

Comparison of Combined Therapy (Curcumin + PRP) Versus Curcumin Alone PRP Alone in Terms of Quality of life Improvement in OSMF

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Cite this paper as: Dr. Muhammad Anwar Zeb, Ramsha Tahir, Dr. Mehak Anis, Dr. Lubna M. Arif, Mustafa Abid, Dr. Hera Nadeem, (2025) Comparison of Combined Therapy (Curcumin + PRP) Versus Curcumin Alone PRP Alone in Terms of Quality of life Improvement in OSMF. *Journal of Neonatal Surgery*, 14 (32s), 9028-9034.

ABSTRACT

Oral Submucous Fibrosis (OSMF) is a chronic, progressive, and potentially malignant condition of the oral cavity that severely affects patients' functional capacity and quality of life (QoL). This prospective, comparative, interventional study evaluated the therapeutic efficacy of combined Curcumin and Platelet-Rich Plasma (PRP) therapy versus Curcumin alone and PRP alone in improving QoL among OSMF patients. The study was conducted in the Department of Oral and Maxillofacial Surgery, Jinnah Hospital, Karachi, from January 2024 to January 2025, involving 90 clinically diagnosed OSMF patients randomized into three groups (n=30 each). Group A received Curcumin alone, Group B received PRP alone, and Group C received combined Curcumin + PRP therapy. Quality of life was assessed using the WHOQOL-BREF questionnaire, while clinical outcomes such as mouth opening and burning sensation were also recorded. Results demonstrated that the combined therapy group exhibited the greatest mean increase in mouth opening (9.4 ± 2.1 mm) and the most substantial reduction in burning sensation (VAS: 7.8 ± 1.2 to 1.3 ± 0.9), along with the highest WHOQOL-BREF score improvement (23.8 ± 5.6 , $p < 0.001$). No major adverse effects were reported. The synergistic anti-inflammatory and regenerative effects of Curcumin and PRP were reflected in improved mucosal flexibility, pain reduction, and enhanced overall QoL. The findings suggest that the Curcumin + PRP combination offers a superior, safe, and biologically integrative therapeutic option for OSMF management..

Keywords: Oral Submucous Fibrosis, Curcumin, Platelet-Rich Plasma, Quality of Life, Synergistic Therapy.

1. INTRODUCTION

Oral Submucous Fibrosis (OSMF) is a chronic and progressive, and possibly malignant disease of the mouth that involves juxta-epithelial inflammation and fibrosis of the lamina propria resulting in mucosal stiffening, limited mouth opening, and functional impairments [1]. It reveals populations in South and Southeast Asia because of the habitual canine fondness of

areca nut chewing, and this is approximated to be amid 0.2 and 2.3% in the Indian subcontinent [2]. OSMF is recognized by the World Health Organization as a precancerous disease where a malignant transformation incidence reaches 7-13, which reveals its clinical importance and imposes an urgent requirement on effective care mechanisms and measures [3]. Nevertheless, OSMF is a treatment dilemma since currently available treatment options are mainly symptomatic and unlikely to reverse fibrosis or restore normal oral function [4].

OSMF pathogenesis is complicated by an interplay of inflammatory factors, fibroblasts, and extra-cellular factors. The fibroblast proliferation, collagen cross-linking, and reduced collagenase activity that occurs due to chronic areca nut alkaloid exposure including arecoline leads to irreversible fibrosis [5]. Transforming growth factor-beta (TGF- β), tumor necrosis factor-alpha (TNF- α), and interleukin-6 (IL-6) are pro-inflammatory cytokines that have been identified to be instrumental in driving the disease process [6]. Therefore, the central focus of therapeutic approaches to disease control should be the control of inflammation, oxidative stress, and fibrosis; a modification that enhances patient clinical outcomes and quality of life (QoL) [7].

