



ORIGINAL RESEARCH PAPER

ENT

"THE INTRAORAL INJECTION OF TRIAMCINOLONE - HYALURONIDASE COMBINATION VERSUS PLATELET RICH PLASMA IN PATIENTS WITH ORAL SUBMUCOUS FIBROSIS IN A TERTIARY CARE CENTRE IN VINDHYA REGION, M. P."

KEY WORDS: Oral Submucous Fibrosis, Injection Triamcinolone-Hyaluronidase, Platelet Rich Plasma, Mean Inter Incisal Distance, Dr. Vineeth Kumar V

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ABSTRACT

Introduction: Oral submucous fibrosis (OSMF) has been defined by Pindborg (1966) as an "an insidious chronic disease affecting any part of oral cavity and sometimes the pharynx, usually preceded by vesicle formation, always associated with fibrotic bands and a juxta epithelial inflammatory reaction followed by fibroelastic change of lamina propria with epithelial atrophy leading to stiffness of oral mucosa, trismus and progressive difficulty in eating." **Material And Methods:** This prospective, observational study included 100 patients aged more than 15 and less than 60 years diagnosed with OSMF. Patients were randomly divided in to two groups, 'A' and 'B' of 50 patients each. In group A, 1 ml injection of Triamcinolone (40mg) reconstituted with hyaluronidase (1500 IU) filled in an insulin syringe, was injected intraorally in the sub mucosal plane, into the retro-molar trigone and in the fibrous band along the soft palate on multiple sites, weekly for 6 weeks. Patients of group B were administered Inj. PRP (1ml) weekly for 6 weeks along the same sites. The Mean Inter Incisal Distance (MIID) was precisely measured with a Vernier caliper initially, before commencing the treatment, and subsequently on all visits. This study was conducted at Department of Otorhinolaryngology, Gandhi Memorial and Sanjay Gandhi Hospital, associated with Shyam Shah Medical College, Rewa (M.P.), during period of 18 months (September 2022 to February 2024). **Results:** Maximum patients were between second and third decades of life, with mean age 33 years. The majority of patients were male and from low socioeconomic strata. The majority of our participants were gutkha chewers (58%), followed by arecanut chewers (19%), tobacco chewers (12%), and betal quid chewers (11%). The duration of substance uses among our participants ranged from 2 to 18 years, with a mean duration of approximately 7.8 years. The mean mouth opening increased from 23.6 mm to 32.9 mm in Group A and from 23.2 mm to 37.9 mm in Group B over 6 month. **Conclusion:** Platelet-rich plasma is the autologous component of the plasma and contains higher concentrations of platelets, growth factors, and cytokines than the basal levels.

INTRODUCTION

Oral submucous fibrosis (OSMF) is a chronic, complex, premalignant (1% transformation risk) condition of the oral cavity, characterized by juxta-epithelial inflammatory reaction and progressive fibrosis of the submucosal tissues (the lamina propria and deeper connective tissues). As the disease progresses, the oral mucosa becomes fibrotic to the point that the person is unable to open the mouth [1,2].

The pathological definition, as provided by Jens J. Pindborg and Satyavati Sirsat (1966), describes it as an insidious chronic disease affecting any part of the oral cavity and sometimes the pharynx. It is always associated with a juxta-epithelial inflammatory reaction followed by a fibro-elastic change of the lamina propria, with epithelial atrophy leading to stiffness, although it is sometimes preceded by vesicle formation. [3]

The term "atrophica idiopathica mucosa oris" was first used by Schwartz. [4] Joshi later referred the ailment as OSMF [4].

It is clinically and histopathologically characterized diffusely blanched mucosa, presence of fibrous bands, depapillated tongue, erosions in the mucosa, where the patients chiefly complains of burning sensation and inability to take spicy food [5,6] Proposed etiological factors include excessive areca nut, chilly consumption, vitamin B12 and iron deficiency, tobacco ingestion, smoking, autoimmunity, genetic and environmental factors. [7]

It is a precancerous condition common in the Indian subcontinent. The incidence varies from 0.2 to 0.5% in India. [8]

In the early stages of OSMF treatment, medication is used. In more severe cases, physical therapy is used, and in the later or advanced stages, surgery is performed. Numerous studies have demonstrated that the signs and symptoms of OSMF can be reduced by taking a combination of medications, such as steroids, enzymes, antioxidants, multivitamins, and minerals.

