

The Efficacy Of Medical Management In Oral Submucous Fibrosis

Research Article

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Abstract

Aim: The Aim of the study is to analyse whether medical treatment has a potential role in the treatment of Oral Submucous Fibrosis.

Materials And Methods: This is a Retrospective study where 86000 patients records were analysed and after fulfilling all inclusion and exclusion criteria, a total of 103 patients with age ranging from 21 years to 70 years suffering from Oral Submucous Fibrosis reported to Saveetha Dental College were enrolled in this study. Subjective and objective observations were recorded that includes age, gender, mouth opening before treatment, mouth opening after treatment. They were treated by administering intralesional injection of Dexamethasone 8 mg, Dexamethasone 8 mg and Hyaluronidase 1500 IU injection intralesionally biweekly for two weeks. All the datas were tabulated and statistics done using SPSS software.

Results: Patients were periodically reviewed for 6 weeks and we noticed that there is improvement in the patient's mouth opening in the follow-up period over 6 weeks for both corticosteroid injections alone and also in treatment with corticosteroid and hyaluronidase injections. The increase in mouth opening is by 2-3 mm in both the groups which are considered statistically significant using paired 't' test and independent 't' test.

Conclusion: Within the limitations of the study there is significant effect in the management of Oral Submucous Fibrosis with medications itself. Oral submucous fibrosis is one of important premalignant condition which if untreated may lead oral cancer. So this study helps in identifying the role of medical treatments used for treating oral submucous fibrosis. Both corticosteroid injection and Injection of hyaluronidase with dexamethasone are an effective method of managing Oral Submucous Fibrosis and can possibly eliminate the morbidity associated with Surgical Management. So this test can pave for further studies which if proven, then medical management can be performed as gold standard of treatment for initial stages of oral sub mucous fibrosis.

Keywords: Dexamethasone; Hyaluronidase; Mouth Opening; Oral Submucous Fibrosis.

Introduction

The Oral Submucous Fibrosis is a chronic fibrotic disease that involves the oral mucosa and occasionally it even affects the upper third of the oesophagus. OSMF is characterized by a juxta epithelial inflammatory reaction followed by fibroelastic changes in the submucosa and epithelial atrophy that leads to stiffness of the

oral mucosa causing trismus and inability to eat [1]. The etiological factors are excessive consumption of spicy foods nutritional deficiencies like chronic iron and Vitamin B complex deficiency, areca nut chewing habits [2].

The main agent involved in the pathogenesis of OSMF is arecanut. Arecanut is made up of alkaloid and flavonoid components.

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Received: January 12, 2021

Accepted: January 22, 2021

Published: January 30, 2021

Citation: Yandeti Srinivasulu, Abdul Wahab, Senthil Murugan. P. The Efficacy Of Medical Management In Oral Submucous Fibrosis. *Int J Dentistry Oral Sci.* 2021;08(01):1523-1529. doi: <http://dx.doi.org/10.19070/2377-8075-21000303>

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Arecoline is the most potent agent and plays a major role in pathogenesis of OSMF. The signs and symptoms are burning sensation in mouth exacerbated by spicy or acidic foods, pain often referred to temporal region, increased or decreased salivation, reduced mouth opening, difficulty in the mastication, difficulty in phonation, and deglutition, and ulceration of oral mucosa [3]. Dentistry comprises of practices related to oral cavity. Dental diseases pose a major problem among general population and there are various procedures carried out to prevent and treat them [4]. The goal of the scientific research is to find the new biological markers which should be able to define the “tumor biological fingerprint” and to identify the molecular key players that are involved in oropharyngeal carcinogenesis [5]. Oral submucous fibrosis is an insidious, chronic, disabling disease that affects the entire oral cavity, sometimes pharynx and rarely larynx [6]. The Aim of the study is to analyse whether medical treatment has a potential role in the treatment of Oral Submucous Fibrosis.

