

Determination of Clinical Efficacy of Lycopene and Curcumin in the Treatment of Oral Submucous Fibrosis Using Ultrasonography: A Comparative Study

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ABSTRACT

Objective: To compare the effectiveness of lycopene and curcumin using ultrasonography to assess changes in fibrous bands in patients with oral submucous fibrosis (OSMF).

Methodology: This comparative prospective study was conducted at the Department of Oral Diagnosis, Bhitai Dental & Medical College, Mirpurkhas, Sindh, from March 2023 to February 2024. Patients were randomly allocated into two equal groups: Group A and Group B. At baseline, all patients underwent clinical examination. Mouth opening was measured using a Vernier caliper, burning sensation was assessed using a Visual Analog Scale (VAS), and ultrasonography was performed to evaluate the extent of fibrous bands. Patients in Group A received lycopene 4 mg twice daily for three months, whereas patients in Group B received curcumin 4 mg twice daily for the same duration. Mouth opening, burning sensation, and ultrasonographic findings of fibrous bands were assessed monthly throughout the treatment period.

Results: Of the 40 patients included, 33 (82.5%) were males and 7 (17.5%) were females. The mean age of the male patients was 32.8 ± 7.5 years, while the mean age of the female patients was 29.6 ± 6.5 years. Following treatment, both groups showed improvement; however, Group A demonstrated a significantly greater increase in mean mouth opening (5.5 mm) than Group B (3.0 mm) ($P < 0.001$). Lycopene was also more effective than curcumin in reducing burning sensation.

Conclusion: Lycopene was more effective than curcumin in improving mouth opening and reducing burning sensation in patients with oral submucous fibrosis.

Keywords: Curcumin, Lycopene, Oral submucous fibrosis, OSMF, Ultrasonography.

Introduction

Oral submucous fibrosis (OSMF) is a protracted, progressive, and oral precancerous condition that disturbs the mucous membrane of the mouth and throat.¹ It is described by the presence of tough bands of flesh in the 'submucosal layer', which leads to imperfect mouth germinal (trismus) and difficulty in swallowing. The main indications of OSMF include a scorching impression in the mouth, trouble in opening the mouth, and a feeling of tightness in the mouth and

throat. The disease can progress to the point where the person is unable to eat solid food or speak clearly.²

OSMF was first characterized by Schwartz in 1952, and at that time it was known as atrophic idiopathica (tropica) mucosae oris.³ It is thought that the fibrosis seen in OSMF is the result of a complex interplay between multiple factors, including the chemical components of tobacco and areca nut, nutritious lack ("deficiency of vitamins and iron"), usage of "chilies"

(Spices), and immune system dysfunction.⁴ The alkaloids and other compounds in these substances can cause swelling, DNA damage and oxidative stress, in the "oral mucosa", leading to the activation of fibroblasts and the deposition of collagen and other extracellular matrix proteins. The Oral submucous fibrosis" (OSMF) is primarily a sickness in Southeast and South Asia, where the habit of mastication of areca and tobacco nut is widespread.⁵ The prevalence of OSMF varies widely across different regions and populations within this area. In India, OSMF is estimated to affect between 2.5 to 4.5 million people, with higher rates observed in certain regions such as the northeastern states and the state of Maharashtra.⁶ In Bangladesh, the occurrence of OSMF is estimated to be about 2%, with higher rates reported in some areas.⁷ In Pakistan, the reported prevalence of OSMF ranges from 0.2% to 7.6%, depending on the population studied.⁸ Other countries in the region where OSMF has been reported include Sri Lanka, Myanmar, Thailand, Malaysia, and Indonesia. However, the available data on the prevalence of OSMF in these countries is limited and varies widely.⁹

The high prevalence of OSMF in these regions is a chief community health apprehension, as the condition is associated with a significantly increased risk of oral cancer, which has a poor prognosis if not detected and treated early. Other risk factors for developing OSMF include tobacco use, alcohol consumption, poor nutrition, and genetic predisposition.¹⁰

There is no recognized cure for OSMF, and management focuses on managing symptoms and preventing the disease from progressing. This includes quitting betel nut chewing and other risk factors, nutritional support, mouth opening exercises, and in severe cases, surgical intervention.¹¹ Early detection and intervention are important in preventing the disease from progressing to advanced stages. The most usual treatment is with antioxidants. Antioxidants work by stimulating the immune system or directly attacking tumor cells, they are antimitogenic and antimutagenic with the same mechanism of interrupting free radical chain reaction.¹² Therefore the goal of learning was to evaluate the efficacy of two antioxidants Lycopene and Curcumin in OSMF patients and evaluate them by ultrasonography in order to determine the effects of the drug on fibrous bands after treatment.

