APPLICATION OF LASERS FOR ORAL SUBMUCUS FIBROSIS - AN EXPERIMENTAL STUDY

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ABSTRACT

Aim: Oral submucous fibrosis is a chronic disease characterised by progressive inability to open the mouth. Various treatment modalities are available for its management, but these have largely been ineffective.This preliminary study indicates that adequate release of oral submucous fibrosis can be achieved by using a diode laser, with minimal morbidity and satisfactor results.

Materials and Methods: 50 cases of oral submucous fibrosis underwent fibrous band resection using diode laser under Local anesthesia, from 2011 to 2013. All the patients were encouraged to carryout regular physiotherapy exercises, and were followed for period of 6 months.

Results: Pre- and post-operative mouth-opening were compared using repeated measure ANOVA test. The mean pre operative mouth opening was 23.04 mm and mean postoperative mouth opening at the end of 6 months was 27.97 mm and significant difference observed (F value - 619.750, P value - 0.00).

Conclusion: This preliminary study indicated that adequate release of oral submucous fibrosis can be achieved by using a diode laser, with minimal morbidity and satisfactory results. But the maintenance of intra operative results, post operative entirely depends on patients compliance.

Keywords: Oral Submucous Fibrosis (OSMF),Trismus,Diode Laser.

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INTRODUCTION

Oral submucous fibrosis {OSMF} has been well established in Indian medical literature since the time of Sushruta, a renowned Indian physician who lived in the era 600 B.C and was termed as "Vidari"[1]. This condition was first described in the modern literature by Schwartz in 1953, who coined the term "Atrophica idiopathica mucosa oris". Joshi subsequently coined the termed oral submucous fibrosis for the condition in 1953[2].However there are various synonyms proposed by different authors such as "Diffuse oral submucous fibrosis", "Idiopathic scleroderma of the mouth", "Idiopathic palatal fibrosis", "Sclerosing stomatitis" and "Juxta-epithelial fibrosis"[3].Pindborg (1966) defined oral submucous fibrosis as, "An insidious, chronic disease affecting any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by and/or associated with vesicle formation, it is always associated with juxta-epithelial inflammatory reaction followed by fibroelastic change of the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa and causing trismus and inability to eat"[3].

Geographically, OSMF has a specific distribution and affects predominantly Asians (and particularly Indians) from the southern states, and Taiwanese[4,5]. Global estimation indicates 2.5 million to 5million people in India are affected by OSMF from 1996 to 2002 respectively,[6] with male to female ratio being 2.36:1[7].Epidemiological data and intervention studies suggest that areca nut is the main aetiological factor for OSMF. Other etiological factors are chillies, lime, tobacco, nutritional deficiencies such as iron and zinc, immunological disorders, and collagen disorders[8].

The possible precancerous nature of OSMF was first described by Paymaster,[9] who observed the onset of slow-growing squamous cell carcinoma in one third of such patients. Studies showed malignant transformation rate of 2.3% in 10 years,8 4.5% in 15 years[10] and 7.6 % in 17 years[11] during follow up period.

Various treatment modalities are followed in treating this condition which includes medical and surgical. Medical management is indicated in the initial stages of OSMF, with mouth opening more than 25 mm. Intralesional injections of steroids, gamma interferon, hyaluronidase, placental extracts, triamcinolone and chymotrypsin are tried with varying results.

Oral submucous fibrosis does not regress either spontaneously or with cessation of betel quid chewing. For this reason, release of fibrotic bands by surgical means is necessary, with the primary aim of enabling mouth-opening sufficient for oral hygiene and feeding and also to facilitate inspection and management of subsequent cancer[12].

Surgery is indicated in moderately advanced cases of oral submucous fibrosis, as defined by maximum mouth-opening of 25 mm by Khanna, Andrade (1995). Simple division of fibrotic bands using blade with secondary healing has resulted in more fibrosis and disability[13]. So, various methods have been described including Split thickness skin grafts, Buccal Fat Pad grafts, Microvascular Free Radial Forearm Flaps, Tongue Flaps and Nasolabial Flaps to reconstruct the defect.

The main disadvantage with all the above described method is either prone to early recurrence of fibrosis or more importantly, they make reg-

ular monitoring of the affected mucosa to be difficult or even impossible for assessing carcinomatous changes[14].

