



Efficacy of oral pentoxifylline in conjunction with physiotherapy exercises for the management of Oral submucous fibrosis: A clinical trial

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Abstract

Background: Oral submucous fibrosis (OSMF) is a chronic disease of the oral cavity including pharynx which is most encountered in patients chewing areca nut in the Indian subcontinent. It is characterized by the formation of constricting bands of collagen in the oral cavity which can severely restrict mouth opening, and tongue movement can lead to difficulty in swallowing and chewing for the patients. There are various treatment modalities for the management of OSMF where in recent research has shown strong promising effects of pentoxifylline for treating OSMF. **Method:** A study of 132 clinically and histopathologically diagnosed patients with OSMF was done. They were prescribed oral pentoxifylline 400mg twice a day for a period of 4 weeks and 400mg thrice a day for another 4 weeks. Along with medicinal therapy patients were strictly advised to do physiotherapy exercises like warm water gargles twice a day, ballooning exercises, ice cream stick exercises. **Results:** Statistical analysis was done and it was found that burning sensation was reduced by 75.8%, tongue protrusion was increased by 50%, fibrosis was reduced by 55%. The total reduction in signs and symptoms score was 56.6%. **Conclusion:** In present study we found that the relapses were less as physiotherapy exercises were advised along with pentoxifylline drug. Pentoxifylline is good substitute to injectable management of OSMF as patient compliance is more as compared to injectable, also the drug is easily available and very cheap as compared to other treatment modalities.

Keywords: OSMF, Pentoxifylline, Physiotherapy Exercises.

Introduction

Oral submucous fibrosis (OSMF) is an insidious chronic and a well-known Oral potentially malignant disorder of oral cavity associated with areca-nut chewing habit which is characterized by generalized blanching and fibrosis of oral soft tissue mucosa resulting in marked rigidity and progressive reduced mouth opening¹⁻³. OSMF is mainly associated to South East Asian countries particularly in the Indian subcontinent. Pathogenesis is not yet clearly known but multifactorial causes are considered to be as an etiology. This premalignant condition initially presents as a burning sensation in the oral cavity⁴.

Treatment modalities includes multivitamins including antioxidant lycopene - an extract of tomato, and a range of various medications (intralesional injection of steroids, hyaluronidase, human placenta extracts, chemotrypsin, Oral Pentoxifylline and collagenase)⁵⁻⁶. Laser and surgery, including excision of the fibrous bands of the muscles of mastication has been indicated for severe OSMF cases. Pentoxifylline is a dimethyl xanthine derivative. It's a vasodilator with fibrinolytic properties used for the management of burns. It is having fibrinolytic properties. Various studies have been conducted by using pentoxifylline for the management of OSMF.

Materials and Methods

The study was conducted after the approval from the institutional ethical committee (SDK/IEC/2014/4658). The procedure of the study was explained to the patients and after making them understand the procedure a written consent of all the patients who have participated in the study were taken. 30 calculate subjects clinically and histopathologically diagnosed with oral submucous fibrosis were selected from Outpatient Department of Oral Medicine and Radiology

Inclusion criteria

Patients with Difficulty in swallowing and chewing, and burning sensation on eating spicy foods.

Restricted mouth opening and presence of palpable vertical fibrous bands, stiffness, and blanching.

Exclusion Criteria

Patients having Systemic illness, undergone surgery or under any drug therapy.

Patient previously undergone treatment for oral submucous fibrosis.

Patients with Trismus due to any other cause.

Methodology

Informed consent and case history was obtained from the patients. The symptoms and signs were noted on a working proforma. Interincisal distance was measured from mesioincisal edge of the upper left central incisor to the mesioincisal edge of the lower left central incisor with the help of Vernier Callipers.

After clinical and histopathologically examination patients, were given oral pentoxifylline 400mg twice a day for period of 4 weeks and then 400mg thrice a day for another 4 weeks.