MATERIALS AND METHODOLOGY

Study Center: Department of Otorhinolaryngology, Gandhi Memorial and Sanjay Gandhi Hospital, associated with Shyam Shah Medical College, Rewa (M.P.)

Duration Of Study: 18 months (September 2022 to February 2024)

Study Design: This study is a Prospective study.

Study Population: Patients more than 15 years and less than 60 years.

Sample Size:

Approximately 50 patients in each group, so we planned to have 100 patients as an adequate number of samples in the study.

Inclusion Criteria

- 1) Patients of age ranging from 15 years to 60 years attending ENT OPD with OSMF
- 2) All patients not having local disease or pathology in oral cavity like lichen planus,

Exclusion Criteria

- 1) Patients with temporomandibular joint disorder.
- 2) Patients with uncontrolled diabetes, uncontrolled hypertension, malignancy, abnormal thyroid status.
- 3) Patients with trismus due to any other cause and those with other premalignant lesions like leucoplakia.
- 4) Patients who had undergone any other treatment for OSMF

Materials Required

Vernier Calipers.
Insulin Syringe
Freshly prepared PRP (Platelet Rich Plasma)
Inj Triamcinolone–Hyaluronidase combination.
Cryofuge machine to prepare PRP (available in pathology department)

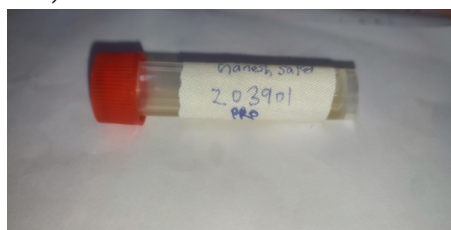


Figure 2: Freshly prepared PRP



Figure 3: Insulin Syringe

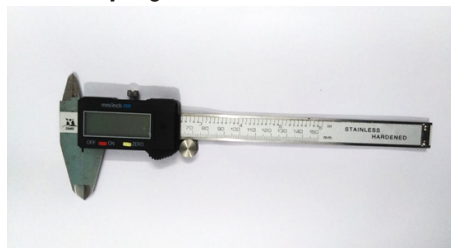


Figure 4: Vernier Calipers



Figure 5: Centrifugation machine (cryofuge 6000i)



Figure 6: The mouth opening was recorded using a graduated

vernier gauge to measure the distance between the upper and lower central incisal edges at maximal unaided mouth opening (IID—interincisal distance).

After approval by the Institutional ethics committee and obtaining written informed consent, patient fulfilling inclusion criteria were chosen for the study.

Pre-anaesthetic examination of the patient was done. Each patient was subjected to complete general physical and systemic examination and detailed history was taken. Basic demographic characteristics such as age, height, sex, weight and BMI grading were noted.

The patient was explained about the procedure and educated. Thereafter, they were shifted to the minor operation theatre (adjacent to ENT OPD).

Procedure Plan

Patients were randomly divided into two groups, 'A' and 'B' of 50 patients each. In group A, 1 ml injection of Triamcinolone (40mg) reconstituted with hyaluronidase (1500 IU) filled in an insulin syringe, was injected intraorally in the sub mucosal plane, into the retro-molar trigone and in the fibrous band along the soft palate on multiple sites, weekly for 6 weeks.

Patients of group B were administered Inj. PRP (1ml) weekly for 6 weeks along the same sites.

The Mean Inter Incisal Distance (MIID) was precisely measured with a Vernier caliper initially, before commencing the treatment, and subsequently on all visits.