In the modern era, the use of laser to release fibrotic bands leads to healing with minimal scarring, thereby decreasing the probability of procedure induced trismus. Laser is also associated with early wound healing. The other advantages of using laser include spontaneous occlusion of small, transected vessels, providing good haemostasis. The laser also assists the surgeon in making precise incisions with minimal collateral damage.

Diode laser is a portable device which delivers rays through a fiber-optic cable and hence can be delivered to relatively "difficult-to-access" areas. Its cutting depth is less than 0.01 mm, and thus preserves tissues beyond this depth. It gives a precise line of controlled cutting without damaging the muscles and deeper structures. Hence, laser therapy eliminates the use of grafts, to close the defect in spite of extensive resection. It yields excellent functional results[15].

In this study we would like to evaluate 50 cases of OSMF where diode laser will be used to release fibrotic bands and its influence on maintaining adequate mouth opening which is evaluated pre operatively (Fig.1),immediate post operatively, at 10th day, 3 months and 6 months.

MATERIALS AND METHODS

Study deisgn: Experimental study

Study setting: This study was carried out in KLE`S Society`s Institute of Dental Sciences, Bangalore (Karnataka, India) from 2011-2013.

Study population: Patients suffering from oral submucous fibrosis in the age group of 18- 60 years.

Sample size: Considering alpha at 0.03, power of the study at 0.95, and Essect size at 0.25. The minimum sample size estimated was 40, anticipating dropout sample size was increased to 50.

Sampling technique: Consecutive sampling technique.This is a type of random non probability sampling technique, where it includes all accessible subjects as part of the sample. This non-probability sampling technique can be considered as the best of all non-probability samples because it includes all subjects that are available that makes the sample a better representation of the entire population.

Material used: Sunny GOLD 6 Surgical Laser, 980 nm - Mikro Scientific Instruments Pvt. Ltd.

METHOD

A total of 50 cases with OSMF were undertaken for the study. All the procedures were carried out under local anesthesia.

PROCEDURE

Under strict aseptic precaution, operation was carried out in dark room. Protective eyewear was worn by the entire operating team and the patient. A 600 micrometer diameter fibre optic cable was used for delivery of the beam. Straight handpiece was used to place the incision at the desired site. Only plastic and wooden instruments were used in the surgery.

2% local anesthesia with adrenaline 1: 80,000 dilution, infiltrated bilaterally all over buccal mucosa.'Y' shaped incision with 2 limbs facing anteriorly were made from the retromolar area extending up to the premolar region or angle of mouth. The incision was made approximately 2 mm deep until the muscle layer was reached, incising only the fibrous mucosa and submucosal layer using Diode Laser at 6watts in continuous mode along the buccal mucosa at the level of occlusal plane away from Stenson's duct orifice(Fig.2). After resection of fibrous bands, the mucosa was further freed by finger dissection and undermining was done by blunt dissection until no resistance was felt. The procedure was repeated on the other side, and the mouth was then forced open (intraoperatively) with Hister's mouthgag. Mouth opening was measured immediate post operatively from the incisal edges of the maxillary and mandibular central incisors and recorded . Hemostasis achieved. Patients were discharged.

All patients received antibiotics for 5 days, and multivitamin and antioxidants for 6 months post operatively.

Patients were started on mouth opening exercises (using wooden sticks) from the 1st postoperative day, with a frequency of four times a day with duration of half an hour, and later the frequency and duration was increased to facilitate improvement in the mouth opening until adequate values were achieved. Patients were evaluated for mouth opening at 10th day, 3 months and 6 months respectively (Fig.3).

RESULTS

A prospective clinical study was conducted on 50 patients who were diagnosed with oral submucous fibrosis based on clinical and histopathological reports. Out of 50 patients, 49 were male and 1 female who enrolled, aged from 15-40 year. The disease was more common in 2nd decade of life. Out of 50 patients, 88 %(n=44) were addicted to gutka, 10%(n=5) consumed betel nut and 2%(n=1) had a habit of sweet supari chewing. In our study we observed mean number of times/daytobacco chewing habit was 18. The frequency of tobacco chewing habit ranged

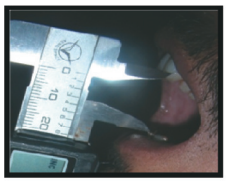

Fig.1- Pre-operative

Fig.2 – Intra operative

Fig.3 – Post- operative

from 1-15 years, mean was 8 year . Patients gave history of burning sensation of mouth ranging from 1- 8.9 years with mean of 5 year . Majority of patients, 56 % (n=28) experienced trismus from 1-2.9 years (Graph.1). All 50 patients under went resection of fibrous bands using diode laser under local anesthesia and forceful mouth opening was achieved using Histers mouth gag. Mouth opening was documented immediate postoperatively, at 10th day, 3 months and 6 months.

