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A Comprehensive Review of Treatment Options of OSMF along with Future Developments

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Oral potentially malignant disorders(opmds) are defined by WHO as "the risk of malignancy being present in a lesion or condition either at the time of initial diagnosis or at a future date." OSMF(oral submucous fibrosis) being an opmd carries a very high chance of cancer if left untreated or undiagnosed in the long run. However there are no definitive guidelines for the treatment of osmf ranging from conservative(non invasive) options to radical surgical options. The primary objective of this article was to critically analyse the studies regarding the treatment options for osmf and to provide the clinician in a comprehensive manner all the available options in one place. A thorough electronic search was carried for relevant articles published until January 2022. Thirty two studies were included in this review after initial screening of 340 articles. The review found that inspite of there being so many available treatment options for osmf no sole therapy can be successfully advocated for the complete resolution of the disease therefore the clinician should rely on a combination of treatment options to achieve good results along with improving patient outcomes and overall quality of life thereby significantly reducing morbidity and mortality among patients suffering from osmf.

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1. INTRODUCTION

Oral Submucous Fibrosis (OSMF) is a potentially malignant disorder which was described by Schwartz in 1952 as “Atropicaidiopathica mucosae oris” and later by Jens J. Pindborg in 1966 as an insidious, chronic disease that affects any part of the oral cavity and sometimes the pharynx. Although occasionally preceded by, or associated with, the formation of vesicles, it is always associated with a juxtaepithelial inflammatory reaction followed by fibroelastic change of the lamina propria and epithelial atrophy that leads to stiffness of the oral mucosa and causes trismus and an inability to eat” [1].

When the disease might be undiagnosed and is progressed to the advanced stages it can lead to progressive fibrosis of pharyngeal & esophageal mucosa,sometimes hearing impairment, xerostomia, hypomobility of soft palate & tongue, loss of gustatory sensations, sunken cheeks, hoarseness of voice, nasal twang and can cause a considerable degree of difficulty in mouth openings.

Development of Vertical fibrous bands in labial and buccal tissues leads to increasingly high fibrosis and loss of elasticity leading to inablitity to open the mouth. The disease is seen in any age group, with prevalence being high in 18–35 years. It carries a considerable public health burden in India, and because of its high malignant transformation rate it contributes significantly to mortality of the individual. There is convincing evidence to point to the chewing of areca nut and its commercial preparations with the development of OSMF.The pooled effect of alkaloids and tannins in areca nut forms the basis for fibrosis.The chewing of areca nut and its commercial preparations (gutkha, mawa, pan masala, flavored supari, etc.) is a common and widespread practice in asian countries, irrespective of age and sex .Once the process of uncontrolled fibrosis is initiated, the condition is not reversible at any stage of the disease process even after cessation of chewing areca nut or its substitute.

Pindborg JJ [2] separated OSMF into three stages based on clinical features:

Stage 1: Stomatitis includes erythematous mucosa, vesicles, mucosal ulcers, melanotic mucosal pigmentation and mucosal petechiae.

Stage 2: The hallmark of this stage is the fibrosis which occurs in healing vesicles and ulcer. Blanching of oral mucosa is seen early on. Vertical and circular palpable fibrous bands in the buccal mucosa and around the mouth opening or lips are palpated in advanced stages, resulting in a mottled marble like appearance of the mucosa because of the vertical thick, fibrous bands associated with blanched mucosa.

Specific finding include the following: Reduction of mouth opening (trismus)

- Restricted tongue movements
- Blanching seen in the floor of the mouth
- Decrease mobility of soft palate and rubbery consistency
- Blanching in faucial pillars and retromolar area along with tonsils
- Shrunken bud like uvula/deviated uvula /hockey stick shaped uvula.
- Inability to blow the cheeks

Stage 3: Sequelae of OSMF

- Over 25% of individuals with OSMF might present with a leukoplakia.
- Speech and hearing deficits may occur because of involvement of the Eustachian tubes.

Pindborg JJ and Sirsat SM [3] were the first to divide OSMF depending only on histopathological features alone are as follows:

1.1 Very Early Stage

“Finely fibrillary collagen dispersed with marked edema. Plump young fibroblast containing abundant cytoplasm. Blood vessels are dilated and congested. Inflammatory cells, mainly polymorphonuclear leukocytes with occasional eosinophils are found” [3].