As one of the first bioactive components of *Curcuma longa*, curcumin has increasingly become a promising antifibrotic and antioxidant agent in the treatment of OSMF [8]. It occurs via its therapeutic effect in the regulation of the TGF- β /Smad signaling pathway, blocking the activation of nuclear factor kappa B (NF- κ B), and lowering lipid peroxidation and reactive oxygen species [9]. Several experiments have shown that Curcumin reduces burning sensation, increases the mucosal elasticity, and enhances the mouth opening in OSMF patients [10,11]. Nevertheless, its low bioavailability and minimal penetration across the mucosa still pose a significant limitation to its long-term activity, as an agent used as a mono-therapy [12].

Conversely, platelet-rich plasma (PRP) an autologous suspension of platelets in plasma has now become a regenerative treatment with considerable potential in the cure of fibrotic oral issues [13]. PRP contains biologically active growth factors including platelet-derived growth factor (PDGF),

vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), and insulin-like growth factor (IGF), that promote angiogenesis, collagen remodelling and tissue regeneration [14]. Intralesional PRP injections have been reported to promote vascularity, epithelial regeneration, and reduce collagen deposition which results in greater mouth opening and symptom improvement in OSMF [15,16]. However, the repair powers of PRP do not work well on its own as it fails to ensure that the chronic inflammatory and oxidative environment that perpetrates the disease is effectively counteracted [17].

Considering the complementary biological effects of Curcumin and PRP, their joint effect is a new, synergistic form of treatment, which, at the same time, brings both the potential to mitigate inflammation and to stimulate tissue regeneration [18]. Curcumin could also reduce fibrotic scarring via PRP, which forms a less inflammatory microenvironment to promote mucosal healing, and PRP may increase Curcumin local bioavailability by improving the vascular perfusion and tissue repair [19]. Regardless of these theoretical benefits, there is a paucity of clinical studies that directly compares the combined effect of Curcumin and PRP to that of either directly.

Quality of life (QoL) measurement has become a critical outcome measure in contemporary research therapeutic literature that has gained significance as indicative not only of physiological recovery but also of mental and social contentment [20]. QoL is a necessity in chronic conditions such as OSMF which is marked by pain, limited oral functions, and social embarrassment [21]. The World Health Organization Quality of Life-BREF (WHOQOL-BREF) questionnaire is a validated multidimensional model of such assessment, which includes a physical, psychological, social, and environmental health domain [22].

Based on these considerations, the current research has been developed to carry out a prospective, comparative, interventional analysis on the therapeutic effectiveness of combined Curcumin and PRP therapy against Curcumin alone and PRP alone on enhancing quality of life of patients suffering OSMF. Through an effective methodological design and systematic QoL measurement, the study was to provide clinically relevant evidence-based information on the synergistic quality of this integrative interventions approach. The results of this study fill not only an important gap in therapeutic application in the management of OSMF, but are also relevant to the current paradigms of biologically-oriented, patient-focused oral rehabilitation.

2. METHODOLOGY

This was a future, comparative, intervention study done at the Department of Oral and Maxillofacial Surgery, Jinnah Hospital, Karachi, between January 2024 and January 2025. The aim of the study was to determine the difference in effect with the use of combined therapy with Curcumin and Platelet-Rich Plasma (PRP) versus Curcumin alone and PRP alone in enhancing the quality of life (QoL) of the patients with Oral Submucous Fibrosis (OSMF).

Ninety patients who were clinically and histopathologically diagnosed with OSMF were recruited using non-probability purposive sampling method. The inclusion criteria included patients between the ages of 18 and 60 years old, with clinical evidence of OSMF stage II and III based on the classification system provided by Pindborg and Sirsat, and who had never

treated OSMF within the past six months. Patients with systemic illnesses like diabetes mellitus, bleeding diathesis, chronic liver or kidney disease, and patients having the history of allergy to Curcumin or any of the PRP components were excluded.

