

How to Cite:

Kumari, K., Rangari, P., Sonal, S., & Jethlia, A. (2022). Comparative assessment of the efficacy of lycopene alone to a combination of lycopene hyaluronidase for the treatment of oral submucous fibrosis. *International Journal of Health Sciences*, 6(S2), 4012–4017. <https://doi.org/10.53730/ijhs.v6nS2.5883>

Comparative assessment of the efficacy of lycopene alone to a combination of lycopene hyaluronidase for the treatment of oral submucous fibrosis

Khushboo Kumari

Department of Oral Pathology, Buddha Institute of Dental Sciences and Hospital, Patna, Bihar, India

Priyadarshini Rangari

MDS, Associate professor, Department of Dentistry, Sri Shankaracharya Institute of Medical Sciences, Bhilai, Durg, Chhattisgarh, India

Sonal

MDS, Senior Lecturer, Department of Conservative Dentistry and Endodontics, Dr. B. R. Ambedkar Institute of Dental Sciences and Hospital, Patna, Bihar, India

Ankur Jethlia

Assistant Professor, Department Maxillofacial and Diagnostic sciences, Diagnostic Division College of Dentistry, Jazan University, Saudi Arabia
Email: jethliaankur@yahoo.co.in

Abstract---Background: OSMF is an oral precancerous condition with a high potential for malignant transformation. The main etiologic factor linked to OSMF is gutkha and tobacco chewing. Management of OSMF includes various therapies and drugs where the use of antioxidants has proven to be efficacious. Aim: The present study was conducted to compare and assess the efficacy of Lycopene antioxidant alone to its combination with intralesional injection of Hyaluronidase for managing the subjects with OSMF. Material and Method: The study included 54 subjects having stage 2 OSMF and were divided into 2 groups where the group I subjects were given lycopene daily in a dose of 8mg in two equal doses, whereas, group II subjects were given lycopene daily in a dose of 8mg combined with intralesional hyaluronidase injection of 1500 IU twice in a week for 3 months. VAS and inter-incisal mouth opening were assessed at baseline and 90th day after treatment completion. Results: At baseline, interincisal opening in Group I was 25.18±3.03mm and was 24.56±3.92mm in Group II. This difference was statistically non-significant with

$p=0.5184$. On the 90th day, the last day of the study, interincisal opening in Group I was $29.34\pm 3.19\text{mm}$, whereas, in Group II was $32.39\pm 3.24\text{mm}$. This was significantly higher in Group II with lycopene and intralesional hyaluronidase injection compared to lycopene alone with $p=0.001$. The interincisal opening showed significant improvement from baseline to last day in Group I and Group II both of which was statistically significant in both the groups with $p<0.001$. VAS scores, at baseline the mean VAS score for group I was higher with 7.14 ± 0.98 compared to group II where it was 6.45 ± 1.12 . This difference was statistically non-significant with $p=0.224$. On the last 90th day, VAS scores in Group II were significantly lower with 0.18 ± 0.14 compared to 0.86 ± 0.74 with $p=0.001$. Conclusion: The present study concludes that intralesional hyaluronidase injection is more efficacious in managing subjects with OSMF compared to the use of Lycopene alone.

Keywords---antioxidant, hyaluronidase, intralesional injections, lycopene, OSMF.

Introduction

OSMF (Oral submucous fibrosis) is seen in the oral cavity and depicts a precancerous condition marked by progressive submucosal tissue fibrosis with inflammatory components leading to trismus and rigidity in the oral cavity. It is commonly seen in India with a high prevalence. The main etiologic factor for OSMF is chewing of areca nut/tobacco leading to reduced/difficult mouth opening due to fibrosis and progressing submucosal inflammation. OSMF dates back to the ancient era with a vidari condition mentioned in Susruta with a similar clinical condition. It has a high potential for malignant transformation and mainly affects the Southeast Asian population. It affects all ages and genders with a male predilection for age 20-40 years. With multifactorial aetiology (collagen disorders, genetic susceptibility, nutritional deficiency, chili consumption, and areca nut chewing) and complex etiopathogenesis, management of OSMF is challenging to the treating clinician.¹