1.2 Early Stage

“Juxta-epithelial area showing early hyalinization. Collagen seen in separate thick bundles. Moderate number of plump young fibroblasts are seen. Dilated and congested blood vessels. Inflammatory cells such as lymphocytes, eosinophils and occasional plasma cells present” [3].

1.3 Moderately Advanced Stage

Moderately hyalinized collagen. Slight residual edema between the thickened collagen bundles. Fibroblastic response is less apparent .Normal or compressed blood vessels. Inflammatory exuadate-lymphocytes and plasma cells.

1.4 Advanced Stage

Entirely hyalinized collagen. Collagen bundles seen not seen apart. Edema is absent. Hyalinized area is devoid of fibroblasts. Completely obliterated or narrowed blood vessels. Inflammatory cells are lymphocytes and plasma cells.

2. CLASSIFICATION BASED ON CLINICAL AND HISTOPATHOLOGICAL FEATURES

For the surgical management of OSMF a group classification system was developed by Khanna JN and Andrade NN [4]:

2.1 Group I:Very Early Cases

“Very early cases Burning sensation in the mouth, acute ulceration and recurrent stomatitis and not coupled with mouth opening limitation” [5].

2.1.1 Histology

“Fine fibrillar collagen network interspersed with mark edema, blood vessels dilated and congested, large aggregate of plump young fibroblasts present with abundant cytoplasm, inflammatory cells mainly consist of polymorhonuclear leukocytes with few eosinophils. The epithelium is normal” [5].

2.2 Group II: Early cases

Mottled and marble like buccal mucosa, extensive sheets of fibrosis palpable, interincisal distance-26 to35mm.

2.2.1 Histology

“Juxta-epithelial hyalinization present, collagen present as thickened but separate bundles, blood vessels dilated and congested, young fibroblasts seen in moderate number, inflammatory cells mainly consist of polymorph nuclear leukocytes with few eosinophils and occasional plasma cells, flattening or shortening of epithelial rete-pegs evident with varying degree of keratinization” [6].

2.3 Group III: Moderately Advanced Cases

“Moderately advanced casestrismus is present, interincisal distance-15 to 25 mm, buccal mucosa is pale and tightly attached to underlying tissues, atrophy of vermilion border, vertical fibrous bands palpable at the soft palate, pterygomandibular raphe and anterior faucial pillars” [6].

2.3.1 Histology

“Juxta-epithelial hyalinization present, thickened collagen bundles, residual edema, constricted blood vessels, mature fibroblasts with scanty cytoplasm and spindle-shaped nuclei, inflammatory exudates which consists of lymphocytes and plasma cells, epithelium markedly atrophic with loss of rete pegs, muscle fibers seen with thickened and dense collagen fibers” [6].

2.4 Group IVA

Advanced cases show severe trismus, interincisal distance-less than 15mm, thickened faucial pillars, shrunken uvula, restricted tongue movement, presence of circular band around entire lip and mouth.

2.5 Group IVB

Very Advanced cases show presence of hyperkeratotic leukoplakia and squamous cell carcinoma.

2.5.1 Histology

“Collagen hyalinized smooth sheet, extensive fibrosis, obliterated the mucosal blood vessels, and eliminated melanocytes, absent fibroblasts within the hyalinized zones, total loss of epithelial rete pegs, presence of mild to moderate atypia and extensive degeneration of muscle fibers” [6].

Several medical and surgical approaches have been tried for the management of OSMF over the decades. The results of these treatments are not predictable and none has been consistently successful. Therefore it is suggested that a combination therapy including medicinal, adjuvants therapy and physiotherapy can provide the best results in terms of reducing morbidity

and improving quality of life of the patient thereby reducing the mortality associated with this precancerous condition.

This article reviews all the effective treatments modalities for osmf that were discovered over the years. This is an attempt to provide a clearer picture of most effective treatment modalities to clinicians and researchers.

