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ORIGINAL ARTICLE

Comparative Study of the Efficacy of Newer Antioxitands Lycopene and Oxitard in the Treatment of Oral Submucous Fibrosis

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Abstract

Objective: To compare the efficacy of oxitard and lycopene in the management of Oral Submucous Fibrosis (OSMF). **Material and Methods:** 120 subjects with clinic-pathologically diagnosed OSMF were included in the study and divided equally in 2 groups, Group A (oxitard) and Group B (lycopene). Group A was administered 2 oxitard capsules twice daily and Group B was given 8 mg lycopene in 2 divided doses of 4 mg for 3 months. Gingival index and plaque index were documented for all patients and compared. Evaluation for different clinical parameters was done at regular intervals and data was analyzed using the Student's paired t test and Chi-square test. P-value <0.001 was considered to be statistically significant. **Results:** Clinical improvements in mouth opening and tongue protrusion was significant in Group A ($p<0.001$). Subjective symptoms of pain associated with the lesion ($p=0.0001$), difficulty in swallowing ($p=0.0004$) and speech ($p=0.0002$) significantly improved in the Group A. However, there was no significant improvement in burning sensation ($p>0.001$) among the 2 groups. Although the mean gingival index and plaque index in group A was reduced but it was found to be not statistically significant. **Conclusion:** Oxitard capsules can bring about significant clinical improvements in the symptoms like mouth opening, tongue protrusion, difficulty in swallowing and speech and pain associated with the lesion when compared to lycopene, thereby improving the quality of life of the affected individuals.

Keywords: Oral Submucous Fibrosis; Antioxidants; Burning Mouth Syndrome.

Introduction

Oral submucous fibrosis (OSMF) is a potentially malignant disorder of oral cavity, pharynx and upper digestive tract, characterized by progressive inability to open the mouth and by inflammation and progressive fibrosis of the submucosal tissues [1]. The pathogenesis of the disease is not well known, but the etiology is believed to be multifactorial. The condition is particularly associated with areca nut chewing, which is the main component of betel quid. The habit of betel quid chewing is practiced predominately in the Indian subcontinent from a long time [2].

The ingredients of arecanut induce excessive reactive oxygen species, which damages the cell structures [3]. Accompanied with this, vitamin deficiency, iron deficiency anemia, and poor nutrition can disturb the repair of the inflamed oral mucosa, leading to poor healing. This results in atrophic oral mucosa, which becomes more susceptible to the effects of areca nut. The antioxidant vitamins are thus employed to stabilize and deactivate the free radicals before they attack cells [4].

Treatment modalities for relieving the symptoms have been advocated, but have not been successful so far. The first step of preventive measure should be in discontinuation of habit, which can be encouraged through education, counseling and advocacy and to maintain proper oral hygiene. Medical treatment is symptomatic and predominantly aimed at improving mouth movements. Specific treatment includes administration of steroids, placental extracts, IFN gamma, pentoxifylline, lycopene, surgical excision, etc [2-5]. Oxitard capsules have been successfully tried in the treatment of OSMF [6]. Lycopene has also been proved to be the most potent radical scavenger in various studies and it has been tried in the treatment of leukoplakia and also in OSMF [7,8]. But each treatment has its own limitations. The present study was carried out to compare the efficacy of these newer antioxidants in the management of oral submucous fibrosis.

Material and Methods

Study Design and Data Collection

The present prospective study included 120 subjects with clinico-pathologically diagnosed OSMF reporting to the Department of Oral Medicine and Radiology, Jodhpur Dental College General Hospital. Patients of either gender with OSMF were included in the study. Those with any evidence of severe psychiatric, cardiac, gastrointestinal or metabolic disorders and pregnancy and lactation were excluded from the study. Detailed family and medical history with a history of associated habits and the course of the disease was recorded.

A thorough clinical examination was carried out and relevant findings were recorded. The subjects were randomly divided equally in 2 groups, Group A (Oxitard) and Group B (Lycopene). Group A was administered 2 oxitard capsules twice daily and Group B was given 8 mg lycopene (LycoredTM, Jagsonpal Pharmaceuticals, New Delhi, India) in 2 divided doses of 4 mg for 3 months.

Mouth opening was measured by measuring the distance between the centre of incisal edges of maxillary central incisors and mandibular central incisor at maximum opened mouth. In edentulous patients, the inter ridge (alveolar) distance along the midline was measured. Three

measurements were recorded consecutively and the average value was calculated and recorded. Tongue protrusion was measured as distance between lower central incisor and tip of the tongue on protrusion.

Evaluation for presence, absence or reduction of other clinical parameters such as burning sensation, pain associated with the lesion, difficulty in swallowing and speech was done at regular intervals of 1 month, 2 month and 3 months. Gingival index [9] and plaque index [10] was recorded before and after the treatment for each patient in both groups.