Lycopene is a "carotenoid pigment" present in a variety of foods, but especially tomatoes and tomato-based products. A red carotenoid that does not convert to vitamin A. The antioxidant lycopene has been linked to a wide range of health benefits. Researchers have shown that it may help prevent cancers such as prostate, lung, and cancer of the stomach. By lowering inflammation and oxidative stress, it may also assist to reduce the risk of cardiovascular disease. Phytochemicals like lycopene

are only created by vegetation ("like tomatoes") and microbes but not by humans and animals, so they must get their lycopene needs met through diet or pharmacological supplements. Numerous studies have been conducted on lycopene because of its many purported health advantages. However, the Curcumin, a chemical found naturally in spice turmeric, is thought to have antioxidant and anti-inflammatory and qualities and has been the subject of much research. Turmeric is extensively used in Indian and Southeast Asian cuisine. Free radicals, chemicals that may cause oxidative destruction of cells and contribute to chronic illnesses, including cancer, cardiovascular disease, and Alzheimer's, are effectively mopped up by this compound. The health advantages it has the potential to provide numerous, including relief from pain and other symptoms. Overall the natural antioxidants like lycopene and curcumin have revealed anti-inflammatory and antifibrotic properties, but comparative evidence on their effectiveness is very limited specifically at local level. Hence present was aimed to assess and comparative effectiveness of lycopene and curcumin in improving clinical symptoms and ultrasonographic fibrous bands among patients of OSMF, which may helpful for the clinicians in the selection of more effective management option to improve outcomes among such patients.

Methodology

This current study was carried out at the "Oral diagnosis department Bhitai Dental & Medical College Mirpur-khas Sindh after taking ethical approval from the parent institution ref no BDMC/R &D/ERC/2023-12. This study was carried out from 1st March 2023 to 28th February 2024. A total 40 number of patients were comprised in learning and randomly separated into two Groups A and Group B equally. The study purpose and follow-up period were informed to patients and a written consent was filled by all participants. Patients were informed about the OSMF and chances of malignancy and were advised to quit the habit of chewing betel nuts (pan, gutka, and chalia) before starting treatment. Those patients who were unable to come for follow- up examination, patients with hypertensive, systematic disease, pregnant women, and who were allergic to the drug were excluded from the study. Patients who were well oriented and physically healthy and in time and place, with a optimistic antiquity of "chewing areca nut" or one of its profitable arrangements. Patients with symptoms of OSMF included a scorching feeling while eating spicy meals, difficulties with crediting and oral mucosa boiling, chewing, perceptible fibrous bands, and a limited opening in the mouth (20-30 mm) were included in the study.

Patients of Group A (n=20) and Group B (n=20) were clinically examined, mouth opening of patients was dignified by a Vernier caliper scale, burning sensation was measured by visual analog scale (VAS), patient's age, gender, and ultrasonography was performed in each patient to the evaluate the number of fibrous bands before the treatment.

Group A patients have treated with lycopene 4mg (Product name: Advance, Nature's Bounty) twice a day for three months, while patients under Group B were given Curcumin 4mg (Product name: turmeric Curcumin, Nutrifactor pharma) twice in a day for three months. Mouth opening, burning sensation, and fibrous bands by ultrasonography were recorded every month after treatment. All the data were recorded in MS Excel (2013) worksheet, data were analyzed by SPSS version 16.0.

Results

Overall 40 patients were comprised in the study, with majority of males (82.5%), while females were (17.5%), with overall mean age of male patients, 32.8 ± 7.5 years, and female patients as 29.6 ± 6.5 years, indicating male predominance and mostly belonging to the young adult age group as shown in table I.

According to the comparison of mean mouth opening between Group A and Group B on different time intervals, the group B showed a slightly higher mean mouth opening (26.2 ± 2.9 mm) in contrast to group A (25.1 ± 2.1 mm), at baseline (pre-treatment). However, after one month, both groups showed improvement, with higher mean value (27.9 ± 3.1 mm) in group B

compared to group A (26.9 ± 1.9 mm), ($p = 0.03$), while after two months of treatment, the mean mouth opening further improved in both groups (28.2 ± 1.5 mm and 28.7 ± 3.3 mm) respectively, without significant difference ($p = 0.05$). Moreover, after three months of treatment, group A showed a higher mean mouth opening (30.6 ± 1.2 mm) versus group B (29.2 ± 3.3 mm); while the difference was statistically insignificant ($p = 0.12$), indicating that the mean mouth opening was progressively improved in both groups over the time in both groups. Table II

Table I: Mean age and gender distribution of OSMF patients.