3. TREATMENT OPTIONS

3.1 Conservative Options

In vitro studies [7] performed on "the effect of alcoholic extracts of turmeric (TE), turmeric oil (TO) and turmeric oleoresin (TOR), on the incidence of micronuclei (Mn) in lymphocytes from normal healthy subjects observed that all three treatment modalities decreased the number of micronucleated cells both in exfoliated oral mucosal cells and in circulating lymphocytes".

Pratik r piplia et al. [8] found that "Turmeric with black pepper and nigella sativa given every 15 days enhanced mouth opening,reduced burning sensation, and serum superoxide dismutase SOD levels in the present OSMF study patients; nonetheless, further investigations are needed". Sarwaralam et al. [9] in a group of 60 subjects receiving aloevera as an adjuvant found that it was helpful as an adjuvant.

"Earlier studies had acknowledged nutritional deficiencies as a probable causative factor in OSMF" [10]. "Other reports have shown that many patients diagnosed with OSF had nutritional deficiencies, particularly in iron and B vitamins. In view of these findings, several authors have attempted nutritional supplementation as a measure of adjunctive treatment for OSF. Amongst the supplements used, vitamins A, B complex, C, and E have been tried alone or in combination with other agents" [10].

"Recent work has shown that Manuka honey, an increasingly popular wound additive with potent antibacterial properties, also has anti-inflammatory properties" [11]. "The outcomes indicate a cytotoxic limit of 3-5% v/v. The presence of 1% honey decreased superoxide release at 24 hours. Reduced chemotaxis and IκBα phosphorylation in a dose-dependent fashion was seen with the use of honey in concentrations of 0.5, 1, and 3%. Suggesting that Manuka honey significantly reduces neutrophil recruitment and inflammatory behavior in the wound site in a dose-dependent fashion under the cytotoxic limit" [11].

3.2 Medical Management

Jksharma et al. [12] showed "that Conventional therapies, when pooled with the peripheral vasodilator, improved the magnitude of remissions remarkably, reduced the treatment duration, dosages of associated drugs and frequency of relapses". In a series of treatment conducted by R M borle et al in 1991[13] "three hundred twenty-six patients with oral submucous fibrosis were divided into two groups and treated either with conventional submucosal injections of steroids and hyaluronidase, or with topical vitamin A, steroid applications, and oral iron preparations".

Jayachandtran et al. [14] showed that "pentoxifylline therapy results in significant improvement in clinical symptoms such as burning sensation, mouth opening,tongueprotrusion,relief from perioral fibrotic bands,reduced difficulty in swallowing, speech and submucosal layer thickness and echogenicity using ultrasonography, both pre- and post-operatively".

Abhinav kumar et al. [15] treated "56 patients of osmf with 16 gm lycopene biweekly and found that Mouth-opening values for the patients showed an average increase of 3.4 mm, 4.6 mm, and 0.0 mm for patients in groups A, B, and C, respectively. These values were statistically found to be highly significant. Suggesting that lycopene can and should be used as a first line treatment in initial management" [15]. Wanninayake et al. [16] "In selecting patients for treatment with corticosteroid injection the degree of preinterventional mouth opening is the single factor that we can rely on. In the study, they injected corticosteroids to a group of selected patients who had 30 mm or a less of mouth opening at the preinterventionalstage.Consequently, an interincisal mouth opening of 30 mm or less can be regarded as a reference point for corticosteroid therapy".

In a clinical trial by M F Haque et al. [17] using "Interferon gamma reported its immuno-regulatory effect and has anti-fibrotic cytokine effect and hence its major role in altering collagen synthesis. In vivo studies of Intra-lesional injection of 0.01- 10.0U/ml 3 times a day

for 6 months showed improvement of symptoms". "There appears to be a key to the treatment of these patients, and intra-lesional injections of the cytokine may have a significant therapeutic effect on OSF.

Steroids boast their therapeutic effects due to their anti- inflammatory and immune-suppressive action for prevention or suppression of the fibro prolific inflammation seen in OSF, thus ameliorating the fibrocollagenous condition. It can be applied topically or intra-lesional injections depending upon the clinical stage of the disease" [16]. "4 mg/ml/biweekly injections of Betamethasone diluted in 1.0 ml of 2% xylocaine for 6 months given on buccal mucosa, bilaterally, using an insulin syringe, with a half dose on each side, and showed significant improvement of mouth opening and reduction in burning sensation in a stage II and stage III OSMF group ($p < 0.0001$), in comparison to a control group which received no treatment over two years" [6].