To know the effect of laser treatment on mouth opening in OSMF patients at different time intervals Repeated measures ANOVA was used.(Table1,Graph.2) Mauchly's test indicated that the assumption of sphericity was violated ($p< 0.05$). Therefore degrees of freedom were corrected using Greenhouse - Geisser estimates of Sphericity ($e= 0.382$). The results show that there is statistically significant effect of laser treatment on mouth opening in OSMF patients at different time intervals .

Pairwise Comparisons of effect of laser treatment on mouth opening at all time intervals was statistically significant ($p < 0.05$),(Table 2). Mean pre-operative mouth opening was 23.04 mm. After resection of fibrous bands using diode laser, mean immediate post-operative mouth opening was improved to 32.74 mm, which on follow up on 10th day, 3 months and 6months, it was 31.57mm, 29.73mm, and 27.97mm respectively.

Graph 1: Distribution of subjects according to trismus.

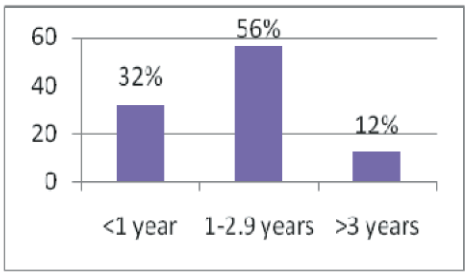

Table 1: Test of within subjects effects/ Repeated measures ANOVA.

Time period	N	Mean	Std. Deviation	Estimate of Sphericity test
Pre-operative	50	23.04	1.56	Greenhouse – Geisser
Immediate post-operative	50	32.74	2.64	
Tenth day	49	31.57	2.56	df – 2.328
Three months	49	29.73	2.68	F value – 619.750
Six months	49	27.97	2.80	P value – 0.00

Graph 2: Test of within subjects effects/ Repeated measures ANOVA.

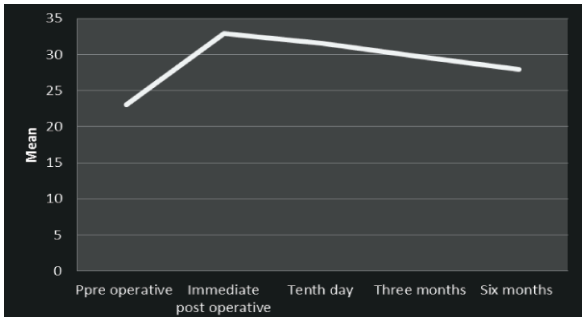

Table 2: Pairwise comparison of mouth opening at different time intervals

Visits	Follow up	Mean Difference	Std. Error	Sig.[a]	95% Confidence Interval for Difference[a]	
					Lower Bound	Upper Bound
Pre op	Post op immediate	-9.796*	.275	.000	-10.605	-8.986
	Tenth day	-8.469*	.284	.000	-9.306	-7.633
	Three months	-6.633*	.276	.000	-7.445	-5.820
	Six months	-4.878*	.278	.000	-5.694	-4.061
Post op Immediate	Baseline	9.796*	.275	.000	8.986	10.605
	Tenth day	1.327*	.135	.000	.930	1.723
	Three months	3.163*	.161	.000	2.691	3.636
	Six months	4.918*	.208	.000	4.307	5.530
Tenth day	Baseline	8.469*	.284	.000	7.633	9.306
	Post op immediate	-1.327*	.135	.000	-1.723	-.930
	Three months	1.837*	.121	.000	1.479	2.194
	Six months	3.592*	.206	.000	2.986	4.198
Three months	Baseline	6.633*	.276	.000	5.820	7.445
	Post op immediate	-3.163*	.161	.000	-3.636	-2.691
	Tenth day	-1.837*	.121	.000	-2.194	-1.479
	Six months	1.755*	.122	.000	1.396	2.114
Six months	Baseline	4.878*	.278	.000	4.061	5.694
	Post op immediate	-4.918*	.208	.000	-5.530	-4.307
	Tenth day	-3.592*	.206	.000	-4.198	-2.986
	Three months	-1.755*	.122	.000	-2.114	-1.396

DISCUSSION

Oral submucous fibrosis is a chronic, progressive, debilitating disease that was first reported in India in the year 1953[2,16].Initially the disease was found only amongst people living in the Indian subcontinent or in Indian migrants. Later, cases where reported from many South-east Asian, and other western countries[17].

