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Comparative Study of Intralesional Dexamethasone, Hyaluronidase & Oral Pentoxifylline in Patients with Oral Submucous Fibrosis

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Strictly as per the compliance and regulations of:

Comparative Study of Intralesional Dexamethasone, Hyaluronidase & Oral Pentoxifylline in Patients with Oral Submucous Fibrosis

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Results : In the present study, improvement in all the parameters except tongue protrusion were statistically significant ($p < 0.001$), improvement in tongue protrusion was statistically not significant ($p>0.05$).

Conclusion : In the present study, it was found that all the parameters showed significant improvement in dexamethasone group compared to pentoxifylline group. Nevertheless pentoxifylline group also showed statistically significant improvement in all the parameters. For this reason, it is concluded that Pentoxifylline is a good alternative treatment for oral submucous fibrosis in patients in whom dexamethasone is contraindicated, or those who cannot make frequent visits for intralesional injections. In such oral submucous fibrosis patients it is better to substitute pentoxifylline therapy.

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Keywords : Oral submucous fibrosis, pentoxifylline, Dexamethasone, Hyaluronidase Lignocaine, burning sensation, mouth opening, tongue protrusion, cheek flexibility.

I. Introduction

Oral submucous fibrosis (OSF) is a chronic disease of insidious onset featuring the deposition of fibrous tissue in the submucosal layer of the pharynx, palate, fauces, cheek and lips and esophagus.[1] Pindborg and Sirsat have defined OSF 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 epithelial inflammatory reactions followed by a fibro elastic change of the lamina propria, with epithelial atrophy leading to stiffness of the oral mucosa and causing trismus and inability to eat".[2]

The term oral submucous fibrosis (OSF) follows from oral (meaning mouth), submucosal (meaning below the mucosa of the mouth) and fibrosis (meaning hardening and scarring).[3]

Submucous fibrosis of the oral cavity was first described by Schwartz in 1952 in five Indian females from Kenya and East Africa. Initially the term "atrophia idiopathica mucosae oris" was proposed, which was later replaced by the term currently being used ie, oral submucous fibrosis. The prevalence in India ranges from 0.2 to 0.5percent with a higher predominance in the southern parts of the subcontinent. Individuals between the ages of 20 & 40 years are most commonly affected but cases have been reported in patients ranging from two years to eighty nine years of age.[4]

OSF has a multifactorial etiology. Several factors such as chilli consumption, nutritional deficiency states, areca nut chewing, genetic susceptibility, autoimmunity & collagen disorders have been suggested to be involved in the pathogenesis of the condition.[5]

OSF is a chronic progressive disorder and its clinical presentation depends on the stage of the disease at detection.[4] Clinical features of OSF include

burning sensation on taking spicy food, excessive salivation, dryness of the mouth, defective gustatory sensation and progressive restriction of mouth opening and the protrusion of the tongue.

It is characterized by excessive production of collagen leading to inelasticity of the oral mucosa and atrophic changes of the epithelium.[6] with the progress of the disease, fibrosis may extend from the lamina propria through entire submucosa to the muscle layer. Thick inelastic rope like fibrous bands appear vertically in the buccal mucosa, along the contours of the faucial pillars and around the entire circle of lips thus leading to difficulty in mouth opening and narrowing of the rima oris.[7] The fibrosis also leads to difficulty in mastication, speech and swallowing, pain in the throat and the ears, and a relative loss of auditory acuity due to stenosis of the opening of the eustachian tube.4 The most outstanding feature and the most reliable sign of oral submucous fibrosis is the presence of palpable bands in the oral mucosa, especially in the buccal mucosa. The disease, however, has other characteristic signs, such as diffuse blanching of the mucosa, occurrence of hyperpigmented areas adjacent to zones with loss of pigment, loss of tongue papillae, and a leathery consistency of the mucosa.[8] A more serious complication of this disease is the risk of the development of oral squamous cell carcinoma (SCC), estimated to be 7.6 percent of cases over a 10 year period.

The reasons for the rapid increase of the disease are reported to be due to an upsurge in the popularity of commercially prepared areca nut preparations (pan masala) in india[9] and to an increased uptake of this habit by young people[10] due to easy access, effective price changes and marketing strategies. OSF has been reported in the Indian population and established in the Indian literature since the time of sushruta.[11]

The various treatment modalities proposed for OSF include nutritional support, immunomodulatory drugs, physiotherapy, local drug delivery, combined therapy and surgical management. [12]

Since long, intralesional injections of Dexamethasone (4mg/ml) and Hyaluronidase 1500 IU and 0.5 ml of lignocaine 2% have been the treatment modality in the management of OSF patients with variable success rates in different clinical studies.[13,14]

Pentoxifylline has been recently shown to have significant improvement in the management of OSF patients.[15]

In the course of disease treatment, convenience of drug administration is one of the factor for successful management of disease. As oral administration of drug is more convenient compared to intralesional drug administration, it would be ideal if a oral substitute to intralesional drug delivery is available in the management of OSF.

This study is intended to compare the efficacy of oral Pentoxifylline 400 mg Tablets with intralesional injections of Dexamethasone (4mg/ml) and Hyaluronidase 1500 IU and 0.5 ml of Lignocaine 2% in OSF patients for 12 weeks period of active treatment.

II. Materials and Methods

Dexamethasone Injection 4 mg/ml is a synthetic analogue of prednisolone, having similar but more potent anti-inflammatory therapeutic action and diversified hormonal and metabolic effects. Modification of the basic corticoid structure as achieved in Dexamethasone Injection 4 mg/ml offers enhanced anti-inflammatory effect compared to older corticosteroids. [16]

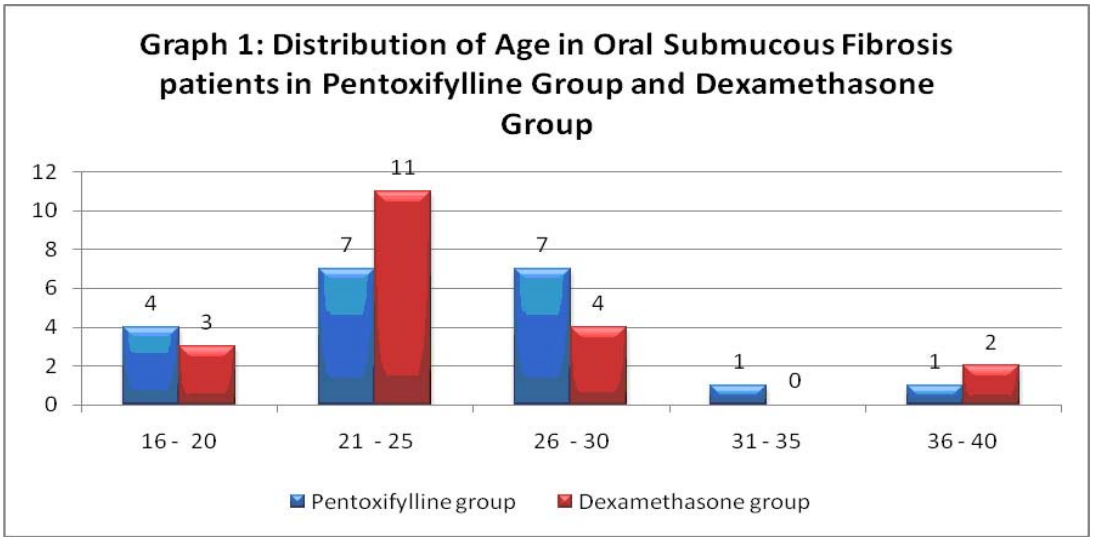
Hyaluronidase is an enzyme which depolymerise the mucopolysacchride hyaluronic acid. It is prepared from the testes and semen of mammals and purified so as to remove most of the inert material. The resulting solution is sterilized and freeze dried. It is a sterile, white or yellowish white powder.

