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Research Article

Efficacy of Lycopene on Burning Sensation and Mouth Opening in Oral Submucous Fibrosis

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Abstract

Introduction: Oral submucous fibrosis is a chronic premalignant condition of oral cavity, pharynx and upper digestive tract [1]. Primary etiology is areca nut, chewing. Nutritional deficiencies increases the risk of severity [3]. Areca nut disrupting the homeostatic balance between synthesis, and degradation of extra cellular matrix [4]. Lycopene is newer Antioxidants restrict the free radical injury to cells and cellular components [5]. Lycopene gives curative effect by inhibition of abnormal fibroblast, up regulation of lymphocytes resistance to stress.

Objective: Determine the efficacy of Lycopene on burning sensations, and mouth opening, in Oral submucous fibrosis.

Duration of Study: 6 months after approval of synopsis (18 August 2015 to 18 February 2016).

Study Type: Descriptive, case series

Sitting: Out patients department, Oral and Maxillofacial Surgery Nishtar Institute of Dentistry Multan.

Materials and Methods: After approval of ethical committee and taking written consent patient were included in the study. Data was collected using structured questionnaire. Pretreatment mouth opening using divider and burning sensation on VAS recorded and compared to post treatment.

Result: The present study comprised of 101 patients of oral submucous fibrosis (OSMF). OSMF patients included 53 (52.4%) male and 48 (47.05%) female patients. Majority 70 (69.3%) have habit of pan chewing. Efficacy of lycopene for burning sensations pretreatment and post treatment were analysed. P value 0.00001(statistically significant). Similarly for mouth opening compared. P value 0.002 (statistically significant).

Conclusion: Lycopene is effective in the management of oral submucous fibrosis.

Keywords: *Colorectal Cancer; Review; Screening; Treatment*

Introduction

Oral submucous fibrosis is a chronic, progressive, irreversible premalignant disease of oral cavity, pharynx and upper digestive tract, characterized by fibrotic change and severe burning sensations with restricted mouth opening [1]. Primary etiology is directly related to areca nut, chewing. Slaked lime used in pan releases alkaloids (arecoline, arecaidine, guvacine, and guvacolin) from areca nut causes euphoria and well-being in users [2,6]. Nutritional deficiencies increases the risk of severity [3,8].

Underlying pathogenic role of areca nut in oral submucous fibrosis is disrupting the homeostatic balance between synthesis and degradation of extra cellular matrix [4]. Cytokines and growth factors activated by inflammatory cells cause up regulation of fibroblast and collagen production and down regulation of collagenase ultimately increase fibrosis [4,10,11]. Also areca nut contains copper that cause up regulation of collagen by enhancing activity of enzyme lysyl oxidase [4].

Lycopene is newer Antioxidants restrict the free radical injury to cells and cellular components5.Lycopene is an open chain unsaturated carotenoid that imparts anti-proliferative properties. Antioxidant properties of Lycopene are twice as compare to B carotene. Lycopene gives this curative effect by inhibition of abnormal fibroblast, up regulation of lymphocytes resistance to stress, and suppress inflammatory response.

Materials and Methods

A Descriptive, case series conducted in outpatients department, Oral and Maxillofacial Surgery, Nishtar Institute of Dentistry Multan from 18 Aug 2015 to 18 Feb 2016, Study conducted after protocol is approved by the ethical committee. All Patients were assured that there name will not be disclosed in final results and a written consent was taken. A structured questionnaire was used to record the patient's demographic data like patient's name, age and gender duration of disease. Pre-treatment mouth opening interincisal distance recorded using divider and simple scale, burning sensation is measured using visual analogue scale. Confounding variables like age and nutritional status (Normal/Malnourished) were controlled by restriction and randomization. Patient labeled as malnourished having BMI (body mass index) less than 18.5. BMI = mass in Kg/height m^2. Bias of observational and recall was controlled by using single observer technique. And bias for lost to follow up was controlled by adding additional number of patients. Bias of measurement was controlled by standardization of measurement technique. Sample size is calculated through computer based software WHO Sample size calculator. Anticipated population proportion 69.8%, confidence level is 95%, and absolute precision 9% [5]. Sample size of at least (n)=101 were required.

In this study patient diagnosed as oral submucous fibrosis having all of the signs and symptoms a history of pan chewing more than 6 months, limited mouth opening less than 45 mm, burning sensation ≥ 1 on VAS, fibrous bands on soft palate retro molar area or buccal mucosa on palpation. Regarding selection of Patients both male and female patients of 15 - 60 years of age have been included after taking a written consent.

Patients having inter incisal distance less than 10 mm, not willing to be a part of study, cannot manage proper and previously treated for OSMF were excluded from study. Data analysed using SPSS 20. Chi square test applied to find out association for confounders.