Literature survey of gender distribution has shown wide variations in the occurrence of OSMF. Some epidemiological surveys in India have shown a female predominance[18,19]. In our study, out of 50 OSMF patients, we observed 98% (n=49) were males and 2% (n=1) was female, which was similar to the study conducted by Chaturvedi VN et al.[20] and Reddy V et al.[7] in India. Male predominance in our study can be

due to easy accessibility for use areca nut and its products more frequently than females in our society and changing lifestyles of the youngsters.

In our study, disease was more common in 2nd decade of life, which was substantiated by the study conducted by Pindborg et al.[5]. The pathogenesis of the disease is thought to be multifactorial. Habitual chewing of gutkha and other areca nut products plays a major role in etiology of this condition[2,17].

Areca-nut contains alkaloids, flavonoids, and copper, which all interfere with homeostasis of the extracellular matrix. Four alkaloids - arecoline (most potent), arecaidine, guvacine, and guvacoline - are known to stimulate fibroblasts to produce collagen. Flavonoids (tannins and catechins) inhibit collagenase, stabilise the collagen fibrils, and render them resistant to degradation by collagenase. The localised mucosal inflammation caused by areca-nut or gutkha results in the recruitment of activated T-cells and macrophages that lead to an increase in cytokines and tumour growth factor beta (TGF- B). The latter considerably increases the production of collagen by activating procollagen genes, and upregulating procollagen proteinase enzymes and lysyl oxidase activity. Simultaneously, TGF- B inhibits collagen degradation by activating the tissue inhibitor of matrix metalloproteinase (TIMP) genes and plasminogen activator inhibitor (PAI). The high concentration of copper in areca-nut has been found to stimulate lysyl oxidase activity, an enzyme essential to the final cross-linking of collagen fibres. Increased copper has been seen in mucosa affected by OSMF, which supports its role in fibrogenesis by enhancing lysyl oxidase activity.

Continually chewing areca-nut leads to increased activity of the masticatory muscles, depletion of glycogen, and muscle fatigue. The reduced blood supply following fibrosis further promotes muscle fatigue and causes extensive degeneration and fibrosis in the muscles[21].

In our series, all the patients gave a positive history of chewing some form of betel nut or tobacco or a combination. 88% (n=44) of patients had habit of chewing gutka, 10% (n=5) with betel nut and 2% with sweet supari chewing habit. When compared to gutkha with betel nut and sweet supari users, gutka users showed a significantly increased severity of OSMF. The reason attributes to the fact that the commercially available products are concentrated, freezes dried and have higher dry weight concentration of tobacco, areca nut, and slaked lime to the traditionally prepared home made products like panmasala[19,22,23]. Another factor supporting this could be the antioxidant capabilities of pan leaf which is known to be rich in beta-carotene, which has the capacity to quench free radicals that are mutagenic which counteracts the different pathology causing irritants[24].

In our study, as the duration of consuming habits increased above 3 years and frequency of habit of consuming for more than 5 times per day resulted in increased burning sensation of mouth and restricted mouth opening. A similar results were found by Tilakaratne et al(2004)[25].

Diagnostic criteria of OSMF are burning sensation of mouth, formation of vesicles/ulcers, dryness of mouth, alteration in taste, blanching, and stiffness of oral mucosa. Palpable fibrotic bands running vertically in the cheek and circumferentially in the lips, limited function of the soft palate, shrunken and bud like uvula, restricted tongue movements are all seen in advanced cases[22].Majority of these diagnostic features were observed in all our patients with varying severity.

Medicinal modalities of treatment like intralesional injections of hyaluronidase, hydrocortisone, placentral extract & triamcinolone along with oral administration of vitamins, iron supplement, antioxidants & peripheral vasodilators like buflomedial hydrochloride & nylhydrin hydrochlorideare effective in treating initial cases of OSMF.Surgery is indicated in moderately advanced to advanced cases, where mouth opening is less than 25 mm. Simple division of fibrotic bands using blade with secondary healing has resulted in more fibrosis and disability[13]. Various methods have been described to reconstruct the defects, which includes Split thickness skin grafts, Buccal Fat Pad grafts, Microvascular Free Radial Forearm flaps, Tongue flaps and Nasolabial flaps.Additional procedures like masticatory muscle myotomy and bilateral coronoidectomycan be performed to enhance mouth opening[14].