Patients were advised and motivated for strict stoppage of the habit. Counseling was done for every patient and physiotherapy mouth exercises were advised along with medicinal treatment follow up were taken every 15 days. After the 8 weeks. Results were carried out as subjective improvement in symptoms By VAS scale 1) Burning sensation in mouth; 2)

Repeated vesiculation/ ulceration in oral mucosa; 3) Resumption of normal food consumption, mastication, and speech.

Results

The results were calculated as a cumulative of score for signs and symptoms before and after the management with pentoxifylline drug in conjunction with physiotherapy exercises based on visual analogue pain scale for 30 patients. The results are shown in chart.

Sr. No	Signs/Symptoms	Pre-treatment score (VAS)	Post-Treatment score (VAS)
1	Burning Sensation	330	80
3	Mouth opening	300	110
5	Tongue protrusion	200	100
6	Ulcers	36	20

The results were calculated by percentile analysis. The post treatment statistically significant results were found. The burning sensation was reduced by 75.8%, vesicle formation was reduced by 14.3%, tongue protrusion was reduced by 50%, ulcers were reduced by 44.4%, fibrosis was reduced by 55%. The total reduction in signs and symptoms score was 56.6%.

Discussion

The management of OSMF remains a challenge. It is said that once the disease has developed, there is neither reversal of the disease nor any effective treatment. Consequently, improvement in mouth opening and symptomatic relief form the main objectives of various form of treatment modalities.

In present study oral pentoxifylline was given for the period of 8 weeks along with physiotherapy mouth exercises. at the end of treatment significant reduction in symptoms and signs was noticed. Because of the physiotherapy exercises relapses found to be less. Basically, the management for OSMF is categorized as conservative and surgical. In conservative management of OSMF recent advances showed that use of combination of triamcinolone acetonide (10 mg/ ml)/ hyaluronidase (1500 IU) at 15 days interval for 22 weeks. The compliance found be more in patients because it required only weekly injections, less daily dosing, better patients' compliance, and improvement in the sign score (trismus, ankyloglossia, vesicle formation and fibrosis). Pathologically, occlusive blood vessels because of the deposition of collagen fibres and hypercoagulability of blood restrict nutrients and therapeutic substances from reaching the affected tissue in OSMF patients, which may be one of the reasons for the unsatisfactory therapeutic effect of drug treatment of OSMF⁸.

Pentoxifylline is a tri-substituted methylxanthine derivative, the biologic activities of which are in abundance. It is popularly term as a "Rheologic modifier." It improves microcirculation as well decreases platelet aggregation and granulocyte adhesion. The pentoxifylline also has antithrombin, antiplasmin activities and fibrinolytic activity. It causes degranulation of neutrophils, enhances natural killer cell activity and inhibits T-cell and B-cell activation. It is used for the management of medical disorders like stroke, aphthous stomatitis, cerebrovascular insufficiency, peripheral arterial occlusion and pretibial myxedema , So after the study of functions of pentoxifylline, it has been used

to alleviate the symptoms in patients suffering with OSMF, as it has role in improving the vascularity of the tissue⁹. Most common side effects caused by Pentoxifylline involves the gastrointestinal tract and central nervous system. The frequently found gastrointestinal complaints include dyspepsia, nausea and /or vomiting, bloating, flatus, and bleeding. The central nervous system side effects include dizziness and headache in a small percentage of patients, whereas tremor, anxiety, and confusion occur in others. Both the central nervous system as well as gastro-intestinal side effects are related to the dose of the drug and are therefore managed by dose reduction^{10,11}

Rajendren et al (2006) used Pentoxifylline as an adjunct in OSMF treatment and after 7 months trial and 6-12 months follow-up, the patients showed improvement in signs and symptoms as compared to controls¹². Ravi Mehrotra et al (2011) used 400mg pentoxifylline for a period of 7 months. They found significant improvement in symptoms and sign.

Conclusion

The management of Oral Submucous Fibrosis is a daunting task as there is no 100% disease cure and symptomatic relief is the main concern while managing patients with OSMF. The relapses are found to be more in OSMF patients. After all these considerations, physiotherapy exercises were advised to the patients along with pentoxifylline drug. In our study we found that relapses were less as compared to treatment of OSMF with only Pentoxifylline drug.

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