Pentoxifylline is a tri-substituted methylxanthine derivative, the biologic activities of which are numerous. This includes increasing red cell deformability, leukocyte chemotaxis, antithrombin and anti- plasmin activities, and more importantly to the present context, its fibrinolytic activity.

The study population consisted of 40 male patients with OSF. Patients were divided into two groups. 20 patients are in pentoxifylline group and 20 patients in Dexamethasone group. Pentoxifylline Group received oral Pentoxifylline 400 mg tablets twice daily for first 4 weeks and thrice daily for next 8 weeks. Dexamethasone Group received biweekly intralesional injections of Dexamethasone (4mg/ml), Hyaluronidase 1500 IU and 0.5 ml of Lignocaine 2% for a period of 12 weeks. Parameters taken in the study were burning sensation, mouth opening, tongue protrusion and cheek flexibility.

III. Results

40 patients of OSF were selected for the present study and were divided randomly into two groups with 20 patients of OSF in each group. The patients in the first group were given Pentoxifylline orally 400 mg twice a day for 4 weeks initially, followed by 400mg thrice a day for next 8 weeks and the patients in the second group were given intralesional injections of 2ml of Dexamethasone 4mg/ml, 0.5 ml of Lignocaine 1: 80000 and 1500 IU of Hyaluronidase, biweekly for 12 weeks.



The particulars are given in table no. 1 and graph no.1.

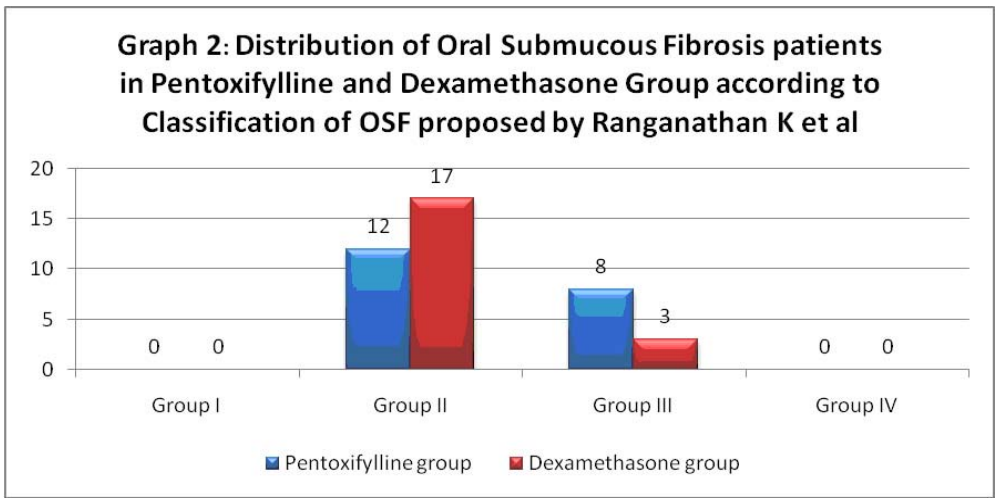
Table 1 : Distribution of Age in Oral Submucous Fibrosis patients in Pentoxifylline Group and Dexamethasone Group.

Age group	Pentoxifylline group	Dexamethasone group
16 - 20	4	3
21 - 25	7	11
26 - 30	7	4
31 -35	1	-
36 -40	1	2
Total	20	20

The age of the 20 patients in the Pentoxifylline group ranged from 18 to 38 years with an average age of 25.05 years. The youngest subject was 18 years old and the oldest was 38 years. Four patients were in the age group of 16-20 years, seven were in the age group of 21 to 25 years and seven were in the age group of 26 to 30 years, one patient in the age group of 31 to 35 years and one patient in the age group of 36 to 40 years. 14 out of 20 patients comprising 70 % were in the age group of 21 to 30 years. The particulars are given in table no. 1 and graph no.1.

The age of the 20 patients in the Dexamethasone group ranged from 18 to 38 years with an average age of 25.15 years. The youngest subject was 18 years old and the oldest was 38 years old. Three patients were in the age group of 16-20 years, eleven were in the age group of 21 to 25 years, four were in the age group of 26 to 30 years, and two patients in the age group of 36 to 40 years. 15 out of 20 patients comprising 75 % were in the age group of 21 to 30 years. The particulars are given in table no. 1 and graph no.1.

All the patients in both, the Pentoxifylline group and the Dexamethasone group were males. These patients were from all the socioeconomic strata.



The particulars are given in table no.2 and graph no.2.

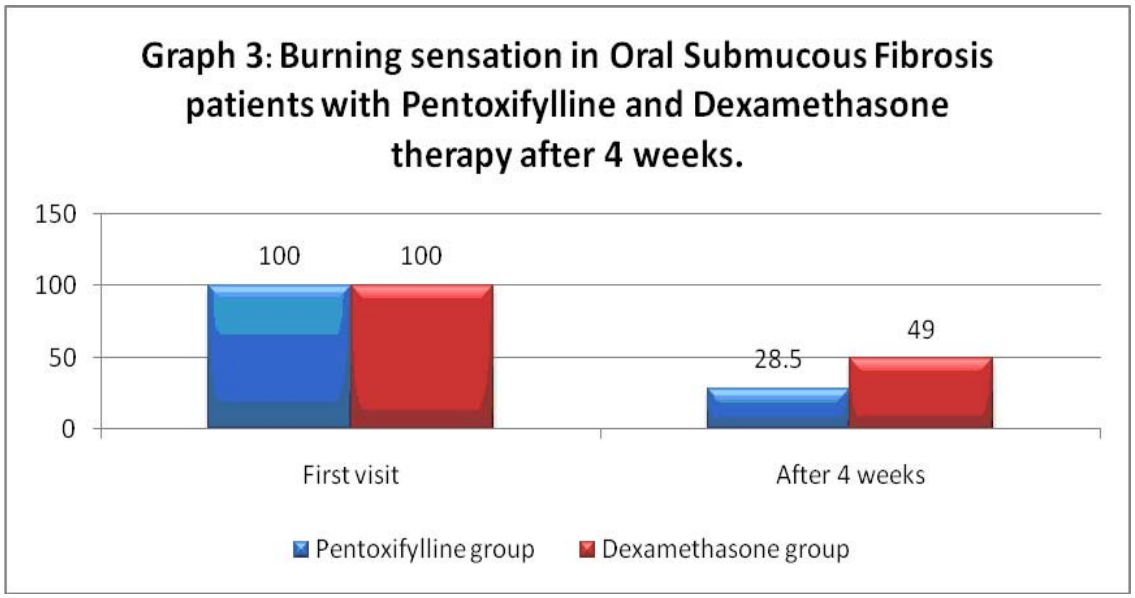
Table 2 : Distribution of Oral Submucous Fibrosis patients in Pentoxifylline and Dexamethasone Group according to Classification of OSF proposed by Ranganathan K et al.