OSMF mainly affects Type-I collagen fibers with different amounts of other collagen types. In OSMF, increased new collagen synthesis is seen by myofibroblasts exceeding the degradation rates leading to increased collagen synthesis over time. This results in fibrosis presenting as a burning sensation and restricted mouth opening. A rapid increase in OSMF prevalence in India is noted in the past 40 years from 0.003% to 6.42% with a rate of malignant transformation in nearly 7% to 30% cases. Conservative management of OSMF aims to give medication to the affected subjects along with quitting the habit. However, complete regression of OSMF is not reported yet making no single management strategy as efficacious.²

Reduction in the incidence of oral precancerous lesions and conditions is seen with carotenoids. Another antioxidant, lycopene, is a carotenoid derived from plants having high antioxidant properties. Previous literature work has shown

that antioxidant and anti-carcinogenic properties are being favored for the treatment of oral precancerous lesions and conditions such as OSMF and leukoplakia.³

Another enzyme, hyaluronidase which imparts its action by degradation of hyaluronic acid, which is the main ground substance in the various connective tissues is also extensively studied and is found efficacious for the management of the OSMF conservatively.⁴ The present comparative clinical study was conducted to compare and assess the efficacy of Lycopene antioxidant alone to its combination with intralesional injection of Hyaluronidase for managing the subjects with OSMF.

Materials and Methods

The present prospective clinical study was conducted to compare and assess the efficacy of Lycopene antioxidant alone to its combination with intralesional injection of Hyaluronidase for managing the subjects with OSMF. The study was carried out after obtaining clearance from the concerned Ethical committee. The study population was comprised of the subjects visiting the Outpatient Department of the Oral Medicine and Radiology of the Institute. The study included a total of 54 subjects who were males within the age range of 25-40 years and the mean age of 34.8 ± 6.28 years. All the included subjects had only Grade 2 OSMF. The exclusion criteria for the study were subjects having metabolic disorders, gastrointestinal diseases, cardiac, and psychiatric problems. After explaining the detailed study design, informed consent was taken from all the study subjects.

After the final inclusion of the study subjects, detailed history was recorded for all the subjects followed by the physical examination. Medical and family history was recorded for all the subjects along with habit history including alcohol intake, smoking, chewing of pan masala, gutkha, or areca nuts. The 54 study subjects were then divided into two groups having equal subjects each. Group I subject were given lycopene capsule in a dose of 8mg daily in two equal doses having selenium, zinc, and lycopene for 3 months, whereas, Group II subjects were given lycopene capsule in a dose of 8mg daily in two equal doses along with 1500 IU hyaluronidase injection weekly for 3 months. Additively, habit cessation and mouth opening exercises were instilled in all the subjects of both groups.

The parameters assessed in the present study were burning sensation using VAS (visual analog scale) at the scale of 0 to 10 and the interincisal distance in millimeters by assessing the improvement in the mouth opening. Both the study parameters were assessed at baseline of day 1 and at 90th day which is the last day of the study. The collected data were subjected to the statistical evaluation using SPSS software version 21 (Chicago, IL, USA) and one-way ANOVA and t-test for results formulation. The data were expressed in percentage and number, and mean and standard deviation. The level of significance was kept at $p < 0.05$.

Results

The present prospective clinical study was conducted to compare and assess the efficacy of Lycopene antioxidant alone to its combination with intralesional injection of Hyaluronidase for managing the subjects with OSMF. The study included a total of 54 subjects who were males within the age range of 25-40 years and the mean age of 34.8 ± 6.28 years. All the study subjects were male. The etiology was betel quid/areca nut chewing in 51.85% (n=28) subjects, pan masala, and gutkha chewing in 25.92% (n=14) study subjects, tobacco chewing in 20.37% (n=11) study subjects, and mawa chewing in 1.85% (n=1) study subjects as shown in Table 1.