Materials And Methods

This Retrospective study was conducted by collecting records of 86,000 patients from June 2019-April 2020 who had reported to Saveetha Dental College for treatments. Patients reporting to the Department of Oral and Maxillofacial Surgery with the diagnosis of Oral Submucous Fibrosis were shortlisted from the main records based on the inclusion/exclusion criteria. So final sample which contains 103 patients were enrolled for the study. Ethical committee approval was obtained from the Institutional Ethics Committee (IEC). The ethical approval number for the present study is SDC/SIHEC/2020/DIASDATA/0619-0320. The study population included patients who underwent treatment for Oral Submucous Fibrosis at Saveetha Dental College by means of Systematic Sampling.

Patients pre op mouth opening is measured in mm.

Group 1 -Patients treated with corticosteroid injection.[8mg Dexamethasone intralesionally].

Group 2 -Patients treated with corticosteroids [8mg Dexamethasone] and 1500IU hyaluronidase injections intralesionally. Inclusion Criteria- Patients of all age groups and gender with diagnosis of Oral Submucous Fibrosis were included. Exclusion Criteria- Patients with other problems like fractures, pathologies, and common dental problems were excluded from the study.

The patients were called for review every 2 weeks and mouth opening is measured in mm and final mouth opening in 6 weeks review were considered for this study.

Duplicate patient records and incomplete data were excluded. Data were reviewed by an external reviewer. Totally, n= 103 patients were included. Demographic data such as the patient's age, gender and their Habits and Systemic Diseases were also recorded. The patients were divided into two groups according to intervention performed. The data obtained were tabulated in Microsoft Excel 2016 (Microsoft office 10) and later exported to SPSS (Statistical Package for Social Sciences) for Windows version 20.0, SPSS Inc, Chicago IU, USA) and subjected to statistical analysis of paired t tests were employed to arrive at a significance level.

Results

There is improvement in the patient's mouth opening with net gain of 2 ±4 millimetres seen. Patients frequency distribution is given in table 1. Patients distribution among Gender and mean values of two groups with std.deviation are plotted in Tables & figures 1,2 and figure 3, 3.1..OSMF is predominant in male and at the age of 60 years of life. It was observed that corticosteroid 8mg was given and observed for any improvement in mouth opening. We observed that there is a small increase in mouth opening of 1 ± 2 millimetres seen. statistical analysis was done. since the two types of management has two independent samples, we have to do independent “t “ test [table & figure 4] for assessing the significance post op mouth opening of two type of treatments. Statistical analysis done using Paired ‘t ‘ test used for statistical

Table 1. Showing frequency of two groups of interventions used for the medical management of oral submucous fibrosis. Patients were divided into two groups based on the intervention or treatment they underwent. 89 patients were treated with corticosteroid injection which accounts for 86.4% of total ,whereas group 2 : 14 patients were treated with Corticosteroid and 1500 IU hyaluronidase injections which accounts for only 13.6%. The patients were mostly treated by corticosteroid injection.

| Groups vs intervention percentage | | | | |
|-----------------------------------|--|-----------|---------|---------------|
| | | Frequency | Percent | Valid Percent |
| | Corticosteroids injection | 89 | 86.4 | 86.4 |
| | Corticosteroid + 1500IU Hyaluronidase injections | 14 | 13.6 | 13.6 |
| | Total | 103 | 100.0 | 100.0 |

Table 2. Frequency distribution of gender in patients with oral sub mucous fibrosis. Incidence of males (87.4%) were more compared to females (12.6%), which indicates male predilection for oral sub mucous fibrosis.

| | | Frequency | Percent | Valid Percent | Cumulative Percent |
|--|--------|-----------|---------|---------------|--------------------|
| | Male | 90 | 87.4 | 87.4 | 87.4 |
| | Female | 13 | 12.6 | 12.6 | 100.0 |
| | Total | 103 | 100.0 | 100.0 | |

Figure 1. Pie diagram showing frequency of two groups of interventions used for the medical management of oral sub-mucous fibrosis. Patients were divided into two groups based on the intervention or treatment they underwent. 89 patients were treated with corticosteroid injection which accounts for 86.4% of total ,whereas group 2 : 14 patients were treated with Corticosteroid and 1500 IU hyaluronidase injections which accounts for only 13.6%. The patients were mostly treated by corticosteroid injection.

