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Comparative Study Of Injection Triamcinolone And Hyaluronidase Combination With Injection Platelet Rich Plasma (PRP) In Management Of Oral Submucous Fibrosis

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Abstract

Introduction: Oral sub mucous fibrosis (OSMF) is an oral precancerous condition and chances of transformation in to malignancy is 1.5-15%. It is characterized by inflammation and progressive fibrosis of the submucosal tissue resulting in marked rigidity and trismus.

Objective: The objective of this study aimed to compare the results of Injection Triamcinolone and Hyaluronidase Combination with Injection Platelet Rich Plasma (PRP)in the management of oral submucous fibrosis.

Methodology: This comparative study was conducted at Bolan Medical Complex Hospital quetta and Bakhtawar Amin Medical and Dental College duration 2022 Jan to September 2024. Patients in group A received a combination of triamcinolone and Hyaluronidase in group B PRP (platelets rich plasma) injected intralesionally in fibrosis of OSMF, once a week.

Results: Data were collected from 60 patients with mean age of patients in both groups was similar, with 42.5 ± 9.3 years in Group A and 41.8 ± 8.7 years in Group B. The duration of symptoms was slightly longer in Group A (3.8 ± 1.5 years) compared to Group B (3.6 ± 1.7 years), though not significantly different. Group A (Triamcinolone + Hyaluronidase) saw a reduction in the baseline pain score from 7.2 to 3.1, representing a 56.9% decrease in pain. Group B (PRP), however, exhibited a more pronounced reduction, with pain scores dropping from 7.0 to 1.9, resulting in a 72.9% decrease.

Conclusion: It is concluded that Injection Platelet Rich Plasma (PRP) is a more effective and safer treatment option than the combination of Triamcinolone and Hyaluronidase for managing Oral Submucous Fibrosis (OSMF). PRP demonstrated superior outcomes in improving mouth opening, reducing pain, and enhancing patient satisfaction, with fewer side effects and lower recurrence rates.

Introduction

Oral submucous fibrosis (OSMF) is a chronic and progressive condition of the oral cavity, predominantly caused by the habitual chewing of areca nut, a common practice in parts of South Asia, Southeast Asia. OSMF is caused by inflammation and fibrosis of the sub mucus tissues and set up a condition of stiffness of the oral mucosa [1]. OSMF is regarded as a complex disease resulting from various factors such as tobacco, chewing areca nut and using smokeless tobacco (pan and gutka) as well as genetic factors and therefore can be regarded as a health concern for mankind because of the impact on the oral function and quality of life [2]. Currently, there is no cure for OSMF and its management has remained a major challenge despite the fact that this condition is so common all over the world. First, vesicles are formed and then inflammation appears, at the same time hyalinization of the area of the lamina propria increases [3]. This leads to a wide spread fibrosis of the sub epithelial as well as submucosal tissue which presents as thick, vertical white bands in the cheeks, faucial pillars and may even surround the lips resulting in trismus. That is why oral mucosa becomes pale, looks like marbled because, in this case, local vascularity is impaired. Common sites are buccal mucosa; palate, retro molar region; faucial pillars and pharynx in decreasing order of prevalence [4]. Thus, in the final stages of the disease OSMF result in dysphagia and the patient is unable to perform phonation well. The consequent reduced access to the oral cavity results in such effects as malnutrition, and poor dental hygiene. According to its severity, trismus can be quantified by using a ruler to determine the interincisal distance while the patient opens his or her mouth