In the modern era, the use of laser to release fibrotic bands leads to healing with minimal scarring, thereby decreasing the probability of procedure induced trismus. The word "Laser" is an acronym for Light Amplification by Stimulated Emission of Radiation. Laser is a device that produces an intense beam by amplifying light.

Unlike other light sources, lasers emit coherent, monochromatic, and collimated electromagnetic radiation, with high intensity, displaying a high optical power per unit area for a given amount of energy as compared to broadband light sources. These characteristics endow the laser with unique applications.

The most common surgical lasers emit wavelengths in the infrared (IR) part of the spectrum: the Nd:YAG (Wave Length=1,064nm), the Er:YAG (Wave Length=2.94 micrometers), and the CO2 laser (Wave Length=10.6 and 9.6micrometers). Within the visible portion of the electromagnetic spectrum, argon lasers emit light between 458 and 515nm, and excimer lasers are located in the ultraviolet part of the spectrum (100 to 400nm). Diode lasers emit wavelengths of 670 to 1551nm. Infrared light is absorbed primarily by water, while visible and ultraviolet light are primarily absorbed by hemoglobin and melanin, respectively.

Lasers within the ultraviolet region (100 to 380nm) are able to ionize tissues, a process known as photochemical desorption. Lasers of longer wavelengths, especially those within the infrared part of the spectrum (700 to 10,000nm), cause significant tissue heating. Most of the surgical lasers are embedded in this group and comprise thermal lasers. The light of these lasers is rapidly converted to thermal energy causing denaturation of proteins, decomposition of tissue, microexplosion of cell water and charring.

Diode lasers have a diversity of applications in the medical field. These devices are compact and portable in design. The active material used is a semi-conducting crystal, usually gallium arsenide (GaAs) or similar compounds. Blood vessels smaller than 0.5mm in diameter are sealed spontaneously, allowing excellent visibility and precision when dissecting through the tissue planes.There is minimal cellular damage adjacent to the plane of excision. This facilitates good wound healing, even large laser wounds heal with good functional results and minimal scar. The laser energy is transmitted through an optical fibre delivery system to access the difficult areas in case of OSMF. Its cutting depth is less than 0.01 mm, and thus preserves tissues beyond this depth. It gives a precise line of controlled cutting without damaging the muscles and

deeper structures. There is minimal damage to adjacent tissue and a coagulum of denatured protein forms on the surface, hence no dressing is required, and the lasered area can be left exposed in the mouth. Skin grafting is not necessary, even for large areas. Denatured protein acts as a dressing layer for the treatment site that may decrease pain and enhances less risk of secondary infection.

Our study included patients with mean pre operative mouth opening of 23.04 mm.

Resection of fibrous bands using diode laser under local anesthesia was carried out in all 50 patients. Intra-operatively very minimal bleeding was seen. Surgical procedure was well tolerated by the patients. Complications like damage to facial vessels, and parotid duct were not encountered in any of the 50 patients. Out of 50 patients, 1 patient lost the follow up.

Post operatively patients were evaluated for mouth opening at different intervals i.e, immediate post operative, after 10 days, 3 months, and 6 months respectively.Intra-oral defect healed uneventfully in all 49 patients.

Mean mouth opening achieved immediate post operatively was 32.74 mm, and on 10th day, it was 31.57mm. On 3 months follow up, mouth opening was reduced to 29.73mm, on 6months follow up, it was further reduced to 27.97 mm. This gradual decrease in mouth opening can be attributed to fibrosis of the tissue while healing and irregular physiotherapy post operatively. The mean increase in mouth opening achieved at the end of 6 months was 4.77mm.

These data shows, even though there is acceptable increase in mouth opening through conservative approach using diode laser in OSMF patients, patient's compliance plays an important role in its maintenance. For this reason, psychologic preparation for the patient before surgery plays a significant role in the success of surgery.

"Although laser excision is not a panacea for oral submucous fibrosis, it is a simple surgical procedure with effective results in the management of this disease. A more extensive study involving a greater number ofcases and including more parameters is necessary to come to final conclusion about this surgical technique and to evaluate the efficacy of lasers in the surgical management of oral submucous fibrosis".

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