

Drug Pentoxifylline in Management of Oral Submucous Fibrosis

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ABSTRACT

Aim: To evaluate the efficacy of pentoxifylline in the management of oral submucous fibrosis.

Material and method: This randomized clinical trial was conducted in the Department of Oral Medicine and Radiology, Darshan Dental College, Udaipur from January 2018 to March 2019 consisted of clinical case series of 40 patients distributed equally among study and control group. Pain and burning sensation were recorded using Visual Analogue Scale (VAS) which consists of a straight line with the end points defining extreme limits such as 'no pain at all' and 'pain as bad as it could be.' 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 using Vernier Calliper. 3 measurements were recorded consecutively and the average value was calculated and recorded in mm. The patients in either group were followed up after 1st month, 2nd month and 3rd month from commencement of the treatment of the respective therapies.

Results: The difference among 1 month, 2 month, 3 month post-treatment pain assessment and mouth opening score among the study group and the control group is found to be statistically significant

Conclusion: Pentoxifylline can be safer and better alternative treatment for oral submucous fibrosis. Larger sample size and longer treatment duration is necessary in this regard to validate results of the current study.

Keywords: Pentoxifylline, VAS, Oral Submucous Fibrosis

INTRODUCTION

Oral submucous fibrosis (OSMF) is defined as the chronic, insidious disease affecting the oral cavity and sometimes pharynx, although occasionally preceded and/or associated with vesicle formation and is always associated with juxtaepithelial inflammatory reaction followed by fibro elastic changes in the lamina propria with epithelial atrophy leading to stiffness of oral cavity leading to trismus and inability to eat¹.

The condition is remotely linked to oral cancers and is associated with areca nut and betel quid chewing, habit similar to tobacco chewing². Pentoxifylline is a tri-substituted methylxanthine derivative. Pentoxifylline a valuable drug for reducing burn scar contractures & immunomodulatory actions of pentoxifylline have definite therapeutic advantages in alleviating the symptoms in patients with OSMF, in addition to its role in improving the vascularity^{3,4}. The present study was conducted to evaluate the efficacy of pentoxifylline in the management of oral submucous fibrosis.

Material and method: This randomized clinical trial was conducted in the Department of Oral Medicine and Radiology, Darshan Dental College; Udaipur from January 2018 to March 2019 consisted of clinical case series of 40 patients of both sexes and all age groups with Oral Submucous Fibrosis. 20 patients were included in the study group and 20

patients, age and sex matched were included in the control group after approval from Institutional Ethical Committee. A Proforma was used to record the related information (patient data, clinical findings) from the individual cases for the study. The subjects were selected according to the following inclusion and exclusion criteria:

Study Group: This group comprised of 20 patients with OSMF who received Pentoxifylline extended release tablets containing pentoxifylline 400 mg given twice daily after food for a period of 3 months. The patients were asked to report for follow-ups every 30 days till end of 3 months.

Control Group: This group comprised of 20 patients with OSMF who received multivitamin capsule containing calcium pantothenate 50 mg, vitamin B12 15 mcg, folic acid 1.5 mg, thiamine mononitrate 10 mg, riboflavin 10 mg, pyridoxine hydrochloride 3 mg, niacinamide 100 mg, ascorbic acid 150 mg, biotin 100 mcg given twice daily after food for a period of 3 months. The patients were asked to report for follow-ups every 30 days till end of 3 months.

Inclusion Criteria:

1. Patients of either sex diagnosed clinically and histopathologically as oral submucous fibrosis.
2. Patients above 18 years of age.
3. Patients who had not undergone any treatment for oral submucous fibrosis for past three months.
4. Patients who were willing to quit arecanut, gutkha or pan masala habit.
5. Patients who were willing to come for regular follow ups for 6 months duration.

Exclusion Criteria:

1. OSMF patients with co-existing systemic illnesses or any debilitating diseases.
2. Patients with severe cardiac disease, gastrointestinal disease or metabolic disorders.
3. Pregnancy and lactating mothers

4. Patients who were already diagnosed as cancer patients.
5. Metastatic lesions to the jaw.
6. Patients who were already taking treatment for OSMF or had taken treatment within last 6 months
7. History of hypersensitivity or intolerance to Pentoxifylline.

Procedure: The patient was relaxed, topical local anaesthetic was sprayed onto the site of injection. 2% lignocaine hydrochloride with 1:80,000 adrenaline was used for local anaesthesia. The incisional biopsy was then carried out and the tissue specimen was immediately placed into 10% formalin until it was processed. The site of biopsy was cleaned using saline and interrupted sutures were placed. Later patient was given post-operative instructions with medications. Patient was recalled after 7 days for suture removal. The biopsy specimen was then sent for histopathological examination to the Department of Oral Pathology and Microbiology.

Pain and burning sensation were recorded using Visual Analogue Scale (VAS) which consists of a straight line with the end points defining extreme limits such as 'no pain at all' and 'pain as bad as it could be'. We used Visual Analogue Scale score ranging from 0 to 10 for pre-treatment pain assessment for the subjects in the study group and control group.