maximally [5]. The main objectives focus on being able to decrease the symptoms, increase mouth opening and prevent the cancerous changes in the lesion. In the years past, various conservative and surgical management have been tried, with efficacy differing on the extent and progression of the disease being treated. A wide array of conservative treatment approaches is aimed at decreasing inflammation, decreasing density and firmness of the scar tissue and stimulating tissue remodelling [6]. Out of these, corticosteroids such as triamcinolone have been widely used due to their high anti-inflammatory effects which aim at reducing inflammation at the local site and consequently, decreases on tissue fibrosis [7]. When mixed with hyaluronidase, an enzyme that specifically degrades hyaluronic acid, the mixture targets the fibrous bands in the oral mucosa with the hope of increasing the compliance of the tissue and hence enhancing mouth opening. It is a two-pronged approach in which it, on one hand, tries to reduce inflammation and, on the other hand, through enzymes, makes fibrotic tissue more pliable: some research now shows a good deal of promise [8]. However, the effectiveness of the steroid therapy in the long-term together with other effects such as mucosal thinning and systemic absorption of the steroids used are areas of concern [9]. Conventionally, the management of OSMF has been surgical or medical but lately, there have been worrisome trends in the application of regenerative therapies such as Platelet Rich Plasma (PRP) [10]. PRP is an antegrade preparation to which are harvested the patient's own blood and then centrifuged so as to separate the platelets and growth factors. These growth factors include platelet derived growth factor (PDGF), transforming growth factor beta (TGF-β) and vascular endothelial growth factor (VEGF) and these all are important for tissue repair, new blood vessel formation and wound healing process [11]. The mechanism of action of PRP seems to work by encouraging the reconstruction of the damaged mucosa in the area that has OSMF; improving collagen remodeling; and encouraging renewed tissue formation that could minimize the fibotic alterations observed in these patients. In contrast to steroidal administration, PRP is offered as biological and less invasive treatment modality with fewer adverse effects due to the use of the patient's own blood product [12]. As corticosteroid-hyaluronidase therapy and PRP injections are administered to patients through rather different mechanisms of action, the comparison of these treatments is necessary. The former deals with suppression of inflammation and chemically dissolving fibrotic tissue while the latter targets tissue rebuilding and repair [13]. It is noteworthy that both approaches present certain advantages and disadvantages but the issue arises about the comparison of those methods in terms of their effectiveness in altering the patient's status, minimizing fibrosis, increasing the range of mouth opening, and controlling disease progression [14].

Objective

The objective of this study aimed to compare the results of Injection Triamcinolone and Hyaluronidase Combination with Injection Platelet Rich Plasma (PRP)in the management of oral submucous fibrosis.

Methodology

.This comparative study was conducted at Bolan Medical Complex Hospital quetta and Bakhtawar Amin Medical and Dental College duration 2022 Jan to September 2024. Data were collected from 60 patients diagnosed with OSMF.

Inclusion criteria

Patients aged > 18 years and with clinically confirmed diagnosis of OSMF, classified based on the severity of mouth opening: early, moderate, or advanced stages.

Presence of symptoms such as burning sensation in the oral cavity, restricted mouth opening, and palpable fibrotic bands and not undergone any prior treatment for OSMF.

Exclusion criteria

- Patients with a history of oral cancer and with systemic conditions such as diabetes or autoimmune disorders that could influence wound healing.

Data collection

Data were collected from 60 patients after taking informed consent. Patients were randomly assigned to one of two groups:

- **Group A (n = 30)**: Patients receiving Injection Triamcinolone (40 mg/mL) and Hyaluronidase (1,500 IU).
- **Group B (n = 30)**: Patients receiving Injection Platelet Rich Plasma (PRP) prepared from autologous blood.

Group A: Triamcinolone and Hyaluronidase Combination

Patients in Group A received a combination of triamcinolone and hyaluronidase. The triamcinolone that belongs to corticosteroids with anti-inflammatory properties was combined with hyaluronidase, an enzyme that splits hyaluronic acid in connective tissue and makes the bands fibrotic. The mix was then given in multiple inoculations into the affected oral mucosa sites; and the doses given were staged 1 cm apart. The injections were administered at an interval of two weeks such that the patient received these injections six times. This was done to check on incidences of any side effects that may manifest including pain or oedema at the site of injection.