Data Analysis

The data was entered using computer software IBM SPSS Statistics for Windows version 20 (IBM Corp., Armonk, NY, USA) and analyzed using the Student's paired t test and Chi-square test. P-value<0.001 was considered to be statistically significant.

Ethical Aspects

Ethical clearance was obtained from the Institutional Ethical Committee of Jodhpur Dental College, Jodhpur National University. A written informed consent was obtained from all the participants prior to the inclusion in the study.

Results

There were 64 males and 56 females with a mean age of 31.6±12.7 years. 56% of the patients had habit of betel nut chewing, while 26% of the patients had tobacco chewing habit. 40% of the patients consumed spicy foods, which were among the main causative factors for OSMF in the study population. Clinical improvements in mouth opening and tongue protrusion was significant in the Group A (p<0.001) (Tables 1 and 2).

Table 1. Effect of oxitard and lycopene in improving mouth opening (mean values in mm).

Evaluation	Oxitard	Lycopene	p-value
Baseline	19.1±2.4	18.2±2.1	
After 1 month	21.6±2.6	20.2±2.2	<0.001
After 2 months	27.2±2.9	22.4±2.5	
After 3 months	31.5±2.9	25.9±2.3	

Table 2. Effect of oxitard and lycopene in improving tongue protrusion (mean values in mm).

Evaluation	Oxitard	Lycopene	p-value
Baseline	10.1±1.4	9.8±2.1	
After 1 month	13.6±2.4	10.3±1.9	<0.001
After 2 months	20.2±2.1	15.7±2.2	
After 3 months	24.5±2.5	19.1±1.9	

The effect of administration of oxitard capsules in the Group A showed significant improvement in the subjective symptoms of pain associated with the lesion (p=0.0001), difficulty in swallowing (p=0.0004) and speech (p=0.0002) when compared to the Group B who were given lycopene (Tables 3 to 5).

Table 3. Effect of oxitard and lycopene on pain associated with pain.

	Oxitard			Lycopene		
Evaluation	Present	Absent	Reduced	Present	Absent	Reduced
Baseline	58	2	-	59	1	-
After 1 month	50	4	6	53	4	5
After 2 months	29	17	14	35	11	14
After 3 months	11	31	18	24	25	11

Table 4. Effect of oxitard and lycopene on difficulty in swallowing.

	Oxitard			Lycopene		
Evaluation	Present	Absent	Reduced	Present	Absent	Reduced
Baseline	57	3	-	58	2	-
After 1 month	38	10	12	50	4	6
After 2 months	24	22	14	36	11	13
After 3 months	7	36	17	23	25	12

Table 5. Effect of oxitard and lycopene on difficulty in speech.

	Oxitard			Lycopene		
Evaluation	Present	Absent	Reduced	Present	Absent	Reduced
Baseline	56	4	-	57	3	-
After 1 month	36	14	10	41	9	10
After 2 months	22	24	14	32	19	9
After 3 months	10	38	12	18	28	14

However, there was no significant improvement in burning sensation ($p>0.001$) among the 2 groups (Table 6). Eight patients experienced mild abdominal discomfort due to oxitard. There were no reported side effects of lycopene. None of the patients withdrew from the study due to any reason.

Table 6. Effect of oxitard and lycopene on burning sensation.

	Oxitard			Lycopene		
Evaluation	Present	Absent	Reduced	Present	Absent	Reduced
Baseline	60	-	-	60	-	-
After 1 month	42	8	10	48	3	9
After 2 months	28	18	14	30	12	18
After 3 months	3	43	14	7	32	21

Table 7 shows a decreased accumulation of plaque, improvement in the gingival health but these findings were statistically non-significant.

Table 7. Comparison of the mean plaque index and gingival index.

	Group A				Group B			
Variables	Baseline (mean±SD)	3 months (mean ± SD)	t-value	**p-value**	Baseline (mean±SD)	3 months (mean ± SD)	t-value	**p-value**
Plaque Index	2.32 ± 0.50 (1.17 – 3.00)	2.30 ± 0.51 (1.08 – 3.00)	- 1.81	0.075	2.31 ± 0.48 (1.21 – 2.92)	2.28 ± 0.48 (1.25 – 2.96)	-1.84	0.071
Gingival Index	2.18 ± 0.24 (1.67 – 2.71)	2.16 ± 0.23 (1.58 – 2.58)	-1.71	0.093	2.24 ± 0.23 (1.75 – 2.79)	2.21 ± 0.24 (1.71 – 2.75)	-1.98	0.052

SD = Standard Deviation.

Discussion

Treatment modalities for relieving the symptoms related to oral submucous fibrosis (OSMF) have been advocated, but have not been successful so far [11-15]. The first step of preventive measure should be in advising the patient to discontinue the habit of betel nut chewing, tobacco, spicy foods and chillies. This can be encouraged through education, counseling and advocacy. Medical treatment is symptomatic and predominantly aimed at improving mouth movements. But each treatment has its own limitations [16,17].