Gender	n	%	Mean SD
Male	33	82.5%	32.8 ± 7.5 years
Female	07	17.5%	29.6 ± 6.5 years

Pre-treatment the burning sensation was moderate to severe in almost all of the cases on both groups ($p=0.429$). After one-month of treatment, moderate burning sensation remained the predominant in both groups (in 17 cases of Group A and in 18 cases of Group B) ($p = 0.834$), followed by after two months of treatment, it was shifted toward mild burning sensation became more frequent, while the moderate burning sensation was still higher ($p = 0.582$). However, after three months of treatment, mild burning sensation was the most common in both groups, while moderate burning sensation was significantly lower in Group A compared to group B ($p = 0.025$), as shown in table III.

The mean of USG fibrous band scores was almost similar in both groups at baseline and after one month

Table II: Comparison of mean mouth opening in both groups

Prospective PeriodMouth Opening	Group A (Mean SD)	Group B (Mean SD)	T-Value	P-Value
Pre-treatment	25.1 ± 2.1	26.2 ± 2.9	1.98	$P=0.03$
1 month	26.9 ± 1.9	27.9 ± 3.1	1.0	$P=0.03$
2 months	28.2 ± 1.5	28.7 ± 3.3	0.51	$P=0.05$
3 months	30.6 ± 1.2	29.2 ± 3.3	1.69	$P=0.12$

Tabl III: Comparison of burning sensation between Group A and Group B at different times of follow-up

Prospective PeriodBurning Sensation	Group A			Group B			p-value
	Mild	Moderate	Severe	Mild	Moderate	Severe	
Pre-treatment	0	17	03	0	15	5	0.429
1 Month	02	17	01	01	18	01	0.834
2 Month	08	10	02	05	13	02	0.582
3 Month	15	05	0	08	12	0	0.025

Table IV: Comparison of USG fibrous band presence in Group A and Group B.

Prospective Period	Group A		Group B		Mean Difference	P-Value
	n	Mean (SD)	n	Mean (SD)		
Before Treatment	20	2.15 ± 0.69	20	2.95 ± 0.79	0.8	$P=0.5$
1 Month	20	2.15 ± 0.69	20	2.95 ± 0.79	0.8	$P=0.5$
2 Month	16	1.72 ± 0.31	15	2.15 ± 0.58	1.63	$P=0.08$
3 Month	2	0.94 ± 0.11	8	1.47 ± 0.34	0.56	$P=0.005$

of treatment, ($p > 0.05$). However, after two months, mean scores decreased in both groups, while the difference remained statistically insignificant ($p = 0.08$), and after three months of treatment, the group A showed significantly lower mean fibrous band score (0.94 ± 0.11) compared to group B (1.47 ± 0.34), ($p = 0.005$), as shown in table IV.

Discussion

OSF has a significant association with oral cancer, particularly squamous cell carcinoma.¹³ Although not all cases of OSF progress to oral cancer, individuals with OSF are at an increased risk of developing malignant transformation over time. The risk of OSF into oral cancer is further increased in patients with OSF who continue to consume betel quid, tobacco, and alcohol.¹⁴ Various research studies were conducted to determine the etiology, Treatment, and risk factors that contribute to the development of OSF, while this focused on the effectiveness of curcumin and lycopene in OSF patients for therapeutic purpose, where OSF patients were treated with lycopene-4mg and curcumin-4mg, where male patients (82.5%) showed higher participation than females (17.5%), with slightly higher mean age among males (32.8 ± 7.5) than females (29.6 ± 6.5). Comparable gender distribution was reported in the study of Piyush et al.,¹⁵ who reported male gender predominance (77.8%) compared to females (22.2%).