A Randomised control trial was performed by X Jiang et al using allicin and triamcinolone acetonide injected intralesionally weekly for 16 weeks in treatment of Stage 2 OSMF in a Chinese patient cohort and established allicin as an adjunctive treatment improved mouth opening as well as oral-health related quality of life [18,19].

3.3 Surgical Approaches

Talsania JR et al. [20] performed a prospective clinical study for 4 years(2002-2006) and recommended that Diode laser is a less expensive and alternative method in group III and group IVA cases in whom bilateral temporalis myotomy and coronoidectomy are considered to be the single solution. [20] Zainab C. includes "a case series of 16 cases of moderate OSMF treated with Erbium Chromium Yttrium Scandium Gallium Garnet (ErCr:YSGG) laser fibrotomy under local anesthesia in combination with cessation of habits, topical steroids, lycopene and oral physiotherapy is presented. The mean increase in mouth opening achieved at 1 year was 17.5 mm" [21].

"The pedicled buccal fat pad has been extensively used for the repair of oral defects. A novel application of this flap is in the treatment of patients suffering from trismus caused by oral submucous fibrosis is reported. The patients underwent incision of the fibrotic bands and coverage of the buccal defect with a pedicled buccal fat pad flap. The results suggest that this is a reasonable, convenient, and reliable technique for osmf treatment" [22].

Aafiya et al (2021) in a series of patients showed that coronoidectomy as an adjunctive treatment in OSMF provides comparable treatment outcome in terms of MIO ; also offers a shorter operating time and less blood loss. [23] Utilizing a Platysma-based myocutaneous flap K rajkumar et al(2017) proved it to be durable and aesthetically acceptable for reconstruction of intraoral defects ; hence serving as a viable option for patients with severe OSMF [24].

The use of the nasolabial flap for repair of orofacial defects is well established therefore the nasolabial flap is considered the most successful extraoral flap in the surgical treatment of osmf multiple articles suggest to use it as a donor site [25]. There is an added advantage of non-involvement of flap in the condition too.

4. PHYSIOTHERAPY

"In a randomized control trial conducted by pravinkumar et al found that patients using the MED(mouth exercising device)showed reduction in burning sensation in the range of 64.8% to 71.1% and 27.8% to 30.9%, whereas in non users reduction in burning sensation ranged from 64.7% to 69.9% and from 29.3% to 38.6% after 6 months. The wo-way analysis of variance indicated statistically significant results in changes in initial VAS(visual analog scale) scores to 6-monthly VAS scores between MED users and non MED users. The MED helps to augment the rate of reduction of mucosal burning sensation, in addition to the conventional ice-cream stick regimen, as an adjunct to local and surgical treatment" [27]. "Ultrasound therapy with with thumb kneading physiotherapy for six days/ week for two consecutive weeks showed significant improvement in mouth opening and reduction of burning sensation" [26].

Patients who have undergone surgery along with active physiotherapy showed good results. Thus post operative physiotherapy and cessation of habit are of equal importance for good prognosis in osmf patients.

4.1 Recent Advances

Hyperbaric Oxygen Therapy has been identified as a novel treatment modality in oral submucous fibrosis.

The Committee on Hyperbaric Medicine defines HBOT therapy as “A mode of medical treatment during which the patient is entirely enclosed during a pressure chamber and breathes 100% oxygen at a pressure >1 atmosphere absolute (ATA).” “ATA is the unit of pressure and 1 ATA is equal to 760 mm of mercury or pressure at sea level. Widespread fibrosis of the connective tissue causes reduction of vascularity, resulting in subsequent hypoxia in both fibroblasts and surface epithelia. Hypoxia results in atrophy and ulceration of the epithelium by inducing apoptosis. In addition, the over expression of hypoxia-induced factor-1a is seen in OSMF, which indicates changes in cell proliferation, maturation, and metabolic adaptation increasing the likelihood of malignant transformation” [28].