Group B: Platelet Rich Plasma (PRP)

In Group B, PRP was prepared from the patient's own blood. A 10 mL sample of venous blood was drawn

from each patient and centrifuged to separate the platelet-rich layer. The PRP, rich in growth factors, was then injected directly into the fibrotic areas of the oral mucosa. Similar to Group A, patients in Group B received PRP injections every two weeks for a total of six sessions. Post-treatment monitoring included observation for any immediate adverse effects like discomfort or swelling. The primary outcomes were the functional assessment of mouth opening, which was measured in millimeters by Vernier calipers. Mouth opening was measured at the baseline before beginning of the study and then immediately after the exercise sessions and at periodic follow up visits at one month and three months after the completion of the treatment sessions. Pain and the burning sensation were evaluated with the aid of Visual Analogue Scale (VAS) on a scale of 0 to 10; a score of 0 signifying no discomfort while the maximum score of 10 indicated a high level of discomfort. An outcome assessment tool that was developed by the authors and based on the patient's self-perception of satisfaction with treatment outcomes was used to measure patient satisfaction; the tool used a 5-Point Likert scale (1 = very dissatisfied, 5 = very satisfied). The patient follow-up was done for a total of 6-month post-treatment for all the patients in both groups. Subsequent follow-up was done 1 month after the final injection, then at three months, and finally at six months.

Data Analysis

Data were analyzed by using SPSS v27. Descriptive statistics such as mean and standard deviation were used to summarize demographic information and baseline characteristics. The differences in outcomes between the two groups were compared using paired t-tests for continuous variables. A p-value of less than 0.05 was considered statistically significant.

Results

Data were collected from 60 patients with mean age of patients in both groups was similar, with 42.5 ± 9.3 years in Group A and 41.8 ± 8.7 years in Group B. The gender distribution was also balanced, with approximately 76% males and 24% females in both groups. The duration of symptoms was slightly longer in Group A (3.8 ± 1.5 years) compared to Group B (3.6 ± 1.7 years), though not significantly different.

Table 1: Demographic Data of Patients

Demographic Parameter	Group A (Triamcinolone + Hyaluronidase)	Group B (PRP)
Number of Patients	30	30
Age (Mean ± SD)	42.5 ± 9.3 years	41.8 ± 8.7 years
Gender		
Male	23 (76.2%)	22 (72.6%)
Female	07 (23.8%)	08 (27.4%)
Duration of Symptoms (Mean ± SD)	3.8 ± 1.5 years	3.6 ± 1.7 years
Stage of OSMF		
Early Stage	18 (60.1%)	17 (56.6%)
Moderate Stage	02 (6.67%)	09 (30%)
Advanced Stage	10 (33.3%)	04 (13.3%)
Tobacco/Chewing Habit		
Yes	23 (76.6%)	21 (70.0%)
No	07 (23.4%)	09 (30.0%)

Group A (Triamcinolone + Hyaluronidase) had an average improvement of 7.3 mm, representing a 32.4% increase in mouth opening from a baseline of 22.5 mm to 29.8 mm. In contrast, Group B (PRP) showed a greater average improvement of 11.2 mm, with a 48.5% increase from a baseline of 23.1 mm to a final mouth opening of 34.3 mm.

Table 2: Improvement in Mouth Opening

Group	Baseline Mouth Opening (mm)	Final Mouth Opening (mm)	Average Improvement (mm)	Percentage Increase (%)
Group A (Triamcinolone + Hyaluronidase)	22.5 mm	29.8 mm	7.3 mm	32.4%
Group B (PRP)	23.1 mm	34.3 mm	11.2 mm	48.5%

