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THE EFFICACY OF INTRALESIONAL INJECTION OF PLATELET RICH PLASMA FOR TRISMUS MANAGEMENT IN ORAL SUBMUCOUS FIBROUS PATIENTS AT TERTIARY CARE HOSPITAL

Original Research

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ABSTRACT

Background: Oral submucous fibrosis (OSMF) is a chronic, potentially malignant condition predominantly linked to areca nut chewing, commonly seen in South Asian populations. Among its most disabling manifestations is trismus, which significantly impairs essential oral functions such as speech, mastication, and hygiene. Conventional therapies offer only symptomatic relief with limited effectiveness in reversing fibrosis. Platelet-rich plasma (PRP), owing to its regenerative and anti-inflammatory properties, is emerging as a promising alternative for tissue remodeling and functional recovery in OSMF.

Objective: To evaluate the efficacy of intralesional platelet-rich plasma injections in improving mouth opening among adult patients with OSMF-associated trismus at Abbasi Shaheed Hospital, Karachi.

Methods: This quasi-experimental study was conducted over six months (August 2024 to January 2025) in the Department of Oral and Maxillofacial Surgery at Abbasi Shaheed Hospital. A total of 30 patients aged 18–50 years, presenting with bilateral fibrous bands and mouth opening between 15 mm and ≤35 mm, were enrolled using non-probability consecutive sampling. PRP was prepared from autologous blood via temperature-controlled centrifugation and injected bilaterally into the buccal mucosa weekly for six weeks. Mouth opening was recorded using a digital Vernier caliper at baseline and post-treatment. Data were analyzed using SPSS version 26 with significance set at $p < 0.05$.

Results: The study included 21 males (70%) and 9 females (30%) with a mean age of 37.2 ± 6.8 years. Mean mouth opening improved significantly from 24.5 ± 3.4 mm at baseline to 30.2 ± 4.6 mm after six weeks ($p < 0.001$). Stratification by age, gender, and oral habits showed no statistically significant differences in outcome. Mild localized pain at the injection site was reported in 10% of patients and resolved within 24 hours.

Conclusion: Intralesional PRP therapy demonstrated significant improvement in mouth opening in OSMF patients and presents a safe, minimally invasive, and effective alternative to traditional treatments.

Keywords: Angiogenesis, Buccal mucosa, Fibrosis, Growth factors, Mouth diseases, Platelet-rich plasma, Trismus.

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INTRODUCTION

Oral submucous fibrosis (OSMF) is a chronic, progressive, and potentially malignant disorder of the oral cavity, predominantly observed in individuals of Southeast Asian origin, particularly in countries such as India, Taiwan, Sri Lanka, and Pakistan, where the cultural practice of betel nut chewing remains prevalent. First described by Schwartz in 1952 as "Atrophica idiopathica mucosae oris" (1), OSMF is characterized by epithelial atrophy, fibrosis of the oral mucosa, and progressive limitation in mouth opening. Clinically, patients experience symptoms such as burning sensation, stiffness of oral tissues, blanching of buccal mucosa, and trismus, significantly impairing oral functions and quality of life. Alarmingly, the condition holds a malignant transformation rate ranging from 7% to 13% to oral squamous cell carcinoma (OSCC), emphasizing its public health significance (2). While areca nut consumption remains the most well-documented etiological factor, recent evidence has highlighted other contributory elements such as deficiencies in essential micronutrients like iron, zinc, and vitamins, along with irritants like capsaicin, which may exacerbate mucosal damage and fibrosis (3). Histopathologically, the disease progresses through epithelial atrophy, inflammation, and increased collagen deposition, ultimately leading to mucosal rigidity. The hallmark blanching of the buccal mucosa results from ischemia due to compromised vasculature, and once fibrosis becomes established, reversal proves challenging (4).