”HBOT increases oxygen tension ,Enhances the quantity of dissolved oxygen within the plasma, Augments oxygen delivery to the hypoxic areas.It also decreases the expression of HIF-1a thereby improving ischemia.The relief of hypoxia and the down-regulation of HIF-1a are both responsible for the anti-inflammatory effect of HBOT. It may have the potential to improve the vascular situation.Hyperbaric oxygen therapy (HBOT) necessitates inhalation of 100% oxygen at augmented air pressure usually ranging between 2.0 and 2.5 atmospheres for periods between 60 and 120 minutes” [28].

“Pirfenidone slows the progression of fibrotic lesions and inhibits the formation of new lesions following tissue injuries. Pirfenidone has been tested in many in vivo and invitro fibrotic models which demonstrates favourable results” [29].

“Whilst investigating the inhibitory effect of TSN(Tanshinone) on progression of OSMF Zheng et al found that TSNs inhibits arecoline mediated proliferation of primary human oral mucosal fibroblast and reversed the promotive effects of arecoline on epithelial–mesenchymal transition (EMT) process. Oral mucosal tissues in OSMF contain exceedingly little p53 when compared with normal tisues. Arecoline reacts with oral mucosal fibroblasts resulting in reduction of p53 [30] and its associated downstream molecules p21, Bax and p53 upregulated modulator of apoptosis. Even though there are very few studies conducted on effects of TSNs in OSMF till date, yet all of them have yielded encouraging results. For this reason, TSNs appears to be promising in the management of OSMF” [30].

“Mesenchymal Stem Cells (MSCs) are multipotent stromal cells present in adult and birth associated tissue . MSCs possess low immunogenicity as they lack MHC-II and low MHC-I expression making it a suitable candidate for allogeneic transplantation. MSCs can differentiate into a variety of functional cell types and are capable of secreting immunomodulatory factors, proteins, and growth factors. Transplantation of MSCs is found to be effective in several systemic as well as tissue-specific disorders” [31].

“Employing MSCs which hold immunomodulatory, anti-fibrotic, anti-oxidative, and potential for angiogenesis probably can assist in effectively halting the progression of the disease including its malignant potential” [31].

5. CONCLUSION

Although studied intensively over several decades, OSMF is still poorly understood across the globe. The incidence is rising with young individuals getting more affected due to the large span of advertisement that is aimed towards the youth. There has been significant improvements in the management modalities of osmf although no definitive treatment is effective on its own ; a combination therapy along with an early diagnosis can definitely improve treatment outcomes and improve quality of life of the patients.

OSMF being a potentially malignant disorder, intervention should be started timely to improve outcomes, recognizing the stages early and treatment modalities which may be given to the patient will definitely benefit the patients.

Better integration of medical and dental services will reduce patients’ suffering and improve their quality of life.All health care professionals must work together in public education and primary prevention to subsequently reduce the burden of OSMF.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Pindborg JJ, Sirsat SM. Oral submucous fibrosis. Oral Surg Oral Med Oral Pathol. 1966;22(6):764–79.
2. Thakur N and Kumar V. An outline of existing clinical classification system for

oral submucous fibrosis. J Res Adv Dent 2014;3(2):72-5.

3. More CB, Gupta S, Joshi J and Varma SN. Classification system for oral submucous fibrosis. J Indian Acad Oral Med Radiol 2012;24(1):24-9.
4. Khanna JN, Andrade NN. Oral submucous fibrosis: A new concept in surgical managementReport of 100 cases. Int J Oral MaxillofacSurg. 1995;24:433-9.
5. Gupta H, Grover N, Tyagi N, Misra A. Classification systems in oral submucous fibrosis patients: a review. TMU J Dent. 2018;2:13-9.
6. More CB, Gupta S, Joshi J, Varma SN. Classification system for oral submucous fibrosis. Journal of Indian Academy of Oral Medicine and Radiology. 2012;24(1): 24.
7. Hastak K, Lubri N, Jakhi SD, More C, John A, Ghaisas SD, Bhide SV. Effect of turmeric oil and turmeric oleoresin on cytogenetic damage in patients suffering from oral submucous fibrosis,CancerLetters. 1997;116(2).
8. Pipalia PR, Annigeri RG, Mehta R. Clinicobiochemical evaluation of turmeric with black pepper and nigella sativa in management of oral submucous fibrosis-a double-blind, randomized preliminary study. Oral Surg Oral Med Oral Pathol Oral Radiol. 2016;122(6):705-712.