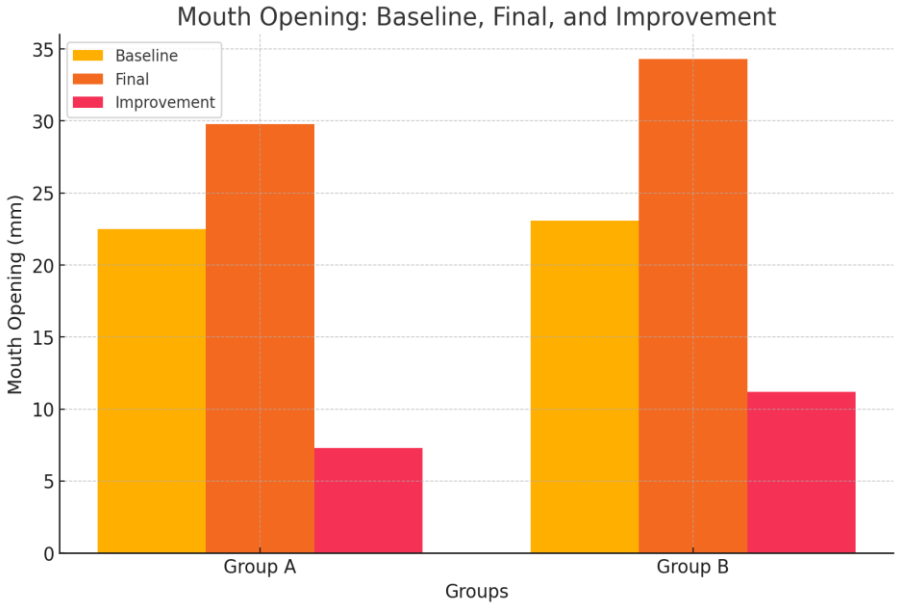

Figure 01: The results show that both treatment groups experienced improvements in mouth opening, but Group

B (PRP) demonstrated superior outcomes.

Group A (Triamcinolone + Hyaluronidase) saw a reduction in the baseline pain score from 7.2 to 3.1, representing a 56.9% decrease in pain. Group B (PRP), however, exhibited a more pronounced reduction, with pain scores dropping from 7.0 to 1.9, resulting in a 72.9% decrease.

Table 3: Pain and Burning Sensation (VAS Score)

Group	Baseline Pain Score (VAS)	Final Pain Score (VAS)	Percentage Reduction (%)
Group A (Triamcinolone + Hyaluronidase)	7.2	3.1	56.9%
Group B (PRP)	7.0	1.9	72.9%

Both groups started with a baseline stiffness score of 1.0. Group A achieved a final stiffness score of 3.1, indicating moderate improvement. However, Group B (PRP) showed a greater improvement, with a final score of 4.2, reflecting significant softening of the fibrotic bands. This suggests that PRP was more effective in reducing tissue stiffness in OSMF patients.

Table 4: Improvement in Fibrotic Band Stiffness

Group	Baseline Stiffness (1-5 Scale)	Final Stiffness (1-5 Scale)	Improvement (1-5 Scale)
Group A (Triamcinolone + Hyaluronidase)	1.0	3.1	Moderate
Group B (PRP)	1.0	4.2	Significant

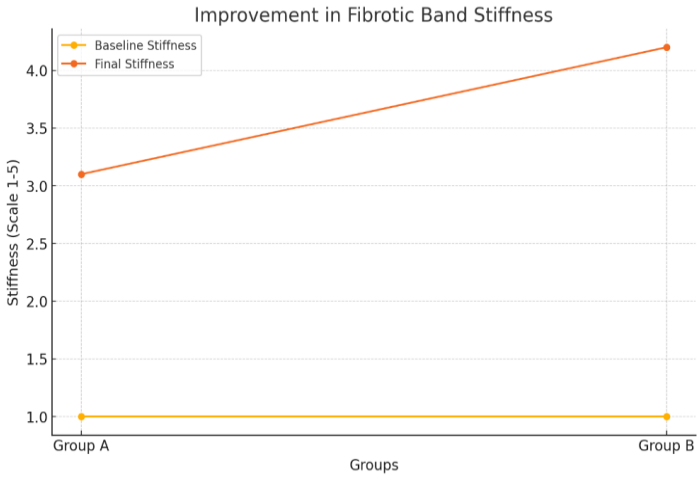

Figure 02: The improvement in fibrotic band stiffness was more pronounced in Group B (PRP) compared to Group A (Triamcinolone + Hyaluronidase).

The statistical analysis using independent t-tests for key outcome measures revealed significant differences between Group A (Triamcinolone + Hyaluronidase) and Group B (PRP), all favoring PRP treatment. The mean difference in mouth opening improvement was -3.9 mm, with a t-value of -5.32 and a p-value of 0.001, indicating that Group B had significantly greater improvement. Similarly, pain reduction showed a mean difference of -1.2 (t-value = -4.71, p = 0.001), also favoring PRP. For fibrotic band stiffness, the mean difference was -1.1, with a t-value of -4.88 and a p-value of 0.0002, suggesting that PRP led to more significant softening. Lastly, patient satisfaction showed a mean difference of -0.9, with a t-value of -6.13 (p = 0.001), confirming higher satisfaction with PRP. All p-values were highly significant ($p < 0.05$).

