B, mean mouth opening at baseline (1st visit) observed was 3.32 ± 0.07 cm which improved to 3.52 ± 0.08 cm after 3 months of the treatment period. On comparing intergroup, the difference was statistically nonsignificant. However, on comparing intergroup, average percent change in mean mouth opening from 1st visit to subsequent time intervals across the time period was found to be statistically significant. Group A showed 11.1 ± 1.0% improvement in mean mouth opening and Group B showed 6.2 ± 0.4% improvement in the mean mouth opening from the 1st visit till the posttreatment period. The change in the mean mouth opening from 1st visit till posttreatment in Group A was 0.35 ± 0.14, and in Group B, it was 0.20 ± 0.09. They concluded that Lycopene showed better results than curcumin in improving mouth opening; both the drugs were equally effective in decreasing burning sensation in OSMF patients.[7, 8]

Karemore TV et al compared the effect of newer antioxidant lycopene with a placebo in conjunction with the cessation of causative habit in the treatment of OSMF. The study group included 92 patients with OSMF. The OSMF diagnosis was established through a composite of accepted clinical and histopathological characteristics. Out of 92, 46 patients were given lycopene and remaining 46 were on placebo drug. Lycopene group patients received 8 mg Lycored TM per day in two divided doses of 4 mg each, while placebo group patients received placebo tablet twice a day. Patients were examined for changes in mouth opening and other clinical symptoms of OSMF during three months and were followed up for next two months. Lycopene was found to be significantly efficacious in the amelioration of signs and symptoms of OSMF. It was effective in reducing the objective signs of OSMF as demonstrated by the improved maximal mouth opening, percentage of which was 69.56%. they concluded that reactive oxygen compounds or free radicals have been implicated as one of the major harmful factors for premalignant and malignant conditions. Piyush P et al evaluated and compared the therapeutic response of lycopene and curcumin with placebo in patients suffering from oral submucous fibrosis (OSMF) and to correlate the habit variables of smoked and smokeless tobacco products in OSMF. A randomized placebo-controlled parallel clinical study was conducted on ninety OSMF patients, who were divided into three treatment groups using computer-generated randomization. Group A patients (n = 30) were given curcumin tablet (300 mg) twice daily, Group B patients (n = 30) received lycopene capsules (8 mg) twice daily, and for Group C (n = 30), placebo capsules were given once daily for a period of six months. Both the participant and outcome assessor were blinded. Pre- and post-treatment comparison of mouth opening, burning sensation, tongue protrusion, and cheek flexibility was analyzed at periodic follow-up of 9 months. The overall improvement in mouth opening, burning sensation, tongue protrusion, and cheek flexibility was 3.9 ± 4.9 mm, 4.8 ± 2.6, 5.0 ± 7.2 mm, & 0.36 ± 0.71 mm, respectively, for curcumin and 4.1 ± 4.2 mm, 5.0 ± 2.3, 2.4 ± 3.5 mm, & 0.66 ± 0.80 mm, respectively, for lycopene with the p value <0.05. Statistically significant improvement in clinical findings was observed in both curcumin and lycopene treatment groups in comparison with placebo. However, the therapeutic efficacy of curcumin and lycopene was found to be almost equal in OSMF patients.[9, 10]

CONCLUSION:

From the results of the present study, we conclude that Lycopene 8 mg with Vitamin E is highly effective treatment for OSMF patients.

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