Clinical classification of OSF	Pentoxifylline Group	Dexamethasone Group
Group I	0	0
Group II	12	17
Group III	8	3
Group IV	0	0

Clinically, all the patients in both the groups were classified according to the classification proposed by Ranganathan K et al. There were 12 patients in group II and 8 patients in group III in the Pentoxifylline group. There were 17 patients in group II and 3 patients in group III in the Dexamethasone group. The particulars are given in table no.2 and graph no.2.

The major presenting complaint among all patients in both the groups was burning sensation in the mouth on eating spicy food and reduced mouth opening. Other features like decreased tongue protrusion, and loss of cheek flexibility were noted in all the patients and were taken as criteria of the study.

Adverse effects as specified in the literature were at long treatment period. In the present study of 12 weeks of treatment, no significant adverse effects were noted, except for transient pain locally when Dexamethasone with Hyaluronidase was given intralesionally which subsided after few minutes.

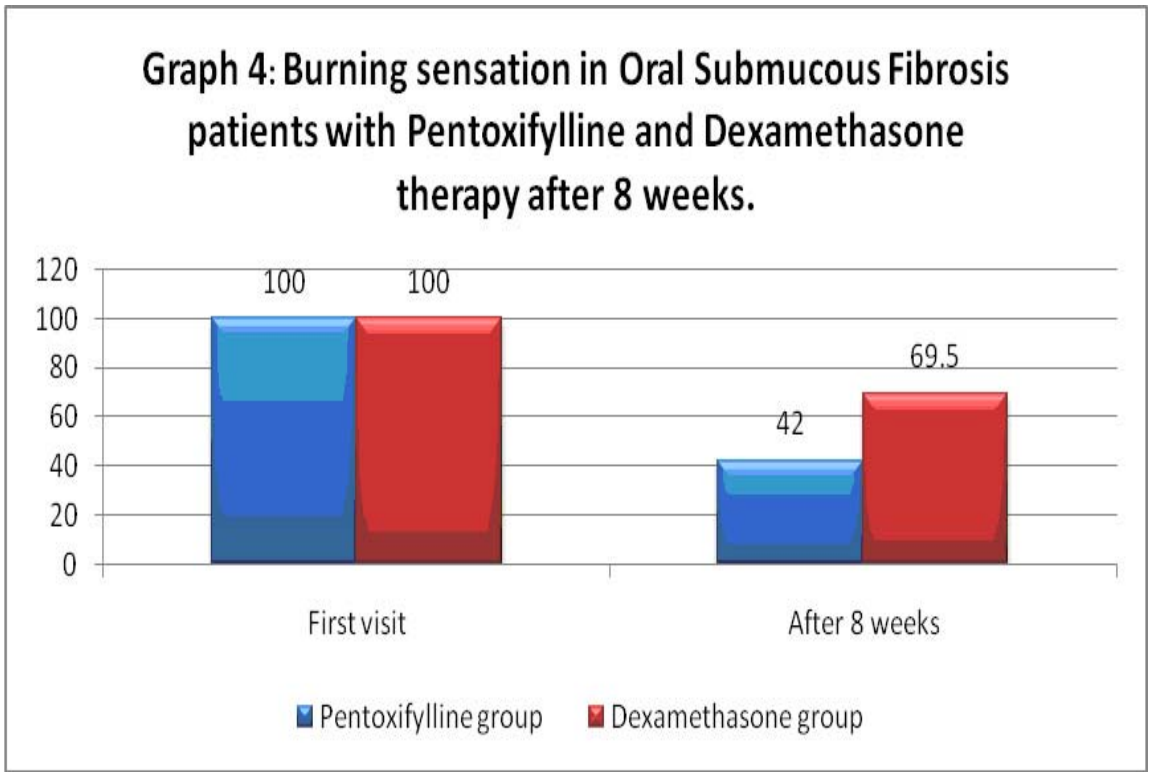


The particulars are given in table no 3 and graph no 3.

Table 3 : Burning sensation in Oral Submucous Fibrosis patients with Pentoxifylline and Dexamethasone therapy after 4 weeks.

		Pentoxifylline		Dexamethasone Intralesional injections		p-value
	No. of patients	Mean	SD	Mean	SD	
First visit	20	100.00	0.00	100.00	0.00	-
After 4 weeks	20	28.50	8.13	49.00	8.52	<0.001

In the present study, all the patients in both the groups showed reduction in burning sensation. The mean reduction in burning sensation in the pentoxifylline group at the end of 4 weeks compared to the first visit was 28.5%. The minimum decrease in burning sensation was 10 % in two patients and maximum decrease in burning sensation was 40 % in three patients. The mean reduction in burning sensation in the Dexamethasone group at the end of 4 weeks compared to the first visit was 49 %. The minimum decrease in burning sensation was 40 % in eight patients and maximum decrease in burning sensation was 60 % in six patients. There was significant reduction in the burning sensation at the end of 4 weeks in dexamethasone group compared to pentoxifylline group ($P < 0.001$). The particulars are given in table no 3 and graph no 3.