   DOI: 10.1016/j.oooo.2016.07.023.

   Epub 2016 Aug 6. PMID: 27720650.
9. Alam S, Ali I, Giri KY, Gokkulakrishnan S, Natu SS, Faisal M, Agarwal A, Sharma H. Efficacy of aloe vera gel as an adjuvant treatment of oral submucous fibrosis. Oral Surg Oral Med Oral Pathol Oral Radiol. 2013;116(6):717-24.

   DOI: 10.1016/j.oooo.2013.08.003.

   PMID: 24237724.
10. Maher R, Aga P, Johnson NW, Sankaranarayanan R, Warnakulasuriya S. Evaluation of multiple micronutrient supplementation in the management of oral submucous fibrosis in Karachi. Pakistan Nutr Cancer. 1997;27(1):41–7.
11. Minden-Birkenmaier BA, Cherukuri K, Smith RA., Radic MZ., Bowlin GL. Manuka honey modulates the inflammatory behavior of a dHL-60 neutrophil model under the cytotoxic limit. Int. J. Biomater. 2019;6132581.

    DOI: 10.1155/2019/6132581.
12. Sharma JK, Gupta AK, Mukhija RD, Nigam P. Clinical experience with the use of peripheral vasodilator in oral disorders. Int J Oral Maxillofac Surg. 1987;16(6):695-9.

    DOI: 10.1016/s0901-5027(87)80055-3.

    PMID: 3125268.
13. Borle RM, Borle SR. Management of oral submucous fibrosis: A conservative approach. J Oral Maxillofac Surg.
14. Sadaksharam J, Mahalingam S. Evaluation of Oral Pentoxifylline in the Management of Oral Submucous Fibrosis - An Ultrasonographic Study. Contemp Clin Dent. 2017;8(2):200-204.

    DOI: 10.4103/ccd.ccd_1192_16.

    PMID: 28839403; PMCID: PMC5551322.
15. Kumar A, Bagewadi A, Keluskar V, Singh M. Efficacy of lycopene in the management of oral submucous fibrosis. Oral Surg Oral Med Oral Pathol Oral RadiolEndod. 2007;103(2):207-13.

    DOI: 10.1016/j.tripleo.2006.07.011.

    Epub 2006 Oct 24. PMID: 17234537.
16. Tilakaratne WM, Ekanayaka RP, Herath M, Jayasinghe RD, Sitheeque M, Amarasinghe H. Intralesional corticosteroids as a treatment for restricted mouth opening in oral submucous fibrosis. Oral Surg Oral Med Oral Pathol Oral Radiol. 2016;122(2):224-31.

    DOI: 10.1016/j.oooo.2015.11.023.

    Epub 2016 Apr 19. PMID: 27422421.
17. Haque MF, Meghji S, Nazir R, Harris M. Interferon gamma (IFN-gamma) may reverse oral submucous fibrosis. J Oral Pathol Med. 2001;30(1):12-21.

    DOI: 10.1034/j.1600-0714.2001.300103.x.

    PMID: 11140895.
18. Goel S, Ahmed J. A comparative study on efficacy of different treatment modalities of oral submucous fibrosis evaluated by clinical staging in population of southern Rajasthan. J Cancer Res Ther. 2015;11(1):113–8.
19. Jiang X, Zhang Y, Li F, Zhu Y, Chen Y, Yang S, Sun G. Allicin as a possible adjunctive therapeutic drug for stage II oral submucous fibrosis: a preliminary clinical trial in a Chinese cohort. Int J Oral Maxillofac Surg. 2015;44(12):1540-6.

DOI: 10.1016/j.ijom.2015.06.015. Epub 2015.

PMID: 26165773.