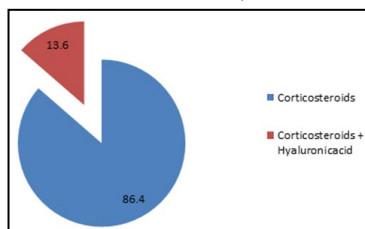


Figure 2. Frequency distribution of gender in patients with oral sub mucous fibrosis. Incidence of males (87.4%) were more compared to females (12.6%), which indicates male predilection for oral sub mucous fibrosis.

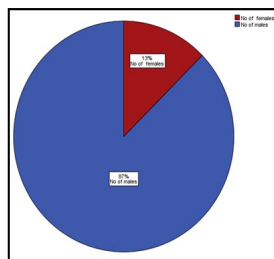


Figure 3. showing association between gender and two medical interventions. 89 oral submucous fibrosis patients treated with Corticosteroid injections and 14 patients treated with Corticosteroids and 1500 IU hyaluronidase injections. Majority of the males with oral submucous fibrosis were treated with corticosteroids (80) and corticosteroids with hyaluronidase (10).

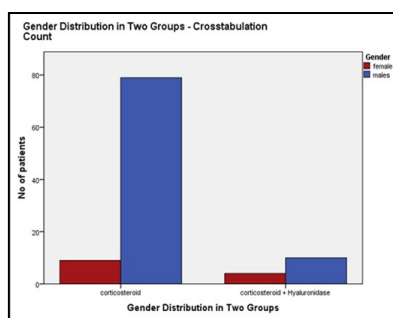
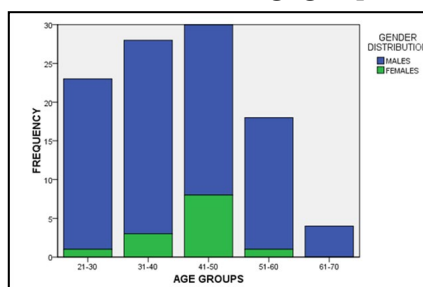


Figure 4. Bar diagram explaining the association of gender with age group patients with OSMF. Where X-axis represents OSMF patients Gender with age group and Y axis represents frequency. Blue bar indicates males and green bar indicates females. From the graph it is evident that males are more affected in all age groups compared to females. While looking among females themselves, females in the age group of 41-50 were affected more.



analysis of individual groups and its significance level is $p = 0.000$ which is statistically significant [$p < 0.005$] (table & figure 5). It was observed that corticosteroid 8mg + hyaluronidase 1500 IU was given and observed for mouth opening there is an increase in the mouth opening of 2 ± 4 millimetres was observed which is also statistically significant p value 0.001 [$p < 0.001$] (table & figure 6).

Discussions

OSMF is a precancerous condition for which many authors have

clinical trials but as such no definitive treatment is currently available. It was observed that patients receiving hyaluronidase alone show a quicker improvement in reduction of burning sensation and healing of painful ulceration produced by the effects of local by-products, so combination of dexamethasone and hyaluronidase give better long term results compared to other regimens [7]. Bacterial endocarditis or infective endocarditis is a serious infection of the heart valves and endocardium that most often is related to congenital and acquired cardiac conditions. Bacterial endocarditis can commonly occur in patients with artificial heart

Table 3. Representing Groups comparison of independent samples-independent 't' test: This table depicts the comparison of pre op and post op mouth opening in oral submucous fibrosis patients treated with corticosteroid injections alone and corticosteroids and 1500IU hyaluronidase injections using Independent 't' test. The mean value of postoperative mouth opening in corticosteroids is 29.11 and corresponding mean for post operative mouth opening in corticosteroid + 1500 IU Hyaluronidase is 30.89. There is a significant improvement in the postoperative mouth opening in oral submucous fibrosis patients who are treated with corticosteroid + 1500 IU Hyaluronidase injection with p value = 0.216 [p > 0.05 statistically not significant] so from the table we observed that there is no statistically significant finding between two type of management of OSMF.