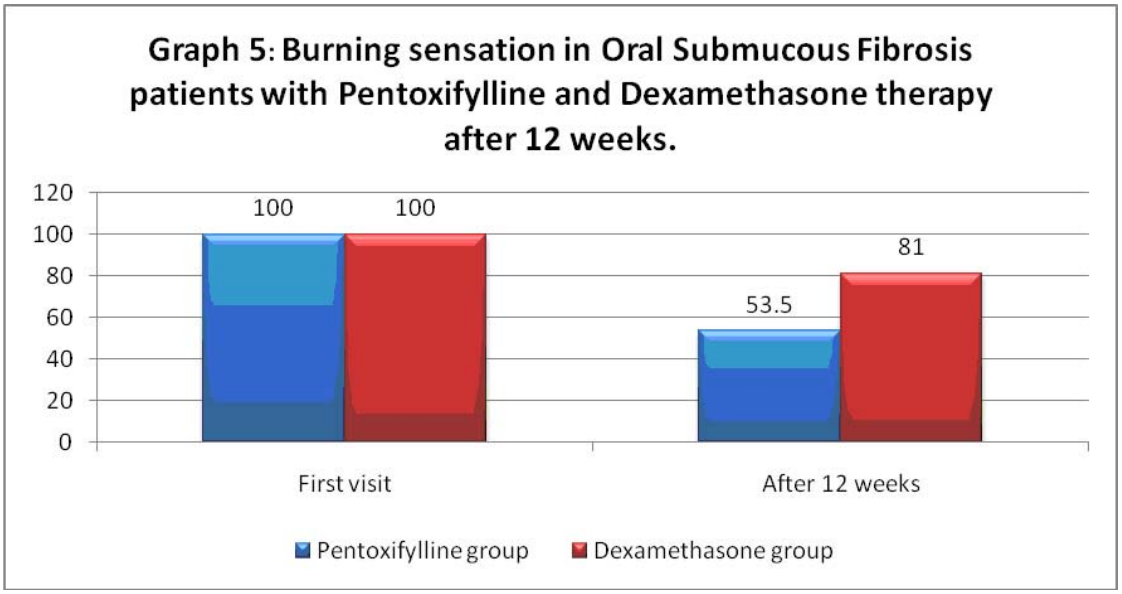


The particulars are given in table no 4 and graph no 4.

Table 4 : Burning sensation in Oral Submucous Fibrosis patients with Pentoxifylline and Dexamethasone therapy after 8 weeks.

		Pentoxifylline		Dexamethasone Intralesional injections		p-value
	No. of patients	Mean	SD	Mean	SD	
First visit	20	100.00	0.00	100.00	0.00	-
After 8 weeks	20	42.00	8.94	69.50	8.87	<0.001

In the present study, the mean reduction in burning sensation in the pentoxifylline group at the end of 8 weeks compared to the first visit was 42 %. The minimum decrease in burning sensation was 20 % in one patient and maximum decrease in burning sensation was 60 % in one patient. The mean reduction in burning sensation in the Dexamethasone group at the end of 8 weeks compared to the first visit was 69.5 %. The minimum decrease in burning sensation was 50 % in one patients and maximum decrease in burning sensation was 80 % in six patients. There was significant reduction in the burning sensation at the end of 8 weeks in dexamethasone group compared to pentoxifylline group ($P < 0.001$). The particulars are given in table no 4 and graph no 4.

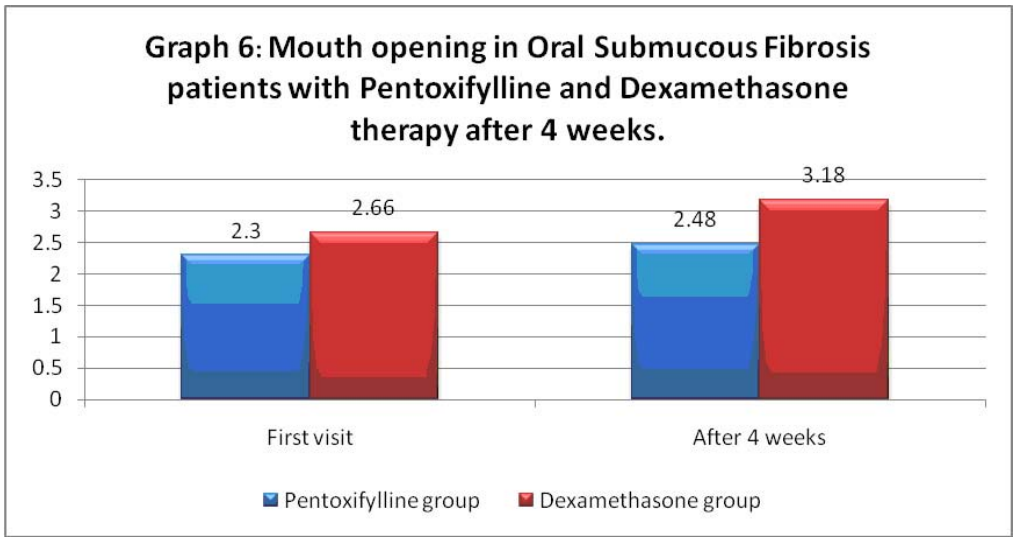


The particulars are given in table no 5 and graph no 5.

Table 5 : Burning sensation in Oral Submucous Fibrosis patients with Pentoxifylline and Dexamethasone therapy after 12 weeks.

		Pentoxifylline		Dexamethasone Intralesional injections		p-value
	No. of patients	Mean	SD	Mean	SD	
First visit	20	100.00	0.00	100.00	0.00	-
After 12 weeks	20	53.50	8.75	81.00	6.41	<0.001

In the present study, the mean reduction in burning sensation in the pentoxifylline group at the end of 12 weeks compared to the first visit was 53.50 %. The minimum decrease in burning sensation was 30 % in one patient and maximum decrease in burning sensation was 60 % in eleven patients. The mean reduction in burning sensation in the Dexamethasone group at the end of 12 weeks compared to the first visit was 81 %. The minimum decrease in burning sensation was 70 % in three patients and maximum decrease in burning sensation was 90 % in five patients. There was significant reduction in the burning sensation at the end of 12 weeks in dexamethasone group compared to pentoxifylline group ($P < 0.001$). The particulars are given in table no 5 and graph no 5.

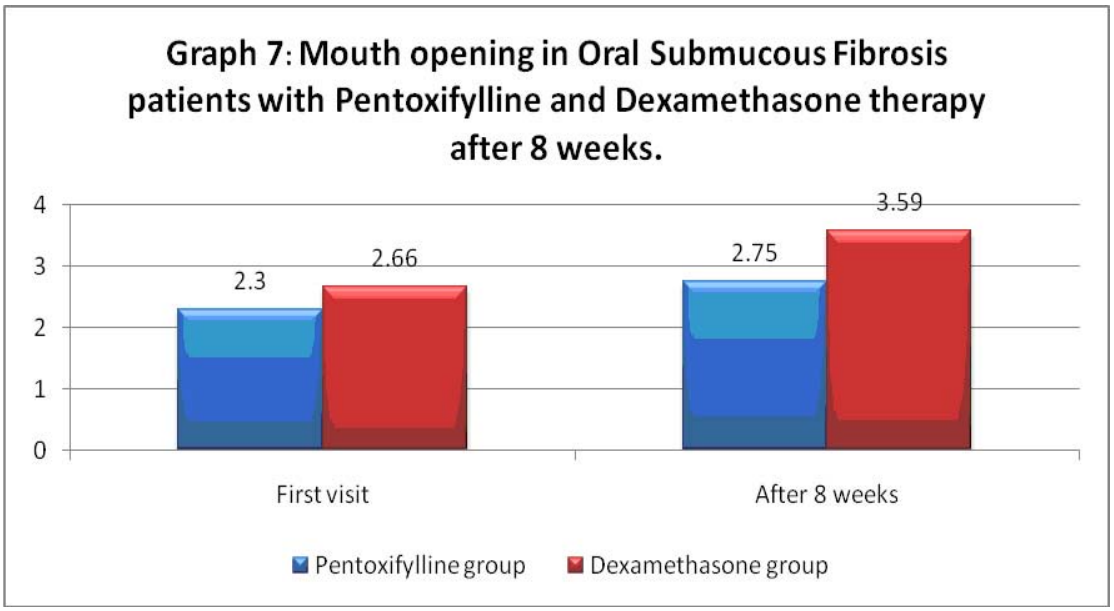


The particulars are given in table no 6 and graph no 6.