20. Talsania JR, Shah UB, Shah AI, Singh NK. Use of diode laser in oral submucous fibrosis with trismus: prospective clinical study. Indian J Otolaryngol Head Neck Surg. 2009;61 (1):22-5.

DOI: 10.1007/s12070-009-0012-x.

Epub 2009 Mar 21. PMID: 23120664; PMCID: PMC3450091.

21. Chaudhry Z, Gupta SR, Oberoi SS. The Efficacy of ErCr:YSGG Laser Fibrotomy in Management of Moderate Oral Submucous Fibrosis: A Preliminary Study. J Maxillofac Oral Surg. 2014;13(3): 286-94.

DOI: 10.1007/s12663-013-0511-x.

Epub 2013 Apr 18. PMID: 25018602; PMCID: PMC4082553.

22. Sharma R, Thapliyal GK, Sinha R, Menon PS. Use of buccal fat pad in the treatment of oral submucous fibrosis. J Oral Maxillofac Surg; 2011.

23. Ambereen A, Bhutia O, Roychoudhury A, Yadav R, Khakhla DH, Vishwakarma K. Is Coronoidectomy Superior to Coronoidotomy for ImprovingMaximum Incisal Opening in Patients With Oral Submucous Fibrosis? J Oral Maxillofac Surg. 2021;79(4):863.e1-863.e7.

DOI: 10.1016/j.joms.2020.11.009.

Epub 2020 Dec 11. PMID: 33345813.

24. Rajkumar K, Roy Chowdhury SK, Vivek Saxena, Ramen Sinha,Superiorly based platysma myocutaneous flap for reconstruction of intra oral defect following fibrotomy in oral submucous fibrosis: Report of a case.

25. Kamath VV. Surgical Interventions in Oral Submucous Fibrosis: A Systematic Analysis of the Literature. J Maxillofac Oral Surg. 2015 Sep;14 (3):521-31.

DOI: 10.1007/s12663-014-0639-3. Epub 2014 Dec 25. PMID: 26225039; PMCID: PMC4510093.

26. Senthilkumar S, Chitra S, Vijayaraghavan RV. Hemaashree, Subhavani Effectiveness of Ultrasound Therapy on Oral Submucosal Fibrosis Indian Journal of Public Health Research & 3 Development, March 2020;11(03).

27. Patil PG, Hazarey V, Chaudhari R, Nimbalkar-Patil S. A randomized control trial measuring the effectiveness of a mouth-exercising device for mucosal burning in oral submucous fibrosis. Oral Surg Oral Med Oral Pathol Oral Radiol. 2016;122(6):713-718.

DOI: 10.1016/j.oooo.2016.07.026.

Epub 2016 Aug 6. PMID: 27720659.

28. Kumar MA, Radhika B, Gollamudi N, Reddy SP, Yaga US. Hyperbaric Oxygen Therapy-A Novel Treatment Modality in Oral Submucous Fibrosis: A Review. J Clin Diagn Res. 2015;9(5):ZE01-4.

DOI: 10.7860/JCDR/2015/11500.5905.

Epub 2015 May 1. PMID: 26155590; PMCID: PMC4484182.

29. More CB, Jatti Patil D, Rao NR. Medicinal management of oral submucous fibrosis in the past decade- A systematic review. J Oral Biol Craniofac Res. 2020;10(4):552-568.

DOI: 10.1016/j.jobcr.2020.08.004.

Epub 2020 Aug 19. PMID: 32939334; PMCID: PMC7479289.

30. Zheng L, Guan ZJ, Pan WT, Du TF, Zhai YJ, Guo J. Tanshinone Suppresses Arecoline-Induced Epithelial-Mesenchymal Transition in Oral Submucous Fibrosis by Epigenetically Reactivating the p53 Pathway. Oncol Res. 2018;10;26(3):483-494.

DOI:10.3727/096504017X14941825760362. Epub 2017 May 21. PMID: 28550687; PMCID: PMC7844836.

31. Suma GN, Arora MP, Lakhanpal M. Stem cell therapy: A novel treatment approach for oral mucosal lesions. J Pharm Bioallied Sci. 2015;7(1):2-8.
DOI: 10.4103/0975-7406.149809.
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