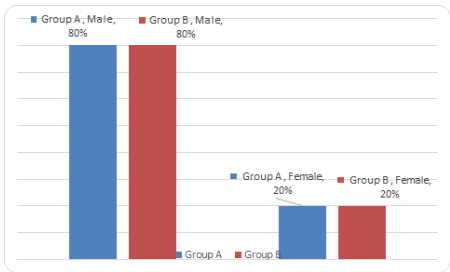
Following the completion of treatment these patients were followed up monthly for a period of 3 months, 6th month and 1 year. IID of 40 mm and above was considered as normal mouth opening score (grade 0, no trismus) 30 to 39 mm (grade 1, trismus); 20 to 29 mm (grade 2, trismus); 10 to 19 mm (grade 3, trismus) and 0 to 9 mm (grade 4, trismus).

RESULTS

Table 1 showing the age-wise distribution of study participants in the two treatment groups: Intraoral Injection of Triamcinolone-Hyaluronidase (Group A) and Platelet Rich Plasma (Group B).

Age Group	Group A	Group B	Total	P Value
15-24 years	10 (20%)	9 (18%)	19 (19%)	0.946
25-34 years	23 (46%)	21 (42%)	44 (44%)	
35-44 years	12 (24%)	13 (26%)	25 (25%)	
45-54 years	4 (8%)	5 (10%)	9 (9%)	
55+ years	1 (2%)	2 (4%)	3 (3%)	
Total	50 (100%)	50 (100%)	100 (100%)	0.590
Mean ± SD	32.7±9.1	33.7±9.4		

The age distribution is very similar between the two treatment groups (Intraoral Injection and Platelet Rich Plasma). The majority of participants (44%) are in the 25–34-year age group, followed by 35-44 years (25%) and 15-24 years (19%). Older age groups (45+ years) represent a smaller portion of participants. The mean ages of the two groups are very similar, with Group A averaging 32.7 years and Group B 33.7 years. The standard deviations are also close (9.1 and 9.4 years respectively), indicating similar age dispersions in both groups. The t-test result ($p=0.59$) shows no statistically significant difference in age between the two groups. This suggests that the age distributions of the groups are well-matched, reducing the likelihood of age being a confounding factor when comparing treatment outcomes.



Graph 2 Gender Distribution Of Patients

The gender distribution is identical between the two treatment groups. Both groups have 40 males (80%) and 10 females (20%). This perfect balance in gender distribution between the groups eliminates any concern about gender being a confounding factor in the study. The chi-square test result ($p = 1$) confirms that there is no difference in gender distribution between the groups.

The overall male predominance (80% of total participants) suggests that oral submucous fibrosis might be more prevalent in males in this study population, or that males are more likely to seek treatment for this condition. This gender imbalance should be considered when generalizing the study results to the broader population.

Table 3 Distribution of study participants according to their substance use

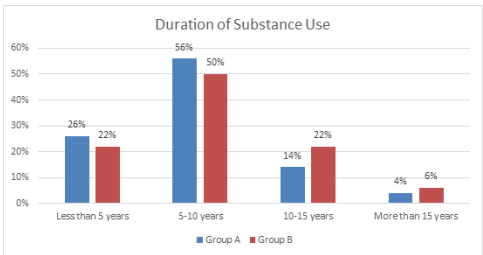
Substance Use	Group A	Group B	Total	P Value
Gutkha chewer	31 (62%)	27 (54%)	58 (58%)	0.776
Areca nut chewer	8 (16%)	11 (22%)	19 (19%)	
Betal quid chewer	6 (12%)	5 (10%)	11 (11%)	
Tobacco chewer	5 (10%)	7 (14%)	12 (12%)	
Total	50 (100%)	50(100%)	100(100%)	

The distribution of substance use is similar between the two treatment groups. Gutkha chewing is the most prevalent form of substance use in both groups (62% in Group A, 54% in Group B), followed by areca nut chewing (16% in Group A, 22% in Group B).The chi-square test result ($p=0.776$) indicates no statistically significant difference in the substance use distribution between the two groups. This suggests that the randomization process was effective in creating balanced groups with respect to the type of substance used.It's noteworthy that gutkha chewing accounts for more than half of the substance use in both groups (58% overall). This high prevalence suggests that gutkha might be the primary substance associated with oral submucous fibrosis in this study population.