Table 6 : Mouth opening in Oral Submucous Fibrosis patients with Pentoxifylline and Dexamethasone therapy after 4 weeks.

		Pentoxifylline		Dexamethasone Intralesional injections		p-value
	No. of Patients	Mean	SD	Mean	SD	
First visit	20	2.30	0.61	2.66	0.52	0.048
After 4 weeks	20	2.48	0.65	3.18	0.60	0.001

In the present study, all the patients in both the groups showed improvement in mouth opening. The mean improvement in mouth opening in the pentoxifylline group at the end of 4 weeks compared to the first visit was 0.18 cm. Two patients showed no improvement in mouth opening and in one patient, maximum improvement was 0.4 cm. The mean improvement in mouth opening in the Dexamethasone group at the end of 4 weeks was 0.52 cm. The minimum improvement in mouth opening was 0.3 cm and maximum improvement was 0.9 cm. There was significant improvement in mouth opening at the end of 4 weeks in dexamethasone group compared to pentoxifylline group. (P = 0.001). The particulars are given in table no 6 and graph no 6.

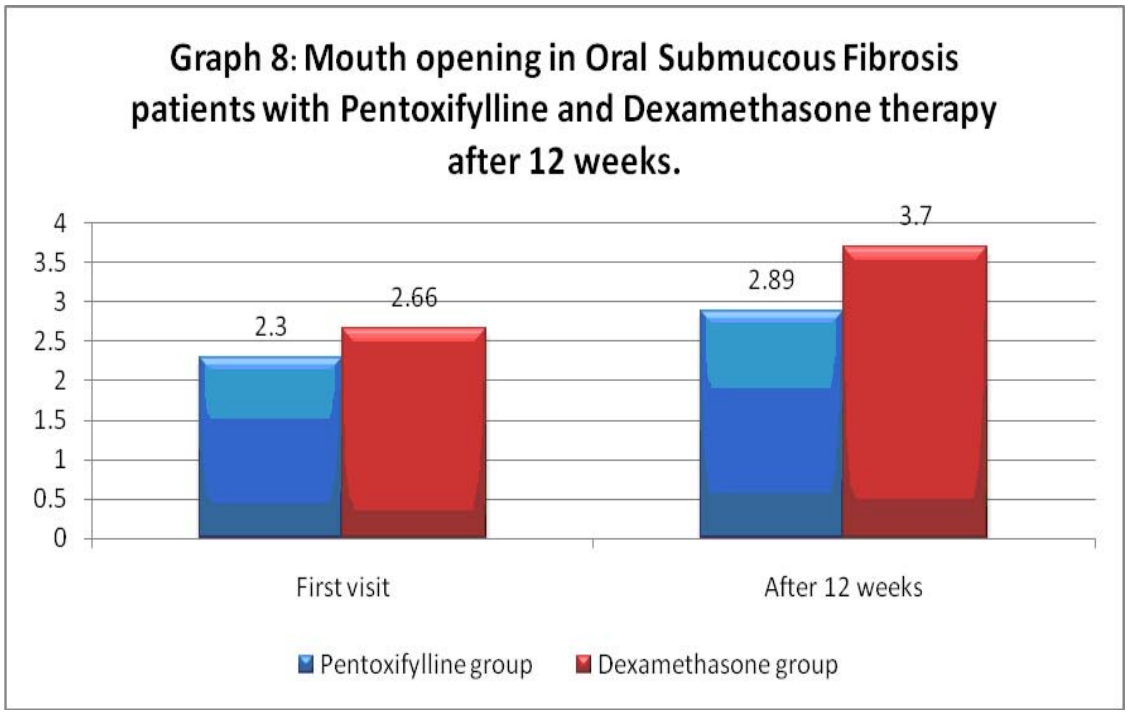


The particulars are given in table no 7 and graph no 7.

Table 7 : Mouth opening in Oral Submucous Fibrosis patients with Pentoxifylline and Dexamethasone therapy after 8 weeks.

		Pentoxifylline		Dexamethasone Intralesional injections		p-value
	No. of Patients	Mean	SD	Mean	SD	
First visit	20	2.30	0.61	2.66	0.52	0.048
After 8 weeks	20	2.75	0.69	3.59	0.57	< 0.001

The mean improvement in mouth opening in the pentoxifylline group at the end of 8 weeks compared to the first visit was 0.45 cm. The minimum improvement in mouth opening was 0.2 cm and maximum improvement was 0.7 cm. The mean improvement in mouth opening in the Dexamethasone group at the end of 8 weeks compared to the first visit was 0.93 cm. The minimum improvement in mouth opening was 0.7 cm and maximum improvement was 0.9 cm. There was significant improvement in mouth opening at the end of 8 weeks in dexamethasone group compared to pentoxifylline group ($P < 0.001$). The particulars are given in table no 7 and graph no 7.

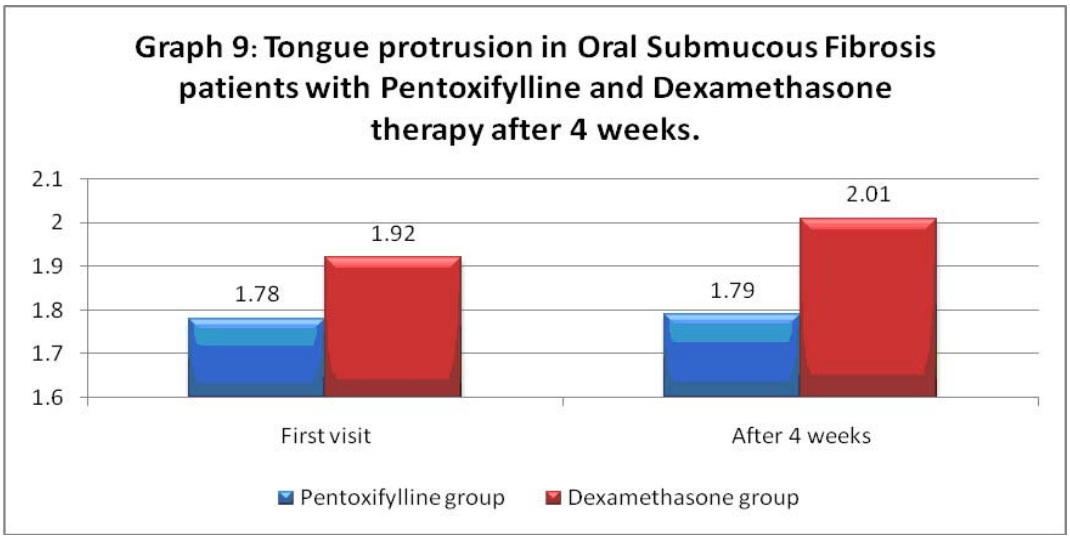


The particulars are given in table no 8 and graph no 8.