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 using Vernier Calliper. 3 measurements were recorded consecutively and the average value was calculated and recorded in mm.

Follow up: The patients in either group were followed up for severity of the clinical sign & symptoms, mouth opening and VAS score was recorded after 1st month, 2nd month and 3rd month from commencement of the treatment of the respective therapies.

Statistical analysis: The data was collected, tabulated and analysed using SPSS software version 24.

RESULTS

In the study group, there were 17 (85%) males and 3 (15%) females and in the control group 16 (80%) males and 4 (20%) females. The mean age of the subjects in the study and control group was 34.3 ± 7.2 and 31.9 ± 6.8 years respectively.

The difference among 1 month, 2 month, 3 month post-treatment pain assessment score among the study group and the control group is found to be statistically significant as shown in the table 1.

The difference among 1 month, 2 month, 3 month post-treatment mouth opening assessment score among the study group and the control group is found to be statistically significant as shown in the table 2.

Table 1: Comparison of VAS Score among Study and Control Groups

Duration	Mean \pm SD		P value
	Study	Control	
Pre-treatment	4.1 \pm 1.34	4.3 \pm 1.53	0.128
1 month post-treatment	3.4 \pm 1.19	3.9 \pm 1.53	0.032
2 months post treatment	3.1 \pm 1.37	4.1 \pm 1.71	0.013
3 months post treatment	2.3 \pm 1.31	3.9 \pm 1.95	0.008

Table 2: Comparison of mouth opening among Study and Control Groups

Duration	Mean \pm SD		P value
	Study	Control	
Pre-treatment	26.32 \pm 4.34	25.57 \pm 3.97	0.152
1 month post-treatment	27.17 \pm 4.32	26.11 \pm 3.78	0.029
2 months post treatment	28.44 \pm 3.81	26.32 \pm 4.15	0.016
3 months post treatment	30.48 \pm 4.28	26.17 \pm 3.61	0.009

DISCUSSION

OSMF has been affecting millions of individuals and is likely to reach an alarming proportion in the near future. 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 mouth, inability to whistle and difficulty in swallowing. Various studies have shown that the malignant transformation rate of OSMF was

found to be in the range of 7-13%. If untreated, the risk of malignant transformation in advanced cases of OSMF is relatively high. It is thus, imperative to treat this condition promptly and aggressively. Pentoxifylline is a methylated xanthine derivative, which causes competitive nonselective phosphodiesterase inhibition which raises intracellular cyclic adenosine monophosphate, inhibits TNF-alpha leukotriene synthesis, reduces inflammation, innate immunity improves red blood cell flexibility, reduces blood viscosity, decreases the potential for platelet aggregation and thrombus formation. It was on this basis that pentoxifylline was administered in OSMF as this is also a disease of the oral cavity characterized by inflammation and progressive fibrosis of the submucosal tissues.

The mean VAS Score for burning sensation and pain at initial visit in the study group was 4.1, during treatment was 3.4, 3.1 and 2.3 after 1, 2 and 3 months respectively. There was significant decrease in burning sensation in subsequent visits in study group patients as compared to the first visit ($p < 0.001$). The above results were in accordance with previous studies done by Gupta M et al (2014)⁵, Kalkur C et al (2016)⁶, Liu J et al (2017)⁷. In control group patients the mean VAS Score for burning sensation and pain at initial visit were 4.3 with standard deviation of 1.53, during treatment was 3.9, 4.1 and 3.9 after 1, 2 and 3 months respectively. There was non-significant decrease in burning sensation with drug Pentoxifylline at 1, 2 and 3 months when compared with the first visit ($p > 0.05$). The results were in accordance with previous study done by Chole RH et al (2016)⁸.

The mean mouth opening reported at the initial visit in study group was 26.32 mm, after 1, 2 and 3 months of the treatment were 27.17 mm, 28.44 mm and 30.48 mm respectively. There was significant increase in mouth opening in study group after 1, 2 and 3 months when compared with the first visit ($p < 0.001$). The results were in

accordance with previous study done by Gupta M et al (2014)⁵, Liu J et al (2017)⁷, Zwiri AM et al (2015)⁹. In the control group patients where multivitamin capsules were given as placebo the mean mouth opening at initial visit was 25.57 mm, during treatment was 26.11 mm, 26.32 mm and 26.17 mm after 1, 2 and 3 months respectively. There was non-significant increase in mouth opening after 3 months when compared with the first visit ($p > 0.05$). The results of our study are at par with studies conducted by Zwiri AM et al (2015)⁹, Deshpande A et al (2015)¹⁰.

CONCLUSION

In the present study Pentoxifylline showed significant increase in mouth opening, decrease in burning sensation and pain in oral submucous fibrosis patients as compared to multivitamin capsules. Occasional gastrointestinal disturbances during pentoxifylline administration can however have poor patient compliance. Pentoxifylline can be safer and better alternative treatment for oral submucous fibrosis. Larger sample size and longer treatment duration is necessary in this regard to validate results of the current study.

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