Results

The present study comprised of 101 patients of oral submucous fibrosis (OSMF). OSMF patients included 56 (55.6%) male and 45 (44.05%) female patients. Mean ± SD of age of OSMF patients is given in table 1. Mean ± SD for duration of disease is given in table 2. Frequencies and percentages of gender, stratified age, mouth opening, burning sensations and stage of OSMF are given in the table 3.

		Female	Male	Total
N	Valid	45	56	
	Missing	56	45	101
Mean		34.2444	32.6607	
Std. Deviation		13.34023	12.94924	

Table 1: *Mean ± SD of age of OSMF patients.*

	N	Mean	Std. Deviation	Std. Error Mean	P value
Pre treatment	101	39.9901	27.40638	2.72704	
Post treatment	101	17.0297	22.56300	2.24510	0.000

Table 2: *Mean ± SD of burning sensations in OSMF patient before and after lycopene treatment.*

Indicator	No of case (%)
Gender	
Male	56 (55.5%)
Female	45 (44.6%)
Age	
18 - 30	49 (48.5%)
31 - 40	24 (23.8%)
41 - 50	15 (14.8%)
51 - 60	13 (12.9%)
Stage of OSMF	
Stage I	55 (54.4%)
Stage II	30 (29.7%)
Stage III	16 (15.8%)
Mouth opening	
10 - 20 mm	25 (24.7%)
21 - 30 mm	45 (44.5%)
31 - 45 mm	31 (30.6%)
Burning sensations	
Mild 00 - 30	50 (49.5%)
Moderate 31 - 60	30 (29.7%)
Severe 61 - 100	21(20.7%)

Table 3: *Demographic data of OSMF patients.*

Lycopene supplementation was started in all 101 patients and efficacy was found out after duration of three months. Pre-treatment and post treatment changes in patients are presented in table 4. Frequencies and percentages of efficacy of lycopene on burning sensation are presented in table 5.

Burning sensations	Pre treatment	Post treatment	X^2	P value
Mild (0 - 30)	50	85	27.40	0.00001
Moderate (31 - 70)	30	10		
Severe (71 - 100)	21	06		

Table 4: *Lycopene pre-treatment and post treatment changes on severity of burning sensations in OSMF patients. Chi square test, significant (P ≤ 0.05).*

Mean ± SD pre and post treatment for burning sensations and T test are given in table 5.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	84	83.2	83.2	83.2
	No	17	16.8	16.8	100.0
	Total	101	100.0	100.0	

Table 5: *Frequency and percentages of efficacy of lycopene in oral submucous fibrosis (burning sensation).*

Efficacy for gender, nutritional status and age groups have been stratified on tables 6-8.

Yes		Burning sensation		Total	P value
		No			
Gender	Male	51	6	57	
	Female	33	11	44	0.054
Total		84	17	101	

Table 6: *Efficacy of Lycopene in terms of burning sensation on gender basis. Chi square test, significant (P ≤ 0.05).*

Yes		Burning sensation		Total	P value
		No			
Nutritional Status	Malnourished	12	7	19	
	Nourished	72	10	82	0.010
Total		84	17	101	

Table 7: *Efficacy of Lycopene in terms of burning sensation according to nutritional status. Chi square test, significant (P ≤ 0.05).*

Yes		Burning sensation		Total	P value
		No			
Age Groups	18 - 30 years	45	4	49	
	31 - 40 years	22	2	24	
	41 - 50 years	10	5	15	0.002
	51 - 60 years	7	6	13	
Total		84	17	101	

Table 8: *Efficacy of Lycopene on Burning sensation in different age groups of OSMF patients. Chi square test, significant (P ≤ 0.05).*

Efficacy for mouth opening is measured using divider and scale. Pre-treatment Mean ± SD for mouth opening meant difference and t test given in table 9. Frequency and percentages of efficacy of Lycopene on mouth opening are given in table 10.

	N	Mean	Std. Deviation	Std. Error Mean	P value
Pre RX	101	24.7525	8.28300	.82419	
Post Rx	101	29.1980	7.83712	.77982	0.000

Table 9: *Mean ± SD of mouth opening in OSMF patient before and after Lycopene treatment. Paired t test applied to find p value.*

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	72	71.3	71.3	71.3
	No	29	28.7	28.7	100.0
	Total	101	100.0	100.0	

Table 10: *Frequency and percentages of efficacy of lycopene in oral submucous fibrosis (mouth opening).*

Efficacy of lycopene in terms of gender, nutritional status and age groups have been stratified on tables 11-13.

