



ASSESSMENT OF THE EFFECTIVENESS OF ANTIOXIDANT THERAPY (LYCOPENE) AND THERAPEUTIC ULTRASOUND IN THE TREATMENT OF ORAL SUBMUCOUS FIBROSIS

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ABSTRACT

Oral Submucous fibrosis is a premalignant condition that has received considerable attention in the recent past because of its chronic debilitating and resistant nature. Various treatment modalities have been proposed for this condition including steroid injections and surgical interventions. In this study a medicinal and a non-medicinal treatment were compared for their effectiveness in treatment of Oral Submucous fibrosis. To evaluate the efficacy of oral lycopene therapy in patients with Oral Submucous fibrosis and compare with the effect with those patients who were administered therapeutic ultrasound with physiotherapy exercises. Thirty (30) patients who enrolled with signs and symptoms of Oral Submucous Fibrosis at Dr D Y Patil Dental College were included in the study. The patients were divided into 2 groups, Group A included 15 patients who were administered Lycopene and Group B, included 15 patients who were administered Ultrasound therapy. Parameters included to assess effectiveness of the two treatments were: mouth opening, burning sensation and tongue protrusion. Results showed that tongue protrusion and burning sensation improved to a greater extent in Group A (lycopene group) as compared to Group B (ultrasound group). Mouth opening improved to a greater extent in Group B (ultrasound group), compared to Group A (lycopene group), but the difference was not statistically significant. Results suggest that lycopene in isolation can be used as the initial treatment modality of Oral submucous fibrosis to relieve burning sensation, but if used in conjunction with therapeutic ultrasound will improve oral opening.

Key Words:- Oral submucous fibrosis, Lycopene, Ultrasound, Burning sensation.

INTRODUCTION

Oral Submucous fibrosis is a chronic disease of insidious onset featuring the deposition of fibrous tissue in the juxta epithelial layer of mucous membrane involving the pharynx, palate, fauces, cheek and lips, pharynx and oesophagus (Canniff JP *et al.*, 1986; Gupta PC, 1999). Oral Submucous Fibrosis (OSF) is a lesion found among

people who chew betel nut (Areca catechu) with or without tobacco and other ingredients. Gutka is the predominant form of areca nut (with or without tobacco) consumption in most parts of India, Gutka (also called gutkha,) is a powdery or granular preparation of areca nut, betel nut, tobacco, lime and savory flavorings. It is a popular product in India and available under several dozen brand names.

A common presenting symptom is a burning when eating hot and spicy food and a progressive decrease in the mouth opening, associated with difficulty in eating,

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changed gustatory sensation, dryness of mouth and nasal voice (Cox SC and Walker DM, 1996). Ulcerations and vesicles are seen in the initial stages of oral mucosa. Periods of exacerbations are manifested by the appearance of small vesicles on cheek and palate (Sirsat MS and Khanolkar VR, 1962). The earliest clinical sign of OSF is blanching of the oral mucosa followed by the appearance of fibrous bands in the areas affected (Pindborg *et al.*, 1980). The bands usually involve the buccal mucosa, palate, posterior pharynx, lips and tongue.

Various treatment modalities have been proposed for this condition including steroid injections, surgical interventions. Non-invasive treatment modalities however have potential for delivering the desired results.

Lycopene a natural carotenoid and antioxidant, extracted from tomato, has been shown to have several potent anti-carcinogenic and antioxidant properties and has demonstrated profound benefits in precancerous lesions such as leukoplakia. Lycopene has been found to inhibit hepatic fibrosis (Kitade Y *et al.*, 2002) in rats as well as human fibroblastic activity *in vitro* suggesting its possible role in the management of Oral Submucous Fibrosis (OSMF).