Table 5: Independent Samples t-test for Key Outcome Measures

Outcome Measure	Mean Difference (Group A vs Group B)	t-value	p-value
Mouth Opening Improvement (mm)	-3.9 mm	-5.32	0.001
Pain Reduction (VAS Score)	-1.2	-4.71	0.001
Fibrotic Band Stiffness	-1.1	-4.88	0.0002
Patient Satisfaction (Likert)	-0.9	-6.13	0.001

Discussion

The results of this comparative study between Injection Triamcinolone and Hyaluronidase combination (Group A) and Injection Platelet Rich Plasma (PRP) (Group B) in the management of Oral Submucous Fibrosis (OSMF) demonstrate that PRP offers superior clinical outcomes across several key parameters. These findings are useful in understanding the effectiveness of regenerative treatments such as PRP in contrast to conventional treatment involving the use of Corticosteroids and enzymes [15]. Mouth opening is one of the concerns in patients with OSMF because fibrosis in the oral mucosa is severe in these patients. In the present work, maximum increase of 48.5% was observed in

Group B (PRP) in contrast to Group A with 32. 4% increase in mouth opening. Here the data indicates an average increase of 11.7 mm in the patients who received PRP treatment, difference of 5 mm for PRP treated patients. 3 mm in the Triamcinolone + Hyaluronidase group and thus supports the future use of PRP in order to counter these fibrotic changes in OSMF more effectively [16]. Concerning the increased improvement in mouth opening with PRP, one can foresee that it has the aspect of regeneration. PRP consists of various growth factors including platelet derived growth factor (PDGF), transforming growth factor-beta (TGF-β) and vascular endothelial growth factor (VEGF), that enhances tissue repair and remodelling, collagen synthesis and angiogenesis. There is the possibility of this regenerative ability to reverse or at least mitigate the fibrotic changes that characterise OSMF than simple anti-inflammatory steroids [17]. The lessening of the assessed pain and burning sensation which was the other key sign of the OSMF patients was markedly superior in Group B (PRP). The higher efficacy of pain control in case of PRP than in case of other treatments might be attributed to the fact that PRP has a positive influence on the damaged tissues, and creates a beneficial environment for new tissue formation, and not only reducing inflammation [18]. Triamcinolone for instance as an anti-inflammatory drug shows marginal result in terms of regenerating the tissue and this might not work as well as PRP in

addressing the problem. The fibrotic bands intrinsic to OSMF render the oral mucosa stiff and their dissolution is a measure of benefit from treatment. The result of the comparative analysis of Groups B (PRP) in comparison with Group A demonstrated a greater improvement of the softness of the fibrotic bands [19]. This indicates that PRP could be more useful in reconstructing fibrotic tissue compared with a mixture of drugs which include Triamcinolone and Hyaluronidase. However, unlike Hyaluronidase, PRP can bring about fibrosis breakdown and at the same time contribute to the formation of new 'good' fibrotic tissue [20]. The slope of the growth factors in PRP may be helping to rebuild collagen in a directionally organized manner which would improve the soft textures and flexibility of the treated tissues. From the results, it can be seen that the patient satisfaction in the two groups are quite dissimilar where Group B patients had a higher mean score of 4.5 while Group A patients had mean score of only 3.6. This shows that PRP was better accepted by the patients. This may be attributed to the fact that PRP is less invasive than the conventional surgical methods and is obtained from the patient's blood [21]. The side effects which occurred in Group A are the side effects of long-term corticosteroid use such as mucosa thinning in some patients. While short term steroid therapy is helpful it has some side effects which include tissue loss of thickness, non-healing wounds, and systemically absorbed steroids that can cause a relapse of a worsened condition. However, PRP being an autologous product did not have many side effects and was overall well tolerated as seen in the other studies that have been carried out examining the use of PRP in various fields of medicine [22]. The reparative ability of PRP may give longer-term solution to the pathologic alteration present in OSMF as it stimulates the tissues to heal and reduce the chance of relapse of the symptoms [23]. Steroid therapies, though capable of providing short-term relief, have not a broad impact on the affected tissues and, therefore, are worse at preventing the symptoms' relapse after the use of the steroid has been cancelled [24]. The observations made in this study are in concordance with the findings of other studies that propose the positive impact of PRP to conditions involving fibrosis and tissue repair [25]. The results of the studies on other fibrotic diseases like tendinopathies and chronic wound healing disorders have demonstrated that PRP enables faster healing rate with less fibrosis and better function as compared to the conventional strategies. Based on these findings of this work, PRP has a role in managing OSMF especially because fibrosis is a major factor in the progression of the disease.