Table 4 Distribution of study participants according to the duration of substance use

Duration of Substance Use	Group A	Group B	Total	P Value
Less than 5 years	13 (26%)	11 (22%)	24 (24%)	0.677
5-10 years	28 (56%)	25 (50%)	53 (53%)	
10-15 years	7 (14%)	11 (22%)	18 (18%)	
More than 15 years	2 (4%)	3 (6%)	5 (5%)	
Total	50 (100%)	50(100%)	100(100%)	

The distribution of substance use duration is similar between the two treatment groups. The majority of participants in both groups (56% in Group A, 50% in Group B) have been using substances for 5-10 years. The chi-square test result ($p=0.677$) indicates no statistically significant difference in the distribution of substance use duration between the two groups. This suggests that the randomization process was effective in creating balanced groups with respect to the duration of substance use. The mean duration of substance use is slightly higher in Group B (8.2 years) compared to Group A (7.4 years), but this difference is not statistically significant (t-test p -value = 0.27)



Graph 5 Distribution of study participants according to the duration of substance use

Table 6 Statistical Analysis OfThe Improvement In Mouth Opening OverThe Treatment Period For Both Groups.

Time Point	Group A	Group B
	Mean ±SD (mm)	Mean ±SD (mm)
0 week	23.6±6.2	23.2±6.3
1st week	24.9±6.3	25.0±6.2
2nd week	26.2±6.4	27.1±6.1
3rd week	27.6± 6.5	29.3±6.0
4th week	29.1±6.6	31.1±5.9
5th week	30.5±6.5	33.0±6.0
6th week	31.8±6.3	34.4±6.2
3rd month	33.0±6.0	35.5±6.4
6th month	32.9±5.7	37.9±6.6

- **1.Repeated Measures ANOVA:**
- **Time effect:** $F = 1245.3, p < 0.0001$
- **Group Effect:** $F = 21.6, p < 0.0001$
- **Time X Group Interaction:** $F = 53.8, p < 0.0001$
- **2. Paired t-tests for within-group comparisons (0 week vs 6th month):**
- **Group A:** $t = 28.4, p < 0.0001$
- **Group B:** $t = 33.7, p < 0.0001$
- **3. Independent t-test for between-group comparison at 6th month:** $t = -4.18, p < 0.0001$

Both groups showed significant improvement in mouth opening over the treatment period. The mean mouth opening increased from 23.6 mm to 32.9 mm in Group A and from 23.2 mm to 37.9 mm in Group B over 6 months.

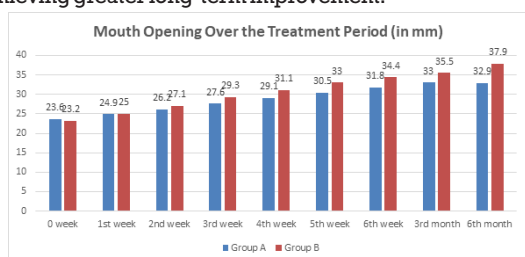
- The repeated measures ANOVA reveals significant effects of time, group, and their interaction. This indicates that:
1. Mouth opening improved significantly over time for both groups.
 2. There was a significant difference between the groups in overall mouth opening.

3. The pattern of improvement over time differed significantly between the groups.

The paired t-tests confirm that the improvement from baseline to 6 months was statistically significant for both groups.

The independent t-test at 6 months shows that Group B (Platelet Rich Plasma) had significantly greater mouth opening than Group A (Intraoral Injection) at the end of the study period.

Group B demonstrated a more substantial and consistent improvement over time compared to Group A. The difference between the groups became more pronounced in the later stages of the treatment period, suggesting that Platelet Rich Plasma therapy may have more sustained long-term effects on mouth opening improvement. These results provide strong evidence that while both treatments are effective in improving mouth opening, Platelet Rich Plasma therapy appears to be significantly more effective than Intraoral Injection of Triamcinolone-Hyaluronidase, particularly in achieving greater long-term improvement.



Graph 6 Improvement in mouth opening over the treatment period for both groups

DISCUSSION

Age Distribution

Our study included participants ranging from 16 to 56 years of age, with a mean age of approximately 33 years in both treatment groups. This age range is consistent with previous studies on OSMF, which have reported that the condition typically affects individuals in their second to fourth decades of life (Pindborg & Sirsat, 1966.^[9] (Tilakaratne et al., 2006)^[10]. The similarity in age distribution between our treatment groups ensures that age-related factors are unlikely to confound our comparison of treatment efficacies.