In recent years ultrasound has been used extensively in physical medicine with considerable success. Ultrasound (US) (Nghiem Doan *et al.*, 1999) can be defined as sound wave or pressure wave with a frequency above the limit of the human hearing range (16 to 20 kHz). The unit of ultrasound is the Hertz or cycle per second. Being a propagating pressure wave, US is capable of transferring mechanical energy into the tissues. The energy of the US signal is absorbed, propagated, or reflected, depending on its frequency. US can be divided into three types:

- 1) Diagnostic US uses a frequency between 3 and 5 MHz and low intensity (1 to 50mW/cm²) to avoid tissue heating;
- 2) Disruptive ultrasound, such as those used in ultrasonic cleaning devices, uses a very low frequency (20 to 60 kHz), and high intensity above 8 W/cm²; and
- 3) Therapeutic US, as used in medicine and physiotherapy, usually uses frequencies between 1 and 3 MHz and intensities of 0.1 to 2.0 W/cm². During ultrasound therapy (Carmine, Samuel and Allan Far man, 1984) cell membrane permeability is increased by altering sodium and potassium ion gradients. This increased permeability improves gas exchange and promotes healing. Ultrasound decreases inflammation, increases vasodilatation and waste removal. Accelerates lymph flow, and stimulates

metabolism. The objectives of ultrasound treatment are to accelerate healing, increase the extensibility of collagen fibers and provide pain relief. Given that these are the requirements of any therapy used for the treatment of OSMF, therapeutic ultrasound as a treatment modality merits investigation.

MATERIALS AND METHODS

Thirty (30) patients who enrolled with signs and symptoms of Oral Submucous Fibrosis at Dr D Y Patil Dental College were included in the study after obtaining their informed written consent.

The following inclusion criteria were selected for enrolling the patients in the study.

Inclusion criteria

Following parameters are to be included in the establishment of diagnosis and any 2 of 3 parameters are to be satisfied for inclusion in the study (Abhinav kumar *et al.*, 2006).

1. Positive history of (H/O) chewing of areca nut or one of its commercial preparations, difficulty in chewing and swallowing, and having burning sensation on eating spicy food.
2. Restricted mouth opening and changes in oral mucosa including presence of palpable vertical fibrous bands, stiffness and blanching.
3. Histopathology confirmation of OSMF by biopsy specimen.

A complete personal history was recorded in a predetermined proforma and a written consent was obtained from the patients which included a complete explanation of their present condition, the severity of the condition, the urgent need to stop the habit and the procedure for the treatment with the requirement to report time to time and the need to come for follow up examination after 3 months.

The patients were divided into 2 groups, Group A included 15 patients who were administered Lycopene and Group B, included 15 patients who were administered Ultrasound therapy.

1. Group A received 16 mg of lycopene (Lycored, from Jagson Pal Pharma) daily in 2 equally divided doses (8mg each) for a period of 6 weeks.
2. Group B received 15 consecutive sittings of therapeutic ultrasound of 5 minutes to left and right cheek each for 15 consecutive days, with permissible one day off each week. (Figure 4,5 and 6) (Frequency of 3 MHz and Intensity 0.8 to 1.5W/cm²). Muscle kneading exercises were also done like buccinator stretch, finger kneading and TMJ mobilization (anterior capsule stretch, TMJ joint mobility exercises). (Fig 7 and 8) Patients were evaluated every week during the treatment period for group A. Patients

were evaluated every 5 days during the treatment period for Group B.

Follow up was done after a period of 3 months from first day of starting the treatment for subjects in each group. The findings were compared with those at the beginning of the treatment.

MEASUREMENTS

1. Mouth opening

This was assessed as the interincisal distance as measured from the mesioincisal edge of the upper left central incisor tooth to the mesioincisal edge of the lower left central incisor tooth. The measurement was made using a geometric divider and scale and was recorded in millimeters. (Fig 1 and 2)

2. Tongue protrusion

The degree of protrusion was recorded in millimeters from the incisal edge of the lower teeth. This

was done by viewing the protruded tongue from the lateral aspect of the head and measuring the distance from the mesial contact area of the lower central incisors to the tip of the protruded tongue (Figure 3).