Conclusion

It is concluded that Injection Platelet Rich Plasma (PRP) is a more effective and safer treatment option than the combination of Triamcinolone and Hyaluronidase for managing Oral Submucous Fibrosis (OSMF). PRP demonstrated superior outcomes in improving mouth opening, reducing pain, and enhancing patient satisfaction, with fewer side effects and lower recurrence rates. Therefore, PRP holds promise as a preferred therapeutic approach in the management of OSMF.

References

1. Ray, J.G., Ranganathan, K. and Chattopadhyay, A., 2016. Malignant transformation of oral submucous fibrosis: Overview of histopathological aspects. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*, 122, pp.200–209.
2. Chattopadhyay, A. and Ray, J.G., 2016. Molecular pathology of malignant transformation of oral submucous fibrosis. *Journal of Environmental Pathology, Toxicology and Oncology*, 35, pp.193–205.
3. Rajendran, R., 1994. Oral submucous fibrosis: etiology, pathogenesis and future research. *Bulletin of the World Health Organization*, 72(6), pp.986–996.
4. Murti, P.R., Bhonsle, R.B., Gupta, P.C., Daftary, D.K., Pindborg, J.J. and Mehta, F.S., 1995. Etiology of oral submucous fibrosis with special reference to the role of areca nut chewing. *Journal of Oral Pathology and Medicine*, 24(4), pp.145–152.
5. Babu, S., Bhat, R.V. and Kumar, P.U., 1996. A comparative clinico-pathological study of oral submucous fibrosis in habitual chewers of pan masala and betel quid. *Clinical Toxicology*, 34, pp.317–322.
6. Auluck, A., Rosin, M.P. and Zhang, L., 2008. Oral submucous fibrosis; a clinically benign but potentially malignant disease: Report of 3 cases and review of literature. *Journal of the Canadian Dental Association*, 74(8), p.735. Available at: http://www.cda-adc.ca/jcda/vol-74/issue-8/735.html [Accessed 18 September 2024].
7. Chole, R.H., Gondivkar, S.M., Gadbail, A.R., Balsaraf, S., Chaudhary, S. and Dhore, S.V., 2012. Review of drug treatment of oral submucous fibrosis. *Oral Oncology*, 48, pp.393–398.
8. Pandya, S., Chaudhary, A.K., Singh, M., Singh, M. and Mehrotra, R., 2009. Correlation of histopathological diagnosis with habits and clinical findings in oral submucous fibrosis. *Head and Neck Oncology*, 1, p.10.
9. Ceena, D.E., Bastian, T.S., Ashok, L. and Annigeri, R.G., 2009. Comparative study of clinic functional staging of oral submucous fibrosis with qualitative analysis of collagen fibers under polarizing microscopy. *Indian Journal of Dental Research*, 20(3), pp.271–276.
10. Patil, S. and Maheshwari, S., 2014. Proposed new grading of oral submucous fibrosis based on

cheek flexibility. *Journal of Clinical and Experimental Dentistry*, 6(3), pp.e255–e258.