Table 8 : Mouth opening in Oral Submucous Fibrosis patients with Pentoxifylline and Dexamethasone therapy after 12 weeks.

		Pentoxifylline		Dexamethasone Intralesional injections		p-value
	No. of Patients	Mean	SD	Mean	SD	
First visit	20	2.30	0.61	2.66	0.52	0.048
After 12 weeks	20	2.89	0.65	3.70	0.52	<0.001

The mean improvement in mouth opening in the pentoxifylline group at the end of 12 weeks compared to the first visit was 0.59 cm. The minimum improvement in mouth opening was 0.2 cm and maximum improvement was 0.7 cm. The mean improvement in mouth opening in the Dexamethasone group at the end of 12 weeks compared to the first visit was 1.04 cm. The minimum improvement in mouth opening was 0.8 cm and maximum improvement was 1.5 cm. There was significant improvement in mouth opening at the end of 12 weeks in dexamethasone group compared to pentoxifylline group ($P < 0.001$). The particulars are given in table no 8 and graph no 8.

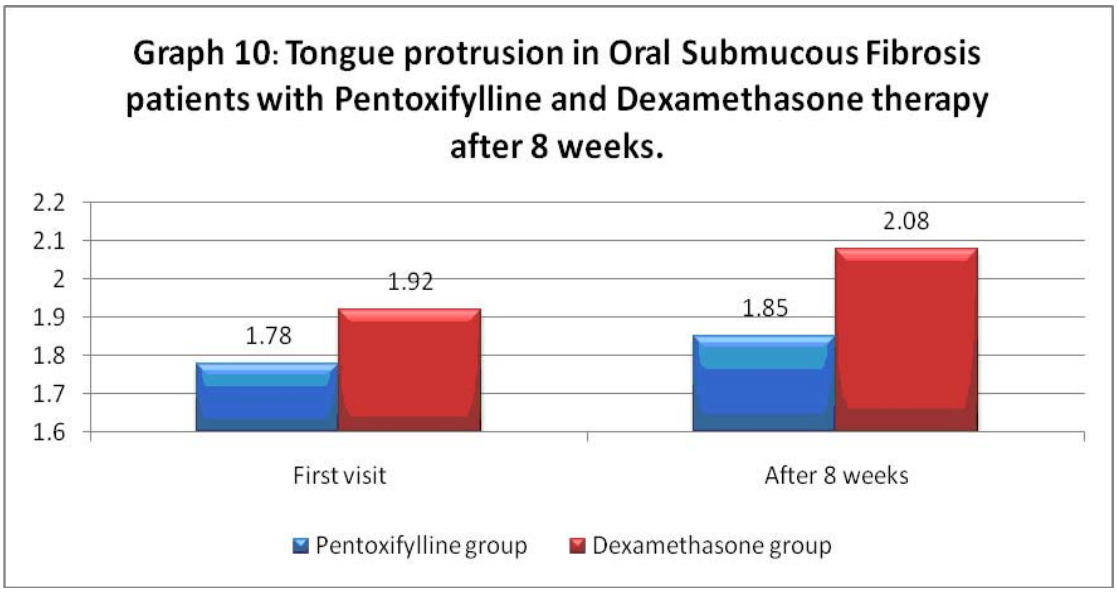


The particulars are given in table no 9 and graph no 9.

Table 9 : Tongue protrusion in Oral Submucous Fibrosis patients with Pentoxifylline and Dexamethasone therapy after 4 weeks.

		Pentoxifylline		Dexamethasone Intralesional injections		p-value
	No. of Patients	Mean	SD	Mean	SD	
First visit	20	1.78	0.66	1.92	0.44	0.418
After 4 weeks	20	1.79	0.61	2.01	0.45	0.213

In the present study, all the patients in both the groups showed improvement in tongue protrusion. The mean improvement in tongue protrusion in the pentoxifylline group at the end of 4 weeks compared to the first visit was 0.01 cm. Two patients showed decrease in tongue protrusion by 0.1 cm and in two patients, maximum increase in tongue protrusion was 0.2 cm. The mean improvement in tongue protrusion in the Dexamethasone group at the end of 4 weeks was 0.09 cm. Twelve patients showed no improvement in tongue protrusion and in one patient, maximum increase in tongue protrusion was 0.4 cm. There was no significant improvement in tongue protrusion at the end of 4 weeks in dexamethasone group compared to pentoxifylline group. (P = 0.213). The particulars are given in table no 9 and graph no 9.

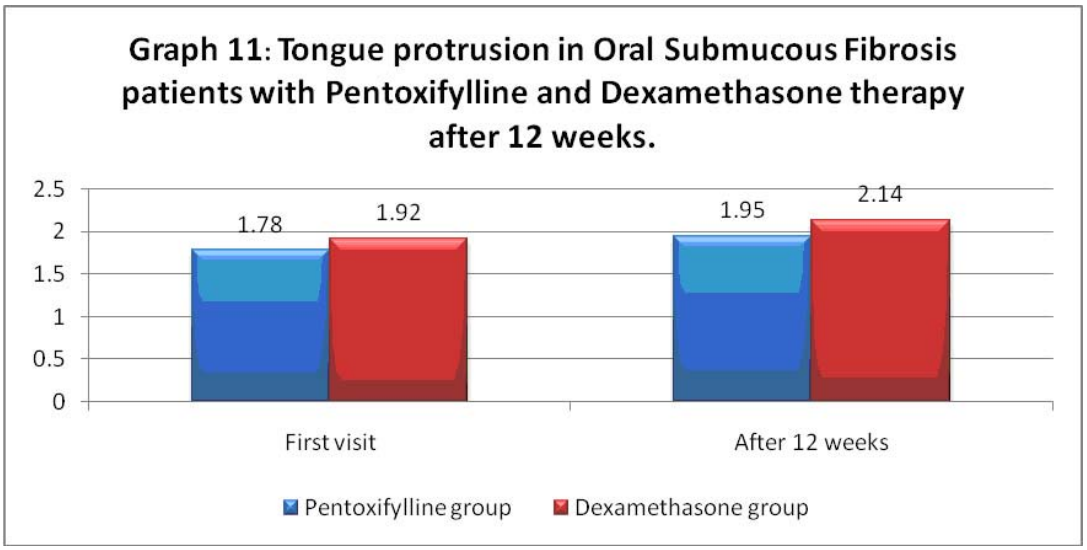


The particulars are given in table no10 and graph 10.