| | GROUPS | N | MEAN | Std. Deviation | Std. Error mean |
|---------------|-----------------------------------|----|--------|----------------|-----------------|
| Preoperative | Corticosteroids | 89 | 26.32 | 5.308 | 5627 |
| | Corticosteroids and Hyaluronidase | 14 | 26.821 | 5.224 | 1.396 |
| Postoperative | Corticosteroids | 88 | 29.11 | 5.993 | 639 |
| | Corticosteroids and Hyaluronidase | 14 | 30.89 | 4.965 | 1.327 |

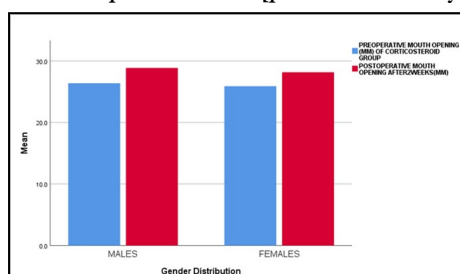
| Hypothesis Test Summary | | | |
|---|---|------|-----------------------------|
| Null Hypothesis | Test | Sig. | Decision |
| 1 The distribution of Preoperative is the same across categories of Group. | Independent Samples Mann-Whitney U Test | .643 | Retain the null hypothesis. |
| 2 The distribution of Postoperative is the same across categories of Group. | Independent Samples Mann-Whitney U Test | .216 | Retain the null hypothesis. |

Asymptotic significances are displayed. The significance level is .05.

Table 4. Depicting the comparison of pre op and post op mouth opening in oral submucous fibrosis patients treated with corticosteroid injections alone using paired t test. The mean value of preoperative mouth opening is 26.371 and corresponding mean for post operative mouth opening is 29.18. There is a significant improvement in the postoperative mouth opening in oral submucous fibrosis patients who are treated with corticosteroid injections alone with p value = 0.000 [p < 0.05 statistically significant].

| Paired Samples Test | | | | | | | | | |
|---------------------|--|--------------------|----------------|-----------------|---|--------|--------|----|-----------------|
| | | Paired Differences | | | | | t | df | Sig. (2-tailed) |
| | | Mean | Std. Deviation | Std. Error Mean | 95% Confidence Interval of the Difference | | | | |
| | | | | | Lower | Upper | | | |
| Pair 1 | PRE & POST OP MOUTH OPENING (MM) AFTER-6 WEEKS | -2.462 | 3.413 | 0.362 | -3.181 | -1.743 | -6.804 | 88 | 0.000 |

Figure 5. Association between preop and post op mouth opening and gender of the patient. Bar diagram depicting the association of gender with treatment effect by comparing pre op and post op mouth opening in oral submucous fibrosis patients treated with corticosteroid injections alone using paired t test. The mean value of preoperative mouth opening is 26.371 and corresponding mean for post operative mouth opening is 29.18. Blue bar represents pre op mouth opening in mm and Red bar indicates post op mouth opening. There is a significant improvement in the postoperative mouth opening in oral submucous fibrosis patients who are treated with corticosteroid injections alone with p value = 0.000 [p < 0.05 statistically significant].



valves [8]. if any simple ranula diagnosed in oral submucous fibrosis as an associated finding, it can be treated by marsupialization or sclerotherapy or complete excision of the associated salivary gland [9].

Hyaluronidase in Oral Submucous Fibrosis: Hyaluronidase breaks down into hyaluronic acid, the ground substance in the connective

tive tissue that lowers the viscosity of intercellular cement substance, better results were observed with respect to the trismus and fibrosis.