In this study, mean mouth opening at baseline was higher in curcumin (group B) compared to patients in lycopene (group-A); 26.2 ± 2.9 mm vs. 25.1 ± 2.1 mm respectively ($p < 0.05$). However, after one month of treatment, both groups showed improvement, with higher mean value in curcumin group (27.9 ± 3.1 mm) compared to lycopene group (26.9 ± 1.9 mm), with significant difference ($p = 0.03$). Moreover, two months post-treatment, the mouth opening further improved in both groups (28.2 ± 1.5 mm and 28.7 ± 3.3 mm respectively), while difference was not significant ($p = 0.05$). Additionally, after three months of treatment, lycopene-4mg group showed a higher mean mouth opening (30.6 ± 1.2 mm) than curcumin-4mg group (29.2 ± 3.3 mm); while the difference was statistically insignificant ($p = 0.12$), indicating that the mean mouth opening progressively improved in both groups over the time. In agreement, in the study of Noor J et al.¹⁶ OSMF patients received daily dose of Lycopene-10 mg and curcumin-500 mg over the period of 3weeks and it was noted that mean mouth opening at baseline (Pre-operatively) were comparable between both the Lycopene group (2.07 ± 0.31) and curcumin group (1.90 ± 0.27) were comparable. However, both groups showed significant improvement in mean mouth opening scores (3.11 ± 0.33 and 2.70 ± 0.33 respectively) at the end of treatment ($p < 0.001$). Aligning with these

findings, the study of Waghmare M et al.¹⁷ found that curcumin effectively alleviated burning sensation and improved mouth opening among OSF patients, with statistically significant difference in mean values of mouth opening ($p < 0.001$). Similarly, the study conducted by Syed AJ et al.,¹⁸ also reported that Lycopene significantly improved mean mouth opening with an average change of 6.32 ± 0.96 mm among OSF patients ($p < 0.001$).

In present study, pre-treatment, burning sensation was moderate to severe in both the lycopene and the curcumin groups ($p = 0.429$). After one-month and two months of treatment, improvement occurred with slight shift towards moderate to mild burning sensation in both groups, while differences were statistically insignificant ($p = 0.834$ and $p = 0.582$ respectively). However, mild burning sensation was the more common in both groups after three months of treatment, while lycopene showed significantly higher reduction of burning sensation to mild level compared to curcumin ($p = 0.025$). In accord with these findings, in the study conducted by Noor J et al.¹⁶ mean burning sensation at baseline between both the Lycopene-10 mg group (83.07 ± 8.99) and curcumin-500 mg group (84.80 ± 9.18). While, over the treatment period of 3weeks both groups showed significant improvement in mean burning sensation scores (69.37 ± 8.69 and 74.83 ± 9.94 respectively) among OSMF patients ($p < 0.027$). Consistently, in the study of Jana BK et al.¹⁹ Significant improvement was observed in burning sensation among patients who received curcumin (300 mg) twice daily, with reduction of burning sensation from 7.1 ± 1.2 at baseline to 2.4 ± 1.1 at 3 months ($p < 0.001$). Correspondingly, in the study conducted by Pérez-Leal M et al.²⁰ significant reduction of burning sensation occurred among OSMF patients who received Lycopene ($p < 0.05$).

In current study, all study subjects were analyzed by ultrasonography to measure the fibrous bands before and after treatment, the mean of USG fibrous band scores was almost similar in lycopene group (2.15 ± 0.69) and curcumin group (2.95 ± 0.79) at baseline, and no change in scores occurred in both groups after one month of treatment ($p > 0.05$). After two months, mean scores insignificant decreased in both groups ($p = 0.08$). However, after three months of treatment, mean fibrous band score reduced significantly more in lycopene group (0.94 ± 0.11) compared to curcumin (1.47 ± 0.34), with significant differences between both groups ($p = 0.005$). Aligning with our findings, in the study carried out by Nigam S et al.²¹ curcumin showed significant reduction in fibrous bands reduction and improved mouth. Overall present study is supported by existing literature, in

terms of both lycopene and curcumin are clinically effective, specifically with some higher effectiveness of lycopene in managing oral submucous fibrosis, with notable improvements burning sensation, and tissue flexibility. Conversely, present was limited by a limited sample size, limited follow-up period, lack of histopathological association, and self-reported patient compliance. Hence further studies involving larger randomized controlled trials, longer follow-up, histopathological and molecular analysis, and dose-optimization studies is suggested to establish standardized treatment protocols and strengthen the overall evidence base for conservative management of OSB.

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Conclusion

This study revealed that the both lycopene and curcumin were observed effective in improving clinical features of oral submucous fibrosis, specifically with higher and more consistent progression, predominantly at three months follow-up, with significantly improved reduction in the fibrous band thickness and burning sensation, indicating the lycopene may be a more effective option of management compared to the curcumin among patients with OSMF. However due to several limitations the further larger-scale studies are recommended to validate the findings.

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