Table 10 : Tongue protrusion in Oral Submucous Fibrosis patients with Pentoxifylline and Dexamethasone therapy after 8 weeks.

		Pentoxifylline		Dexamethasone Intralesional injections		p-value
	No. of Patients	Mean	SD	Mean	SD	
First visit	20	1.78	0.66	1.92	0.44	0.418
After 8 weeks	20	1.85	0.59	2.08	0.43	0.157

The mean improvement in tongue protrusion in the pentoxifylline group at the end of 8 weeks compared to the first visit was 0.07 cm. Two patients showed decrease in tongue protrusion by 0.1 cm and in two patients, maximum increase in tongue protrusion was 0.3 cm. The mean improvement in tongue protrusion in the Dexamethasone group at the end of 8 weeks compared to the first visit was 0.16 cm. One patient showed no improvement in tongue protrusion and in one patient, maximum increase in tongue protrusion was 0.6 cm. There was no significant improvement in tongue protrusion at the end of 8 weeks in dexamethasone group compared to pentoxifylline group (P = 0.157). The particulars are given in table no10 and graph 10.

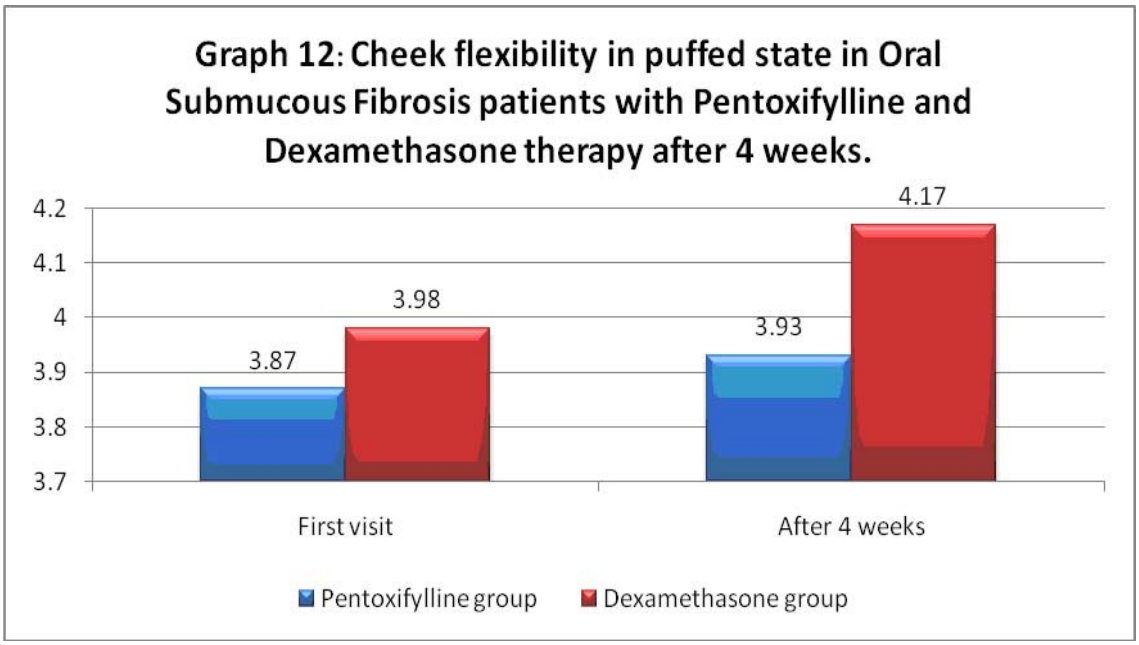


The particulars are given in table no 11 and graph no 11.

Table 11 : Tongue protrusion in Oral Submucous Fibrosis patients with Pentoxifylline and Dexamethasone therapy after 12 weeks.

		Pentoxifylline		Dexamethasone Intralesional injections		p-value
	No. of Patients	Mean	SD	Mean	SD	
First visit	20	1.78	0.66	1.92	0.44	0.418
After 12 weeks	20	1.95	0.61	2.14	0.40	0.24

The mean improvement in tongue protrusion in the pentoxifylline group at the end of 12 weeks compared to the first visit was 0.17 cm. One patient showed decrease in tongue protrusion by 0.1 cm and in one patient, maximum increase in tongue protrusion was 0.7 cm. The mean improvement in tongue protrusion in the Dexamethasone group at the end of 12 weeks compared to the first visit was 0.23 cm. Four patients showed no improvement in tongue protrusion and in one patient, maximum increase in tongue protrusion was 0.7 cm. There was no significant improvement in tongue protrusion at the end of 12 weeks in dexamethasone group compared to pentoxifylline group. (P = 0.24). The particulars are given in table no 11 and graph no 11.



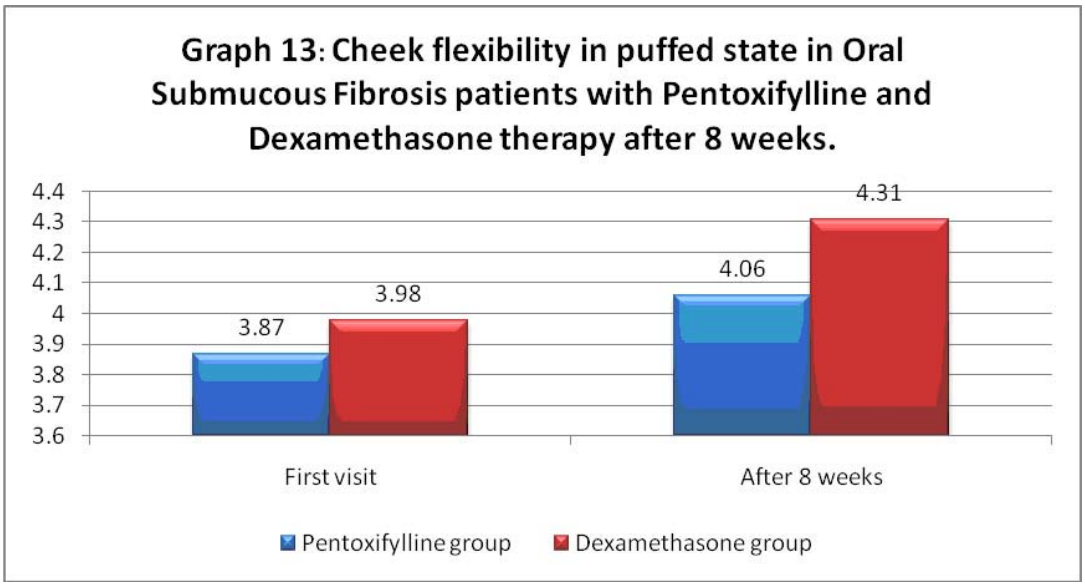
The particulars are given in table no 12 and graph no 12.

Table 12 : Cheek flexibility in puffed state in Oral Submucous Fibrosis patients with Pentoxifylline and Dexamethasone therapy after 4 weeks.