The medical management of oral submucous fibrosis is both empirical and unsatisfactory [13]. Multiple minerals and micronutrients showed significant improvement in mouth opening of 41% of the patients [18]. Whereas, some authors showed improvement in symptoms of OSMF but insignificant improvement in mouth opening with vitamin A [19]. Lycopene has also showed significant improvement in mouth opening [8]. Previous study has shown significant improvement in mouth opening, hyperkeratosis, pain in mouth and size of the lesion with oxitard capsules [6]. However, the present study compared the efficacy of the 2 newer antioxidants oxitard and lycopene in the improvement of clinical parameters such as, difficulty in swallowing, speech, tongue protrusion and burning sensation.

Lycopene is a major carotenoid obtained from tomato, which has potent anticancer activity [20]. The antioxidant properties of lycopene in various types of cancers are thought to be primarily involved in its preventive effects in chronic diseases. It also has potent benefits in oral potentially malignant lesions like leukoplakia. Because of its high number of conjugated dienes, lycopene is one of the most potent antioxidants, with a singlet-oxygen-quenching ability twice as high as that of β-carotene and 10 times higher than that of α-tocopherol [21]. New findings have reported the anticancer activity of lycopene is due to the upregulation of connexin 43 and stimulation of gap junctional communication that does not involve its role as an antioxidant [9].

The formulation of the oxitard capsules contains the extracts of *Mangifera indica*, *Withania somnifera*, *Daucus carota*, *Glycyrrhiza glabra*, *Vitis vinifera*, powders of *Emblica officinalis* and *Yashada bhasma*; and oils of *Triticum sativum*. *Mangifera indica* is shown to have antibiotic, anti-asthamatic, antiseptic, antiviral, hypotensive, anti-emetic properties. *Withania somnifera* provides overall health and wellness with its anti-stress, anti-anxiety, anti-inflammatory, anti-convulsive and anti-arthritic properties. *Daucus carota* acts as a good antiseptic as it is a rich source of vitamin A. *Glycyrrhiza glabra* normalizes the hoarseness in voice and has immunomodulatory and anti-inflammatory properties. *Vitis vinifera* have anti-inflammatory, astringent and an effect to curb the burning sensation. *Emblica officinalis* is a rich source of vitamin C and is a potent antibiotic. *Yashada bhasma* contains zinc, which plays a significant role in protein synthesis, cell division and wound healing. *Triticum sativum* is a rich source of minerals and has an antioxidant property [7].

There was a significant ($p<0.001$) improvement in the mouth opening and tongue protrusion in the patients who were administered oxitard capsules when compared to those who were given lycopene softgel orally. This was similar to previous findings that observed a significant

improvement in the mouth opening of the patients who were given oxitard capsules [6]. It was observed significant improvement in mouth opening in the lycopene group [8,9]. Improvement in mouth opening is not only due to habit intervention but also due to the antioxidant drugs. Although, the mechanism leading to reduced mouth opening is still unclear, it can be due to fibrosis and fibrous band formation in the oral mucosa [9].

Tongue protrusion also showed improvement in both the groups, but Group A showed more significant improvements ($p<0.001$). A significant improvement was observed in the tolerance to burning sensation in both the groups. However, Group A showed more improvement but the difference between the 2 groups was statistically insignificant ($p>0.001$). The effect of administration of oxitard capsules in the Group A showed significant improvement in the subjective symptoms of pain associated with the lesion ($p=0.0001$), difficulty in swallowing ($p=0.0004$) and speech ($p=0.0002$) when compared to the Group B who were given lycopene.

Studies in the literature have shown the influence of betel nut chewing on the periodontium and it has been proposed that the physical action of the components of the betel nut could be the etiological factor [15]. In the present study, improvement in gingival index and plaque index was observed in group A when compared to group B, but these differences were statistically non significant. The improvement in these parameters in the present study could be attributed to the improvement in mouth opening and decrease in pain.

The findings of the present study demonstrate that oxitard capsules are more effective than lycopene as an antioxidant given as the first line of treatment in oral submucous fibrosis. There were improvements in both the groups but significant improvements were observed in the Group A. A larger study with larger sample size and longer follow-up period is encouraged to get more accuracy in the efficacy of the antioxidants.

Conclusion

Oxitard was seen more efficacious antioxidant than lycopene in the management of oral submucous fibrosis. In contrast to other treatment modalities, these drugs offer a non-invasive treatment option with significant improvements in mouth opening, tongue protrusion, burning sensation, difficulty in swallowing and speech. Hence, oxitard is more preferable than lycopene in the management and control of the progression of this chronic debilitating condition of the Indian sub-continent.

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