Conventional treatment modalities for OSMF include intralesional steroids, hyaluronidase, antioxidants, and physiotherapy. These approaches are primarily palliative, providing symptomatic relief without significant reversal of fibrotic changes. Hyaluronidase acts by degrading hyaluronic acid within the connective tissue matrix, reducing the viscosity of intercellular substances (4,5). Steroids exert their anti-inflammatory effects by inhibiting phospholipase A2 activity and downstream inflammatory mediators, while also stabilizing lysosomal membranes and limiting tissue damage (6). Despite partial success, these treatments often fall short in halting disease progression or improving long-term outcomes. Emerging regenerative therapies such as platelet-rich plasma (PRP) have shown promise in overcoming these limitations. PRP, an autologous concentrate of platelets, is rich in growth factors and cytokines that stimulate tissue repair, angiogenesis, and collagen remodeling (7). Recent clinical studies have explored its intralesional administration in OSMF patients with encouraging outcomes. In a study conducted in Rajasthan, the combination of PRP and hyaluronidase with lignocaine was injected weekly, demonstrating statistically significant improvement in symptoms and mouth opening ($p < 0.05$) (8). Another randomized trial at PNS Shifa Hospital in Karachi compared PRP with triamcinolone injections, revealing greater enhancement in maximal interincisal distance (MIID) in the PRP group (mean improvement 1.01 ± 0.05 cm) versus the steroid group (0.783 ± 0.25 cm) (9). Further analysis showed that PRP monotherapy led to a mean MIID improvement of 9.53 ± 1.06 mm, reinforcing its superior efficacy in mitigating trismus and promoting tissue recovery (10). These findings underscore the potential of PRP as a biologically active, minimally invasive, and more effective alternative to conventional treatments. However, there remains a lack of robust, large-scale clinical evaluations assessing its utility in diverse patient populations. Therefore, this study aims to evaluate the effectiveness of intralesional PRP injections in improving trismus among patients with OSMF treated at a tertiary care hospital, with the objective of validating its role as a novel therapeutic intervention.

METHODS

This quasi-experimental study was conducted in the Department of Oral and Maxillofacial Surgery at Abbasi Shaheed Hospital, Karachi, over a six-month period from August 2024 to January 2025. The aim of the study was to evaluate the clinical efficacy of intralesional platelet-rich plasma (PRP) injections in improving trismus among patients diagnosed with oral submucous fibrosis (OSMF). A total of 30 participants were enrolled, consisting of 21 males and 9 females. The sample size was determined using OpenEpi software with 80% power of the test and was expanded to ensure better representation and statistical reliability. Patients were recruited through a non-probability consecutive sampling technique from the outpatient department of the hospital. Participants included in the study were of either gender, aged between 18 and 50 years, and presented with bilateral fibrous bands and a mouth opening ranging from 15 mm to ≤35 mm. Only patients not undergoing any concurrent treatment for OSMF were considered eligible. Exclusion criteria included patients with temporomandibular joint disorders, systemic illnesses such as diabetes mellitus, known hypersensitivity to local anesthetic agents, trismus of non-OSMF origin, mucosal conditions like leukoplakia or lichen planus, and those with radiation-induced fibrosis (11). The

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study was approved by the Research and Ethical Committee of the College of Physicians and Surgeons Pakistan (CPSP/REU/DSG-2021-174-3712), and informed written consent was obtained from all eligible participants prior to their enrollment.

Baseline demographic data, clinical history, and initial mouth opening were recorded using a digital Vernier caliper for precise measurement. PRP was prepared from venous blood drawn aseptically from the cubital vein and collected into sodium citrate tubes to prevent premature platelet activation. The samples were subjected to temperature-controlled centrifugation at 4°C using a two-step spin protocol. The initial centrifugation was performed at 4000 rpm for 6 minutes to separate red blood cells, followed by a second centrifugation at 3500 rpm for 12 minutes to isolate the platelet-rich plasma layer. Approximately 1 mL of PRP was extracted and injected bilaterally into the affected buccal mucosa under aseptic conditions. The PRP injections were administered once weekly for a total duration of six weeks. After the treatment course, post-treatment mouth opening was reassessed using the same digital Vernier caliper to ensure consistency. The data collected were analyzed using SPSS version 26. Descriptive statistics were applied for demographic variables, and paired t-tests were used to compare pre- and post-treatment mouth opening values. A p-value <0.05 was considered statistically significant (12).

RESULTS

A total of 30 patients were enrolled in the study, comprising 21 males (70%) and 9 females (30%), with a mean age of 37.2 ± 6.8 years. The majority of participants reported a history of areca nut use (n = 24, 80%), while the remaining 6 (20%) reported using naswar or gutka. The mean baseline mouth opening was recorded at 24.3 ± 3.4 mm. Following six weeks of intralesional PRP therapy, there was a statistically significant increase in mean mouth opening to 30.2 ± 4.6 mm ($p < 0.001$), indicating substantial clinical improvement. The average increase in interincisal distance across the cohort was 5.9 mm. When stratified by age, patients aged 18–35 years showed a slightly greater mean improvement (6.4 ± 1.1 mm) compared to those aged 36–50 years (5.6 ± 1.3 mm), though the difference was not statistically significant ($p = 0.09$). Similarly, males demonstrated a marginally higher mean gain in mouth opening (6.1 ± 1.3 mm) compared to females (5.8 ± 1.5 mm), without statistical significance ($p = 0.12$). Patients with a history of areca nut use showed a slightly higher mean improvement (6.2 ± 1.2 mm) than those consuming naswar or gutka (5.5 ± 1.4 mm), also not statistically significant ($p = 0.08$).