		Pentoxifylline		Dexamethasone Intralesional injections		p-value
	No. of Patients	Mean	SD	Mean	SD	
First visit	20	3.87	0.30	3.98	0.31	0.129
After 4 weeks	20	3.93	0.29	4.17	0.31	0.001

In the present study, none of the patients showed improvement in cheek flexibility in unpuffed state in both the groups.

Whereas, all the patients are in both the groups showed improvement in cheek flexibility on puffing. The mean improvement in cheek flexibility in the Pentoxifylline group at the end of 4 weeks compared to the first visit was 0.06 cm. The mean improvement in cheek flexibility in the Dexamethasone group at the end of 4 weeks was 0.19 cm. There was significant improvement in cheek flexibility at the end of 4 weeks in Dexamethasone group compared to Pentoxifylline group. (P = 0.001). The particulars are given in table no 12 and graph no 12.

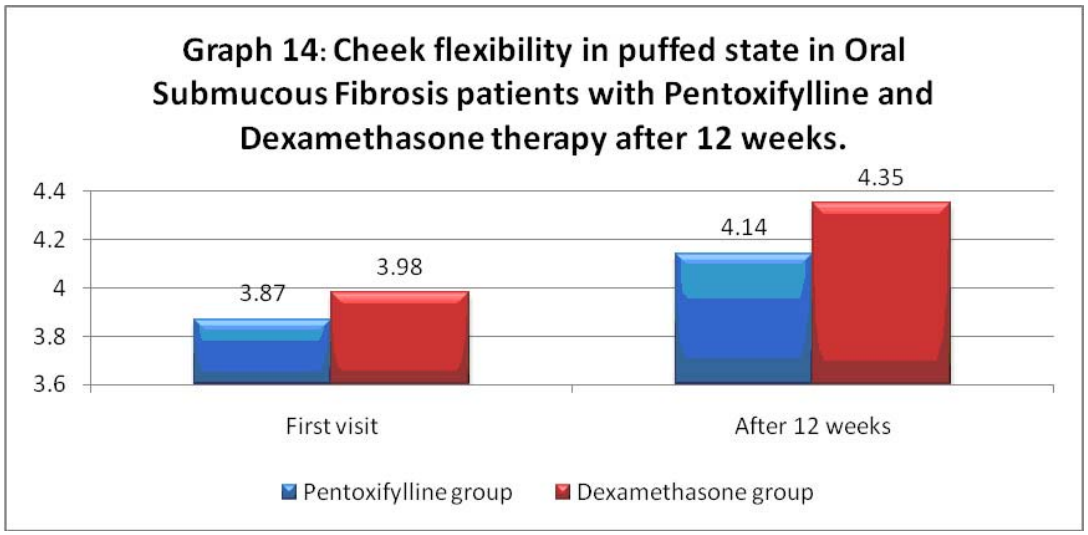


The particulars are given in table no13 and graph 13.

Table 13 : Cheek flexibility in puffed state in Oral Submucous Fibrosis patients with Pentoxifylline and Dexamethasone therapy after 8 weeks.

		Pentoxifylline		Dexamethasone Intralesional injections		p-value
	No. of Patients	Mean	SD	Mean	SD	
First visit	20	3.87	0.30	3.98	0.31	0.129
After 8 weeks	20	4.06	0.32	4.31	0.31	0.001

The mean improvement in cheek flexibility in the Pentoxifylline group at the end of 8 weeks compared to the first visit was 0.13 cm. The mean improvement in cheek flexibility in the Dexamethasone group at the end of 8 weeks compared to the first visit was 0.33 cm. There was significant improvement in tongue protrusion at the end of 8 weeks in Dexamethasone group compared to Pentoxifylline group. (P = 0.001). The particulars are given in table no13 and graph 13.



The particulars are given in table no14 and graph no 14.

Table 14 : Cheek flexibility in puffed state in Oral Submucous Fibrosis patients with Pentoxifylline and Dexamethasone therapy after 12 weeks.

		Pentoxifylline		Dexamethasone Intralesional injections		p-value
	No. of Patients	Mean	SD	Mean	SD	
First visit	20	3.87	0.30	3.98	0.31	0.129
After 12 weeks	20	4.14	0.31	4.35	0.30	0.003

The mean improvement in cheek flexibility in the Pentoxifylline group at the end of 12 weeks compared to the first visit was 0.27 cm. The mean improvement in cheek flexibility in the Dexamethasone group at the end of 12 weeks compared to the first visit was 0.37 cm. There was significant improvement in cheek flexibility at the end of 12 weeks in Dexamethasone group compared to Pentoxifylline group. (P = 0.003). The particulars are given in table no14 and graph no 14.

IV. Discussion

OSF has affected millions of individuals and is likely to reach an alarming proportion in the near future. The onset of oral sub mucous fibrosis is insidious over a period of two to five years. The patients initially complain of burning sensation in the oral cavity while consuming spicy food.

As the disease progresses the oral mucosa becomes blanched, slightly opaque and fibrous bands appear leading to difficulty in opening the mouth, inability to whistle and difficulty in swallowing.

There is constant contact between the areca nut mixture and oral mucosa, in persons with the habit of chewing areca nut. The alkaloids and flavinoids released from the areca nut get absorbed into the oral mucosa and undergo metabolism. In addition to chemical irritation from areca nut, their metabolites facilities diffusion of alkaloids and flavinoids into the sub epithelial connective tissue resulting in the juxtaepithelial inflammatory cell infiltration.[17,18]

V. Conclusion

In the present study, the increase in mouth opening, decrease in burning sensation and improvement in cheek flexibility in puffed state in oral submucous fibrosis patients showed better results by treatment with dexamethasone than pentoxifylline. Also Pentoxifylline and dexamethasone individually showed significant increase in mouth opening, decrease in burning sensation and improvement in cheek flexibility in puffed state in oral submucous fibrosis patients.

When the improvement in tongue protrusion was compared between pentoxifylline group and dexamethasone group, though dexamethasone group showed more improvement in tongue protrusion compared to pentoxifylline group, the improvement was not statistically significant. Even Pentoxifylline and dexamethasone individually did not show any significant improvement in tongue protrusion.

Nevertheless pentoxifylline did show statistically significant improvement in mouth opening, decrease in burning sensation and improvement in cheek flexibility in puffed state in oral submucous fibrosis patients. For this reason, it is concluded that Pentoxifylline is a good alternative treatment for oral submucous fibrosis in patients in whom dexamethasone is contraindicated, or those who cannot make frequent visits for intralesional injections due to disability, far reaching places or any other reason. In such oral submucous fibrosis patients it is better to substitute pentoxifylline therapy rather than not to treat at all.

Pentoxifylline can be safer and better alternative treatment for oral submucous fibrosis than dexamethasone provided local drug delivery systems are invented. Larger sample size and longer treatment duration is necessary in this regard.

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