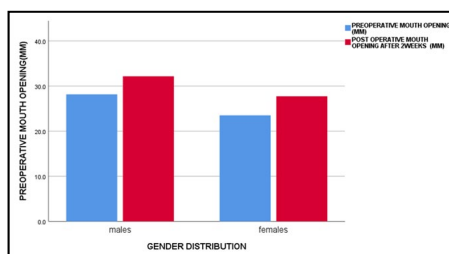
Dexamethasone in Oral Submucous Fibrosis

Dexamethasone acts as an immunosuppressive agent by its an-

Table 5. Depicting the comparison of pre op and post op mouth opening in oral submucous fibrosis patients treated with corticosteroid injections + 1500 IU Hyaluronidase injections using paired t test. The mean value of preoperative mouth opening is 26.821 and corresponding mean for post operative mouth opening is 30.886. There is a significant improvement in the postoperative mouth opening in oral submucous fibrosis patients who are treated with corticosteroid injections + 1500 IU Hyaluronidase injections alone with p value = 0.001[p<0.05 statistically significant].

| Paired Samples Test | | | | | | | | | |
|---------------------|---|--------------------|----------------|-----------------|---|--------|--------|----|-----------------|
| | | Paired Differences | | | | | t | df | Sig. (2-tailed) |
| | | Mean | Std. Deviation | Std. Error Mean | 95% Confidence Interval of the Difference | | | | |
| | | | | | Lower | Upper | | | |
| Pair 1 | PRE & POST OP MOUTH OPENING(MM) AFTER 6 WEEKS | -4.064 | 1.623 | 0.434 | -5.002 | -3.127 | -9.369 | 13 | 0 |

Figure 6. Graph depicting association of gender and drug effect by comparing pre op and post op mouth opening in oral submucous fibrosis patients treated with corticosteroid injections + 1500 IU Hyaluronidase injections using paired t test. The mean value of preoperative mouth opening is 26.821 and corresponding mean for post operative mouth opening is 30.886. Blue bar represents pre op mouth opening in mm and Red bar indicates post op mouth opening. There is a significant improvement in the postoperative mouth opening in oral submucous fibrosis patients who are treated with corticosteroid injections + 1500 IU Hyaluronidase injections and more among males with p value = 0.000[p<0.05 statistically significant].



tagonistic activity on the soluble factors released by the sensitized Lymphocytes succeeding the activation by non specific antigens. Fibrosis is prevented by a decrease in fibroblast proliferation and deposition of collagen. Conservative line of treatment like vitamins, antioxidants, Physiotherapy would give expected symptomatic relief of pain and burning sensation in mouth. In dental treatments, anxiety and fear are said to enhance pain during treatment. It may interfere with patients' compliance during treatment resulting in poor dental and oral health status [10]. A major issue related to present bio medical waste management is that many hospitals dispose their waste in an improper way, which contributes to spread of serious diseases such as hepatitis and human immunodeficiency virus [11]. Kerr et al gave the following classification for OSMF as [12].

Grade 1: Mild : Any features of the disease triad for OSMF like burning, depapillation, blanching or leathery mucosa may be reported and inter incisal opening greater than 35 millimeter.

Grade 2: Moderate: above features of OSMF and inter incisal limitation of mouth opening between 20 to 35 millimeters.

Grade 3: Severe : Above features of OSMF and inter incisal opening less than 20 millimetres.

Grade 4A: Above features of OSMF with other potentially malignant disorders on clinical examination.

Grade 4B: Above features of OSMF with any grade of oral epithelial dysplastic changes on biopsy.

Grade 5: Above features of OSMF with oral squamous cell carcinoma.

Lycopene is a major carotenoid which is found in tomatoes that have antioxidant and chemopreventive properties against potentially malignant disorders. The combination of lycopene with intralesional steroids and hyaluronidase is found to be highly efficacious in reducing symptoms and mouth opening of OSMF patients [13]. Botulinum, is a protein and lethal neurotoxin is one of the most potent biological substances known which is used in bioterrorism as well. It is the first toxin used for therapeutic purposes [14] One of the most common postoperative complications after the extraction of permanent teeth is a condition known as dry socket [5]. It is important for dental students to improve their knowledge to enable diagnosis and management of HIV/AIDS patients to have a more positive attitude toward these patients. Furthermore, as their knowledge improves, dental students may understand methods of infection control and how to prevent HIV transmission [16]. Pharmacological agents have also been used in the recent past as adjuvants in various procedures to aid in the reduction of blood loss. Among these, tranexamic acid has been proven to efficiently reduce bleeding [17].