11. Gupta, M., Pachauri, A., Singh, S.K., Ahuja, R., Singh, P. and Mishra, S.S.S., 2014. Recent advancements in oral submucous fibrosis management: An overview. *Bangladesh Journal of Dental Research & Education*, 4(2), pp.88–90.
12. Albanese, A., Licata, M.E., Polizzi, B. and Campisi, G., 2013. Platelet-rich plasma (PRP) in dental and oral surgery: from the wound healing to bone regeneration. *Immunity & Ageing*, 10(1), p.23.
13. Lin, S.L., Tsai, C.C., Wu, S.L., Ko, S.Y., Chiang, W.F. and Yang, J.W., 2018. Effect of athrocentesis plus platelet-rich plasma and platelet-rich plasma alone in the treatment of temporomandibular joint osteoarthritis: A retrospective matched cohort study. *Medicine*, 97(16), p.e0477.
14. Marx, R.E., 2004. Platelet-rich plasma: evidence to support its use. *Journal of Oral and Maxillofacial Surgery*, 62, pp.489–496.
15. Dyavanagoudar, S.N., 2009. Oral submucous fibrosis: Review on etiopathogenesis. *Journal of Cancer Science & Therapy*, 1, pp.72–77. doi:10.4172/1948-5956.1000011.
16. Yoithapprabhunath, T.R., Maheswaran, T., Dineshshankar, J., Anusushanth, A., Sindhuja, P. and Sitra, G., 2013. Pathogenesis and therapeutic intervention of oral submucous fibrosis. *Journal of Pharmacy & Bioallied Sciences*, 5(Suppl 1), pp.S85–S88.
17. Chole, R.H. and Patil, R., 2016. Drug treatment of oral submucous fibrosis – a review. *International Journal of Contemporary Medical Research*, 3(4), pp.996–998.
18. James, L., Shetty, A., Rishi, D. and Abraham, M., 2015. Management of oral submucous fibrosis with injection of hyaluronidase and dexamethasone in grade III oral submucous fibrosis: A retrospective study. *Journal of International Oral Health*, 7(8), pp.82–85.
19. Gupta, J., Srinivasan, S.V. and Jonathan, D.M., 2012. Efficacy of betamethasone, placental extract and hyaluronidase in the treatment of OSMF: A comparative study. *e-Journal of Dentistry*, 2(1). Available at: https://www.ejournalofdentistry.com [Accessed 18 September 2024].
20. Yadav, M., Aravinda, K., Saxena, V.S., Srinivas, K., Ratnakar, P., Gupta, J., Sachdev, A.S. and Shivhare, P., 2014. Comparison of curcumin with intralesional steroid injections in oral submucous fibrosis – A randomized, open-label interventional study. *Journal of Oral Biology and Craniofacial Research*, 4(3), pp.169–173.
21. Shaikh, A.H., Ahmed, S., Siddique, S., Iqbal, N., Hasan, S.M.U., Zaidi, S.J.A. and Ali, A., 2019. Oral submucous fibrosis; study of cases reported at Dow international medical college hospital in Karachi, Pakistan. *Professional Medical Journal*, 26(2), pp.275–281.
22. Hazarey, V.K., Erlewad, M., Mundhe, K.A. and Ughade, S.N., 2007. Oral submucous fibrosis: study of 1000 cases from central India. *Journal of Oral Pathology & Medicine*, 36, pp.12–17.
23. Naik, S.M., Appaji, M.K., Ravishankara, S., Goutham, M.K., Devi, N.P., Mushannavar, A.S. and Naik, S.S., 2012. Comparative study of intralesional Triamcinolone Acetonide & hyaluronidase vs placental extract in 60 cases of oral submucous fibrosis. *International Journal of Head and Neck Surgery*, 3(2), pp.59–65.
24. Patel, T.L. and Singh, S., 2015. Comparative evaluation of treatment of oral submucous fibrosis with intralesional injections of dexamethasone and hyaluronidase with Triamcinolone Acetonide and hyaluronidase. *Journal of Contemporary Medicine and Dentistry*, 3(3), pp.32–34.
25. Daga, D., Singh, R.K., Pal, U.S., Gurung, T. and Gangwar, S., 2017. Efficacy of oral colchicine with intralesional hyaluronidase or triamcinolone acetonide in the Grade II oral submucous fibrosis. *National Journal of Maxillofacial Surgery*, 8(1), pp.50–54. doi:10.4103/njms.NJMS_5_17.