3. Burning sensation

Burning sensation was recorded as per a verbal analogue scale where values were recorded on a scale of 0 to 10. Patients were explained the scale in native language and asked to mark the appropriate unit on the scale as per the intensity of burning. This was measured at baseline and as per the regular follow up protocol in both the groups.

Statistical Analysis

Data was entered in MS excel and analysed with statistical softwares Epi info and Primer of Biostatistics.

RESULTS

Group A (Lycopene group)

Table 1. Improvement in mouth opening

Sr. No	Day one (in mm)	Third month follow up (mm)	Improvement in mouth opening (mm)
1	33	42	9
2	34	43	9
3	22	24.5	2.5
4	30	32	2
5	24	27	3
6	30	32	2
7	17	22	5
8	20	26	6
9	16	19	3
10	27	31	4
11	29	32	3
12	27	35	8
13	36	43	7
14	18	24	6
15	17	24	7

Table 2. Improvement in tongue protrusion

Sr.No	Day 1 (mm)	3 months follow up (mm)	Improvement (mm)
1	22	26	4
2	13	18	5
3	11	12	1
4	16	17	1
5	17	18	1
6	14	22	8
7	17	18	1

8	17	20	3
9	14	17	3
10	14	19	5
11	17	17	0
12	22	30	8
13	18	23	5
14	18	25	7
15	28	29	1

Table 3. Decrease in burning sensation

Sr. No	Day one (in mm)	Third month follow up (mm)	Improvement in mouth opening (mm)
1	33	42	9
2	34	43	9
3	22	24.5	2.5
4	30	32	2
5	24	27	3
6	30	32	2
7	17	22	5
8	20	26	6
9	16	19	3
10	27	31	4
11	29	32	3
12	27	35	8
13	36	43	7
14	18	24	6
15	17	24	7

Group B (Ultrasound group)**Table 4. Improvement in mouth opening**

Sr. No	First day (mm)	Third month follow up (mm)	Improvement(mm)
1	25.5	29	3.5
2	28	34	6
3	25	33	8
4	22	27	5
5	20	24	4
6	30	33	3
7	21	26	5
8	25	36	11
9	23	33	10
10	27	38	11
11	22.5	29	6.5
12	27	29	2
13	19	27	8
14	21	23	2
15	26	35	9

Table 5. Improvement in tongue protrusion

Sr. No	First day (mm)	Third month follow up (mm)	Improvement(mm)
1	12	12	0
2	19	24	5
3	16	18	2
4	16	19	3
5	13	15	2
6	23	23	0
7	15	15	0
8	18	20	2
9	15	16	1
10	13	15	2
11	19	20	1
12	15	17	2
13	12	14	2
14	19	19	0
15	23	23	0

Table 6. Improvement in burning sensation

Sr. No	First day	Third month	Improvement
1	7	4	3
2	6	5	1
3	6	5	1
4	5	4	1
5	5	4	1
6	5	4	1
7	5	4	1
8	4	2	2
9	5	4	1
10	4	3	1
11	6	5	1
12	5	4	1
13	6	4	2
14	5	3	2
15	4	2	2

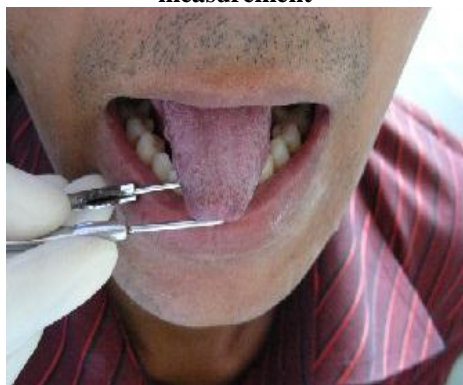
Figure 1. Mouth opening measurement**Figure 2. Reading measured using divider and scale****Figure 3. Tongue protrusion measurement****Figure 4. Ultrasound machine****Figure 5. Transducer probes of 1 Mhz and 3 Mhz**