Pentoxifylline is a methyl xanthine derivative that has vasodilating properties and increases the mucosal vascularity. It acts by suppressing the leukocyte function altering fibroblast physiology and stimulating fibrinolysis and there is significant improvement in mouth opening and burning sensation in the mouth [18]. Maxillofacial trauma is any physical trauma to the facial region, is commonly encountered by maxillofacial surgeons, and is often associated with high morbidity [19] if occurred in OSMF patients then

healing will be much delayed. Surgical alterations in the position of the bony facial skeleton will inevitably affect the soft tissues [20]. Dental anxiety and anxiety-related avoidance of dental care creates significant problems for the patients and dental practitioners. Patients when they experience pain, they will have fear that their visit to the dentist will involve pain. This, in turn, results in exacerbation of their anxiety. It was found that dental anxiety was ranked fifth among the most commonly feared situations [21].

Chillies also plays an etiological role in Oral Submucous Fibrosis as its active ingredient capsaicin acts as a predisposing factor for Fibrosis [22]. Interferon Gamma is proposed to reduce the fibroblast proliferation and collagen synthesis and antifibrotic cytokines. It showed that increase in mouth opening and reduction in burning sensation in the mouth. Surgical modalities for the treatment of OSMF are chosen according to the clinical stage of OSMF surgical excision of fibrotic tissue and covering of defect with buccal fat pad grafts or split thickness skin graft. The nasolabial flap has advantages such as, the donor site is in the same operating field, reliable and rich vascularity, provides versatility in design, proximity to the defect, ease of flap elevation, supple skin, thus aiding in increasing mouth opening and causing minimal esthetic deformity, while the disadvantages being intraoral hair growth, temporary widening of oral commissure and occasional hypertrophic scar at the donor site [6]. Painful Dental extraction is the most common procedure carried out by dentists, and it is a common model for evaluating after the efficacy of analgesics like paracetamol, ketorolac for acute dental pain relief [23].

Other surgical treatment with various flaps like Naso labial, radial forearm microvascular free flap for reconstruction of intra oral defect after release of OSMF revealed that both procedures are equally effective in management but extraoral scar was aesthetically acceptable in the nasolabial flap group. The latest use of lasers in the Surgical Management of OSMF is found efficacious and it is developing as a modern way treating osmf patients.

Conclusion

Oral submucous fibrosis is an pre malignant condition wherein the patients are affected similarly like an typical oral cancer patients in the way that they cannot eat properly, mouth opening reduced, burning sensation, anemia, or some time oesophageal fibrosis. so treating them and bringing them back to lead their normal life is an important tasks that lies in dental and maxillofacial professionals. They have to be treated either conservatively with medications or with aggressive surgical procedures. Surgical treatments has its own disadvantage as associated with morbidities. So most of the patients even prefer medical treatments only. Within the limitations of the study, we observed that there is significant effect in the management of Oral Submucous Fibrosis with medications alone. Both corticosteroid injection and Hyaluronidase with corticosteroids are an effective method of managing Oral Submucous Fibrosis and can possibly eliminate the morbidity associated with Surgical Management.

Clinical Significance

This study helps in identifying the role of medical treatments used for treating oral submucous fibrosis. Both corticosteroid injection and Injection of hyaluronidase with dexamethasone are an

effective method of managing Oral Submucous Fibrosis and can possibly eliminate the morbidity associated with Surgical Management. So this test can pave for further studies which if proven, then medical management can be performed as gold standard of treatment for initial stages of oral sub mucous fibrosis.

Acknowledgement

The authors of this study would like to express their gratitude towards everyone who facilitated and enabled us to carry out this study successfully. We would also thank the institute for helping us to have access to all the case records for collecting the required cases for conducting this study.

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