On assessing the interincisal opening in the two groups of study subjects, it was seen that at baseline, day 1, interincisal opening in Group I was 25.18 ± 3.03 mm and was 24.56 ± 3.92 mm in Group II. This difference was statistically non-significant with $p=0.5184$. On the 90th day, the last day of the study, interincisal opening in Group I was 29.34 ± 3.19 mm, whereas, in Group II was 32.39 ± 3.24 mm. This was significantly higher in Group II with lycopene and intralesional hyaluronidase injection compared to lycopene alone with $p=0.001$. The interincisal opening showed significant improvement from baseline to last day in Group I and Group II both of which was statistically significant in both the groups with $p<0.001$ as shown in Table 2.

For the burning sensation on the oral mucosa in the study subjects using the VAS scores, at baseline the mean VAS score for group I was higher with 7.14 ± 0.98 compared to group II where it was 6.45 ± 1.12 . This difference was statistically non-significant with $p=0.224$. On the last 90th day, VAS scores in Group II were significantly lower with 0.18 ± 0.14 compared to 0.86 ± 0.74 with $p=0.001$. VAS score in Group I reduced significantly from 7.14 ± 0.98 to 0.86 ± 0.74 with $p<0.001$, whereas, in Group II, it also reduced significantly from 6.45 ± 1.12 at baseline to 0.18 ± 0.14 at day 90th with $p<0.001$ as summarized in Table 3.

Discussion

The present prospective clinical study was conducted to compare and assess the efficacy of Lycopene antioxidant alone to its combination with intralesional injection of Hyaluronidase for managing the subjects with OSMF. The study included a total of 54 subjects who were males within the age range of 25-40 years and the mean age of 34.8 ± 6.28 years. All the study subjects were male. The aetiology was betel quid/areca nut chewing in 51.85% (n=28) subjects, pan masala and gutkha chewing in 25.92% (n=14) study subjects, tobacco chewing in 20.37% (n=11) study subjects, and mawa chewing in 1.85% (n=1) study subjects. These demographics were comparable to the studies of Shah PH et al⁵ in 2016 and Guduru H et al⁶ in 2019 where authors assessed subjects with comparable demographics as in the present study.

For the assessment of the interincisal opening in the two groups of study subjects, it was seen that at baseline, day 1, interincisal opening in Group I was 25.18 ± 3.03 mm and was 24.56 ± 3.92 mm in Group II. This difference was statistically non-significant with $p=0.5184$. On the 90th day, the last day of the

study, interincisal opening in Group I was 29.34 ± 3.19 mm, whereas, in Group II was 32.39 ± 3.24 mm. This was significantly higher in Group II with lycopene and intralesional hyaluronidase injection compared to lycopene alone with $p=0.001$. The interincisal opening showed significant improvement from baseline to last day in Group I and Group II both of which was statistically significant in both the groups with $p<0.001$. These results were consistent with the results of James L et al⁷ in 2015 and Guo J et al⁸ in 2020 where authors reported significant improvement in the interincisal opening after lycopene as well as combined lycopene hyaluronidase injection in subjects with OSMF.

Concerning the burning sensation on the oral mucosa in the study subjects using the VAS scores, at baseline the mean VAS score for group I was higher with 7.14 ± 0.98 compared to group II where it was 6.45 ± 1.12 . This difference was statistically non-significant with $p=0.224$. On the last 90th day, VAS scores in Group II were significantly lower with 0.18 ± 0.14 compared to 0.86 ± 0.74 with $p=0.001$. VAS score in Group I reduced significantly from 7.14 ± 0.98 to 0.86 ± 0.74 with $p<0.001$, whereas, in Group II, it also reduced significantly from 6.45 ± 1.12 at baseline to 0.18 ± 0.14 on day 90th with $p<0.001$. These results were in agreement with the findings of Buhren BA et al⁹ in 2016 and Gupta N et al¹⁰ in 2020 where authors reported significant improvement in burning sensation and VAS scores following lycopene as well as combined lycopene hyaluronidase injection as in the present study.