Gender Distribution

In our study, we observed a predominance of male participants, with 80% males and 20% females in each treatment group. This gender disparity aligns with previous epidemiological studies on OSMF. For instance, Hazarey et al. (2007)^[11] reported a male-to-female ratio of 4.9:1 in their study of 1000 OSMF cases in central India. The higher prevalence in males is often attributed to the more common use of areca nut and tobacco products among men in many societies (Gupta et al., 1998)^[12].

Substance Use Profile

The majority of our participants were gutkha chewers (58%), followed by arecanut chewers (19%), tobacco chewers (12%), and betal quid chewers (11%). This distribution reflects the common etiological factors associated with OSMF in the Indian subcontinent. Gupta et al. (1998) highlighted the strong association between areca nut use and OSMF, with gutkha being a particularly potent form due to its fine particulate nature allowing for prolonged contact with oral mucosa.

Duration Of Substance Use

The duration of substance uses among our participants ranged from 2 to 18 years, with a mean duration of approximately 7.8 years. This is consistent with the

understanding that OSMF typically develops after several years of habitual use of areca nut products. Tilakaratne et al. (2006)^[10] noted that the duration and frequency of areca nut use are significant factors in OSMF development and progression.

Improvement in Mouth Opening

One of the primary clinical manifestations of OSMF is the progressive limitation of mouth opening, which significantly impacts patients' quality of life (Arakeri et al., 2014)^[13]. Our study revealed that both treatment groups experienced improvement in mouth opening over the 6-month period. However, the PRP group demonstrated significantly greater improvement compared to the Triamcinolone-Hyaluronidase group.

The superior efficacy of PRP in improving mouth opening can be attributed to its rich content of growth factors and cytokines. PRP contains high concentrations of platelet-derived growth factor (PDGF), transforming growth factor- (TGF-), vascular endothelial growth factor (VEGF), and epidermal growth factor (EGF) (Marx, 2004)^[14]. These growth factors play crucial roles in tissue regeneration and remodelling.

PDGF has been shown to stimulate fibroblast proliferation and extracellular matrix production (Mehrotra et al., 2015)^[15]. In the context of OSMF, where there is excessive collagen deposition and fibrosis, the ability of PRP to modulate fibroblast activity may be particularly beneficial. It's possible that PRP helps to restore a more balanced extracellular matrix composition, potentially reversing some of the fibrotic changes characteristic of OSMF.

Our findings align with those of Kiran Kumar et al. (2020)^[16], who also found PRP to be superior to intralesional steroids in improving mouth opening in OSMF patients. They reported a mean improvement of 8.5 mm in the PRP group compared to 5.7 mm in the steroid group after 6 months, which is comparable to our results.

CONCLUSION

- Maximum patients were between second and third decades of life, with mean age 33 years as reported in literature commonly in the elderly population.
- The majority of patients were male and from low socioeconomic strata.
- The majority of our participants were gutkha chewers (58%), followed by arecanut chewers (19%), tobacco chewers (12%), and betal quid chewers (11%).
- The duration of substance uses among our participants ranged from 2 to 18 years, with a mean duration of approximately 7.8 years. This is consistent with the understanding that OSMF typically develops after several years of habitual use of areca nut products.
- Both groups showed significant improvement in mouth opening over the treatment period. The mean mouth opening increased from 23.6 mm to 32.9 mm in Group A and from 23.2 mm to 37.9 mm in Group B over 6 month.
- The independent t-test at 6 months shows that Group B (Platelet Rich Plasma) had significantly greater mouth opening than Group A (Intraoral Injection) at the end of the study period.
- The superior efficacy of PRP in improving mouth opening can be attributed to its rich content of growth factors and cytokines. PRP contains high concentrations of platelet-derived growth factor (PDGF), transforming growth factor- (TGF-), vascular endothelial growth factor (VEGF), and epidermal growth factor (EGF).

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Conflict Interest: None declared

Ethical Approval: The study was approved by the Institutional Ethics Committee

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