In terms of safety, the treatment was well-tolerated. No serious adverse effects were reported. Mild localized pain or swelling at the injection site was noted in 3 patients (10%), all of which resolved spontaneously within 24 hours without intervention. The remaining 27 patients (90%) reported no adverse effects during the course of therapy. A paired comparison analysis of pre- and post-treatment mouth opening measurements revealed a statistically significant improvement in interincisal distance following six weeks of intralesional PRP therapy. The mean mouth opening increased from 24.71 ± 2.66 mm at baseline to 31.60 ± 3.79 mm post-treatment, with a mean difference of 6.88 mm (95% CI: 5.06 to 8.71; $p < 0.001$). These findings affirm the clinical effectiveness of PRP in managing trismus in OSMF patients. Further subgroup analysis using ANOVA assessed treatment response variations based on age group, gender, and habitual substance use. Although patients aged 18–35 years, males, and those with a history of areca nut use exhibited slightly greater improvements in mouth opening, the differences were not statistically significant across these subgroups. This suggests that PRP therapy demonstrates consistent therapeutic benefit across diverse demographic profiles, independent of age, gender, or specific oral habits.

Table 1: Distribution of Study participants (n=30)

Variable	Classification	n (%)
Gender	Male	21 (70)
	Female	9 (30)
Habits	Areca Nut	24 (80)
	Naswar/Gutka	6 (20)

Table 2: Mean comparison of changes in mouth opening over time

Time point	Mean in mm ± SD	p-value
Base line	24.3±3.4	-
Post-treatment	30.2±4.6	<0.001

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Table 3: Mean comparison of post-treatment mouth opening with demographics

Variable	Classification	Mean in mm ± SD	p-value
Age Group	18-35 years	6.4±1.1	0.09
	36—50 years	5.6±1.3	
Gender	Male	6.1±1.3	0.12
	Female	5.8±1.5	
Habits	Areca nut	6.2±1.2	0.08
	Naswar/Gutka	5.5±1.4	

Table 4: Post—treatment adverse effects (n=30)

Adverse Effects	n (%)
Localized pain/swelling	3 (10)
No adverse effects	27 (90)

Table 5: ANOVA Summary for Subgroup Comparison of Mouth Opening Improvement

Source of Variation	Sum of Squares	Degrees of Freedom	F-value	p-value
C (Age Group)	0.062	1	0.051	0.823
C (Gender)	0.008	1	0.007	0.936
C (Habit)	2.482	1	2.041	0.165
Residual	31.611	26		