Figure 6. Ultrasound probe application**Figure 7. Masseter stretch exercise****Figure 9. Jaw mobilization exercise**

DISCUSSION

The present study was undertaken to assess the efficacy of Lycopene and Ultrasound in the treatment of Oral submucous fibrosis. The present study included a total of 30 patients out of which 76.6% (23) patients were males and 23.3% (7) were females. A higher male predilection for OSMF has been reported in literature and the findings in this study conform to the studies published by Lai *et al* (1995) and Kumar *et al* (2006), where a male predilection of as high as 96.67% and 100% respectively has been reported.⁷³ All patients in the present study gave a positive history of areca nut chewing in the raw form as betel nut proper or as in the form of a commercial preparation called ghutka or pan masala which was proven to be a major causative agent of OSMF.

Mouth opening

The mean improvement in mouth opening in Group A (Lycopene group) was 5.10mm with 75% of patients showing improvement up to 7mm and a maximum improvement of 9mm. The change in mouth opening was considered highly significant statistically ($p=0.001$) and evaluation on a weekly basis showed changes maintained this high significance from the third week onwards, a finding similar to the study by Kumar *et al*, where evaluation on a weekly basis revealed changes maintained high significance from third week onwards in treatment with lycopene.

The change in mouth opening in Group B (Ultrasound group) was considered highly significant statistically ($p=0.001$) and evaluation every 5 days revealed changes maintained this high significance from 10th day onwards.

Tongue Protrusion

The mean improvement in tongue protrusion in Group A was 3.53mm with 75% of patients showing improvement up to 5mm and a maximum improvement of

8mm. The change in tongue protrusion was considered highly significant statistically ($p=0.001$) and evaluation on a weekly basis showed changes maintained this high significance from the third week onwards.

The mean improvement in tongue protrusion in Group B was 1.46mm with 75% of patients showing improvement up to 2mm and a maximum improvement of 5mm. The change in tongue protrusion was considered highly significant statistically $p=0.001$ and evaluation every 5 days showed changes that maintained this high significance from the tenth day onwards.

Burning sensation

The mean of improvement in burning sensation in Group A was 2.73 with 75% of patients showing improvement upto 4 points and a maximum reduction by 5 points. The mean of improvement in burning sensation in Group B was 1.4 with 75% of patients showing improvement upto 2 points with a maximum improvement by 3 points.

Mean of improvement in mouth opening is better in group B (6.20mm) as compared to group A (5.10mm). However, the difference is not statistically significant.

Mean of improvement in tongue protrusion is better in group A (3.53mm) as compared to group B (1.46mm). The difference is statistically significant, $p<0.05$.

Mean of improvement in burning sensation is better in group A (2.73) as compared to group B (1.4). The difference is significant statistically.

SUMMARY AND CONCLUSION

The present study was undertaken to assess the efficacy of Lycopene and therapeutic Ultrasound in the treatment of Oral submucous fibrosis. A total of 30 patients were included in the study. The patients were randomly divided into 2 groups; Group A (15 patients

receiving Lycopene) and Group B (15 patients receiving Ultrasound).

The mean improvement in tongue protrusion and burning sensation is better in group A (lycopene) than in group B (ultrasound) and this has been proved statistically. The mean improvement in mouth opening is better in Group B (Ultrasound group) but the difference is not statistically significant.

In the present study even though the patients on lycopene show an improved response as compared to ultrasound in 2 out of 3 measurable variables, a definite conclusion cannot be drawn as the number of patients subjected to the tests is small. A further study involving a

larger group would be ideal in arriving at definite conclusions.

The two treatment modalities definitely show a significant improvement in the patients' condition with no reported side effects, hence should be included in the treatment protocol for patients with OSMF before a more invasive surgical intervention is sought.

A further conclusion drawn could be that lycopene could be used in the initial part of treatment to decrease burning sensation, while this could be complemented using therapeutic ultrasound to improve mouth opening

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