Yes		Mouth opening		Total	P value
		No			
Gender	Male	35	21	56	
	Female	37	8	45	0.04
Total		72	29	101	

Table 11: *Efficacy Lycopene in terms of mouth opening on gender basis in OSMF patients. Chi square test, significant (P ≤ 0.05).*

Yes		Mouth opening		Total	P value
		No			
Nutritional Status	Malnourished	13	6	19	
	Normal (Nourished)	59	23	82	0.76
Total		72	29	101	

Table 12: *Efficacy of Lycopene on mouth opening according to nutritional status in OSMF patients. Chi square test, significant (P ≤ 0.05).*

Yes		Mouth opening		Total	P Value
		No			
Age Groups	18 - 30 years	35	14	49	
	31 - 40 years	21	3	24	
	41 - 50 years	7	8	15	0.056
	51 - 60 years	9	4	13	
Total		72	29	101	

Table 13: *Efficacy of Lycopene on mouth opening in different age groups of OSMF patients. Chi square test, significant (P ≤ 0.05).*

Discussion

It was a descriptive case series study. One hundred and one subjects were recruited randomly from OPD in department of oral and maxillofacial surgery Nishtar institute of dentistry Multan. Stratification of gender, nutritional status and age groups of patients done and analyzed using chi-square test on SPSS (version 20.0). P value < 0.05 was considered significant.

All available treatments for OSMF are symptomatic relief for patients. In this study an attempt was made to assess the efficacy of lycopene on burning sensations and mouth opening. In the current study Mean ± SD of age of OSMF patients was 33.84 ± 12.97 years, slight male predilection, earlier there were definite female predilection. Desa reported maximum incidence in the second and third decade, the average age being 40.5 years. In our study, maximum incidence is seen in the age group of 18 to 30 years, approximately 46.6%. Results were in accordance with other Asian studies [6,7,9].

Main etiological factor of OSMF is chewing of pan and areca nut product [13]. All the patients in the study reported chewing pan or areca nut products. All patients presented with trismus and burning sensations to food. Most of the affected patients had fibrotic bands on retromolar area, buccal mucosa and soft palate. first symptoms most commonly a patient complains of is burning sensation of the oral mucosa, that is aggravated by spicy food, followed by trismus that is not an abrupt change. It is a gradual process taking years in some patients [10,11]. Decrease in mouth opening causes difficulty in eating swallowing, speech and mastication.

Over the years different treatment methods have been used to relieve both sign and symptoms of oral sub mucous fibrosis. Both medical and surgical treatment modalities have been studied [10,11].

Medical management ranging from gold, arsenic trioxide, large dosage of iodine, steroids, liver extracts, placental extracts, hyaluronidase, antioxidant, chymotrypsin. α lipoic acid, Lycopene, immunized cow milk [11,17]. Surgical methods such as partial thickness skin grafts, temporalis, nasolabial, tongue flaps, placental grafts, buccal fat pad grafts, lasers and ultrasonography have been used for OSMF management [16,17].

Lycopene is newer antioxidants twice as compare to B carotene. Antioxidants are biochemical nutrients found in foods that can prevent or slow the oxidative damage to the human body, enhance immune defense and lower the risk of inflammation restrict the free radical injury to cells and cellular components [5]. Lycopene gives curative effect by inhibition of abnormal fibroblast, up regulation of lymphocytes resistance to stress, and suppress inflammatory response. The findings of this study are in concurrence with those of another study which was performed by Haque., et al. [14] Lycopene also up regulates the lymphocytes resistance to stress and suppress the inflammatory response [15]. In this study a significant symptomatic improvement of tolerance to spices and burning sensation was reported in patients after taking Lycopene. Out of 101 subjects taking lycopene 84 (83.2%) were relieved of intolerance to spices and burning sensation, relief from burning sensation and intolerance to spices was found in 83.2% along with significant improvement in burning sensations, erosions and ulcerations. P value was 0.000 (Table 10).

Lycopene supplementation was started in all 101 patients and efficacy was found out after duration of three months. Pre-treatment and post treatment changes in patients are presented in table 4. Frequencies and percentages of efficacy of lycopene on burning sensation are presented in table 5.

For mouth opening lycopene showed significant improvement over all improvement was 71%. In previous studies Patil S, Khandelwal S there was a significant improvement in mouth opening in patients who were given lycopene soft gel orally than those who were given spirulina (P = 0.0006) [13]. Similarly, Karemore and Motwani Kumar., *et al*. observed significant improvement in mouth opening in the lycopene group (P = 0.0001) [11].

Conclusion

Lycopene a newer antioxidant is very effective for mild to moderate cases of oral submucous fibrosis. For severe cases with mouth opening less than 10 mm lycopene can be prescribed as post-operative supplement to decrease symptoms and refibrosis caused by free radical injury.

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