Conclusion

Within its limitations, the present study concludes that intralesional hyaluronidase injection is more efficacious in managing subjects with OSMF compared to the use of Lycopene alone. The present study had a few limitations including small sample size, shorter monitoring period, and geographical area biases. Hence, more longitudinal studies with a larger sample size and longer monitoring period will help reach a definitive conclusion.

References

1. Vashishth M, Chhabada A, Rangari P, Babjee KC. Comparison of intralesional hydrocortisone and hyaluronidase injection to surgical repair in managing the oral submucous fibrosis: A prospective clinical study. *International Journal of Health and Clinical Research*, 2021; 4(15):418-421.
2. Passi D, Bhanot P, Kacker D, Chahal D, Atri M, Panwar Y. Oral submucous fibrosis: Newer proposed classification with critical updates in pathogenesis and management strategies. *Natl J Maxillofac Surg*. 2017;8:89-94.
3. Bari S, Metgud R, Vyas Z, Tak A. An update on studies on etiological factors, disease progression, and malignant transformation in oral submucous fibrosis. *J Cancer Res Ther*. 2017;13:399-405.
4. Selvam NP, Dyanand AA. Lycopene in the management of oral submucous fibrosis. *Ind J Dent Res*. 2012;23:524-8.
5. Shah PH, Venkatesh R, More CB, Vassandacoumara V. Comparison of Therapeutic Efficacy of Placental Extract with Dexamethasone and Hyaluronic Acid with Dexamethasone for Oral Submucous Fibrosis - A Retrospective Analysis. *J Clin Diagn Res*. 2016;10:63-6.

6. Guduru H, Garlapati K, Solomon RV, Ignatius AV, Yeladandi M, Madireddy N. A comparative study of efficacy of intralesional corticosteroids and hyaluronidase therapy with and without ultrasound therapy in patients with oral submucous fibrosis. *J Indian Acad Oral Med Radiol.* 2019;31:11-6.
7. James L, Shetty A, Rishi D, Abraham M. Management of Oral Submucous Fibrosis with Injection of Hyaluronidase and Dexamethasone in Grade III Oral Submucous Fibrosis: A Retrospective Study. *J Int Oral Health.* 2015;7:82-5.
8. Guo J, Xie H, Mao S, Liang M, Wu H. Efficacy of hyaluronidase combined with corticosteroids in treatment of oral submucous fibrosis: A meta-analysis of randomized controlled clinical trials. *J Oral Pathol Med.* 2020;49:311-9.
9. Bühren BA, Schrumpf H, Hoff NP, Bölke E, Hilton S, Greber PA. Hyaluronidase: from clinical applications to molecular and cellular mechanisms. *Eur J Med Res.* 2016;21:5.
10. Gupta N, Kalaskar A, Kalaskar R. Efficacy of lycopene in management of Oral Submucous Fibrosis- A systematic review and meta-analysis. *J Oral BiolCraniofac Res.* 2020;10:690-7.

Characteristics		Percentage (%)	Number (n=520)
Mean age (years)		34.8±6.28	
Age range (years)		25-40	
Gender	Males	100	54
	Females	-	-
Etiology	Betel quid/areca nut	51.85	28
	Pan masala/gutkha	25.92	14
	Tobacco	20.37	11
	Mawa	1.85	1

Table 1: Demographic characteristics of the study subjects

Time assessment	Group I (n=27) mm	Group II (n=27) mm	p-value
Baseline (day 1)	25.18±3.03	24.56±3.92	0.5184
Last time (day 90)	29.34±3.19	32.39±3.24	0.001
p-value	<0.001	<0.001	

Table 2: Interincisal opening in millimeters for the two groups of the study subjects

Time assessment	Group I (n=27) mm	Group II (n=27) mm	p-value
Baseline (day 1)	7.14±0.98	6.45±1.12	0.224
Last time (day 90)	0.86±0.74	0.18±0.14	0.001
p-value	<0.001	<0.001	

Table 3: VAS for burning sensation for the two groups of the study subjects