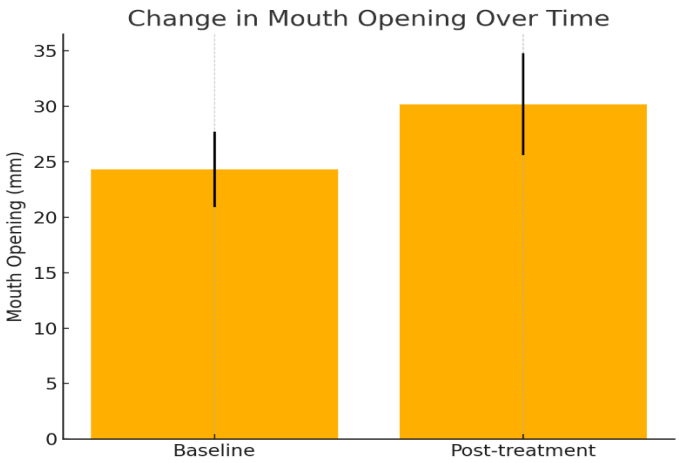

Figure 1 Change in Mouth Opening Over Time

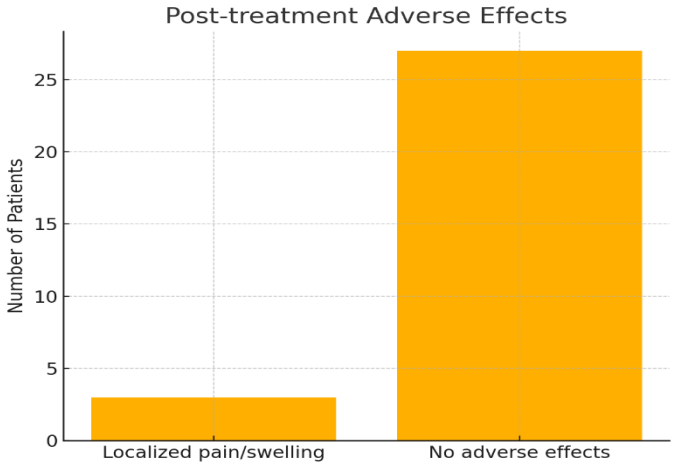

Figure 2 Post-treatment Adverse Effects

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DISCUSSION

The present study demonstrated a clinically and statistically significant improvement in mouth opening following the administration of intralesional platelet-rich plasma (PRP) injections in patients with oral submucous fibrosis (OSMF)-induced trismus. Over a six-week treatment period, mean mouth opening increased from 24.3 ± 3.4 mm to 30.2 ± 4.6 mm, supporting the hypothesis that PRP may serve as a promising adjunctive therapy in managing OSMF. This functional improvement contributed positively to the patients' daily oral functions, such as mastication, speech, and oral hygiene, thereby enhancing overall quality of life and general health. PRP's regenerative potential is attributed to its high concentration of bioactive molecules, including growth factors such as transforming growth factor-beta (TGF-β), platelet-derived growth factor (PDGF), and vascular endothelial growth factor (VEGF), which collectively contribute to collagen remodeling, angiogenesis, and tissue regeneration (13). Unlike corticosteroids and hyaluronidase that primarily target inflammation or enzymatic breakdown of fibrosis, PRP exerts a multifaceted mechanism by simultaneously modulating fibrosis, promoting vascularization, and stimulating cellular proliferation (13,14). The observed reversal of fibrotic tissue and improved interincisal distance may be the result of these synergistic actions. These findings are supported by earlier studies that reported enhanced healing in chronic mucosal lesions with concentrated platelet formulations (15), and others that documented improvements in mouth opening ranging from 6 to 9 mm after PRP treatment, comparable to the outcomes observed in the current study (16).

Demographic subgroup analysis provided additional insight into the variability of treatment response. Younger male patients showed marginally better improvements in mouth opening, potentially due to superior tissue regeneration capacity typically seen in younger age groups (17). Similarly, participants with areca nut habits experienced slightly greater functional recovery than those using other substances. However, this trend lacked statistical significance, which may be attributed to small subgroup sizes or shared pathological effects of various oral habits that promote mucosal fibrosis (18,19). These observations underscore the complexity of OSMF pathophysiology and the multifactorial nature of treatment outcomes. The study's key strengths included a standardized PRP preparation protocol, the use of a consistent delivery technique, and objective pre- and post-treatment evaluation using a digital Vernier caliper. Moreover, the inclusion of a demographic subgroup analysis added depth to the clinical interpretation of outcomes. PRP was well-tolerated by participants, with only 10% reporting mild, transient injection-site pain that resolved spontaneously within 24 hours, highlighting the safety and minimally invasive nature of this approach.

However, several limitations merit consideration. The short duration of follow-up limited the assessment of long-term sustainability of treatment effects. A sample size of 30, though adequate for preliminary evaluation, restricts the generalizability of findings. Furthermore, while the results support PRP's efficacy, the lack of a control group precluded direct comparison with other standard therapies, which would have strengthened the evidence. The absence of long-term histological assessment or imaging-based evaluation also limits the ability to quantify actual reversal of fibrosis at the tissue level. Future research should focus on larger, randomized controlled trials to validate these preliminary findings. Comparative studies with other modalities, such as corticosteroids, enzymatic agents, or combination therapies, would offer more comprehensive insights into therapeutic hierarchies (20). Additionally, exploring different dosages, frequencies, and durations of PRP administration could help identify optimized protocols tailored to disease severity. As PRP preparation is relatively simple, cost-effective, and well-suited for low-resource settings, establishing training modules and clinical guidelines would support broader implementation in primary care and community-level dental practices. Overall, the study supports PRP as a safe and effective therapeutic option for OSMF, offering both functional and symptomatic relief. With further refinement and standardization, PRP may emerge as a frontline treatment modality in the evolving landscape of oral fibrosis management.

CONCLUSION

Intralesional platelet-rich plasma (PRP) therapy offers a promising and clinically relevant advancement in the management of trismus associated with oral submucous fibrosis (OSMF). Unlike conventional treatments such as corticosteroids and hyaluronidase, PRP combines anti-inflammatory effects with tissue regenerative properties, supporting both fibrosis modulation and functional recovery. The findings of this study highlight PRP as a safe, minimally invasive, and effective option that significantly enhances mouth opening and reduces associated discomfort. By demonstrating meaningful clinical improvements, this study reinforces the potential of PRP as a valuable therapeutic alternative in OSMF management, particularly in settings where conventional treatments may fall short.

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Author Contribution

Author	Contribution
Rida Khalid Rafat*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Zahid Ali	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published

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