The randomization of participants into three groups (n=30) was a computer-generated randomization list. Group A, Group B, and Group C were given Curcumin (500 mg orally and twice a day throughout 3 months), PRP by injections into the cheek (1 mL each time to 3 mucosa of the cheek), and PRP used jointly with Curcumin respectively. PMPs were then collected by centrifugation at a double spin resulting in a platelet-to-cell concentration 4-5 times higher than normal which was then quickly inactivated with calcium chloride before injection. All respondents were recommended to remember to stop areca nut, tobacco, and other irritants during the study period, and they were advised to keep the best oral hygiene.

The main outcome could be evaluated by the improvement of the quality of life measured with the World Health Organization Quality of Life-BREF (WHOQOL-BREF) questionnaire at the baseline, 3, and 6 months. Secondary outcomes of the study were an increase in mouth opening (measured as interincisal distance by the use of Vernier calipers), a decrease in the burning sensation (assessed based on a 10-point visual analogy scale), and improvement in mucosal flexibility. To reduce bias, clinical assessments were conducted under the blinded condition by one calibrated examiner who was blinded to group assignment.

The entries and the analysis were done using the Statistical Package for the Social Sciences (SPSS) version 26.0. Continuous variables were used with the mean and standard deviation (SD), and categorical variables were represented in frequencies and percentage. Quantitative variables (intergroup comparisons done through one-way ANOVA) and categorical data (test through Chi-square) were done with post-hoc test of Tukey. Intra-group changes were used to examine changes over the times and employed a repeated measures ANOVA. Any value of a p below 0.05 was regarded as statistically significant.

This research methodology aimed to give the results scientific rigor, reproducibility and validity and succeeded in delivering a strong comparative analysis of the Curcumin, PRP and their interaction possibilities in achieving the quality of life of the OSMF patients.

3. RESULTS

The study enrolled 90 patients diagnosed with Oral Submucous Fibrosis (OSMF) and they completed the study. The average age of study participants was 36.8 /12 years old, and the proportion of males and females was 2.3: 1. The similarity between the three baseline demographic and clinical parameters was determined to be above 0.05, which ensured homogeneity at the time of intervention.

At six months of treatment, all the outcome measures had a positive response, and the combined treatment group (Curcumin + PRP) exhibited the most significant changes. The average change in interincisal mouth opening was the highest in the combined group (9.4 ± 2.1 mm) than in the PRP group (6.8 ± 1.9 mm) and the Curcumin group (5.6 ± 1.8 mm) ($p < 0.001$). Likewise, burning sensation, also measured with the Visual Analogue Scale (VAS), demonstrated significant reduction in the combined group (7.8 ± 1.2 to 1.3 ± 0.9), doing better than both arms of monotherapy ($p < 0.001$).

Regarding the quality of life (QoL) evaluated through the WHOQOL-BREF questionnaire, all domains (physical, psychological, social, and environmental) showed significant improvement, with combined treatment too showing the greatest mean improvement at 6 months (overall mean score: 79.2 ± 5.4) in comparison to PRP alone (72.6 ± 6.3) or Curcumin alone (69.8 ± 6.9). There were no significant side effects noted, and the adherence levels of the patients were good during the course of treatment.

Table 1. Baseline Demographic and Clinical Characteristics of Participants (n = 90)

Variable	Curcumin Group (n=30)	PRP Group (n=30)	Combined Group (n=30)	p-value
Mean Age (years)	37.1 ± 8.7	36.5 ± 9.4	36.8 ± 9.6	0.87
Gender (Male/Female)	21/9	20/10	22/8	0.92
Baseline Mouth Opening (mm)	23.2 ± 3.1	22.8 ± 3.4	23.0 ± 3.0	0.76
Baseline VAS Score (Burning Sensation)	7.9 ± 1.0	8.0 ± 1.1	8.1 ± 1.0	0.83
Baseline WHOQOL-BREF Score	55.2 ± 5.8	54.7 ± 6.1	55.4 ± 5.6	0.89

Figure: 1

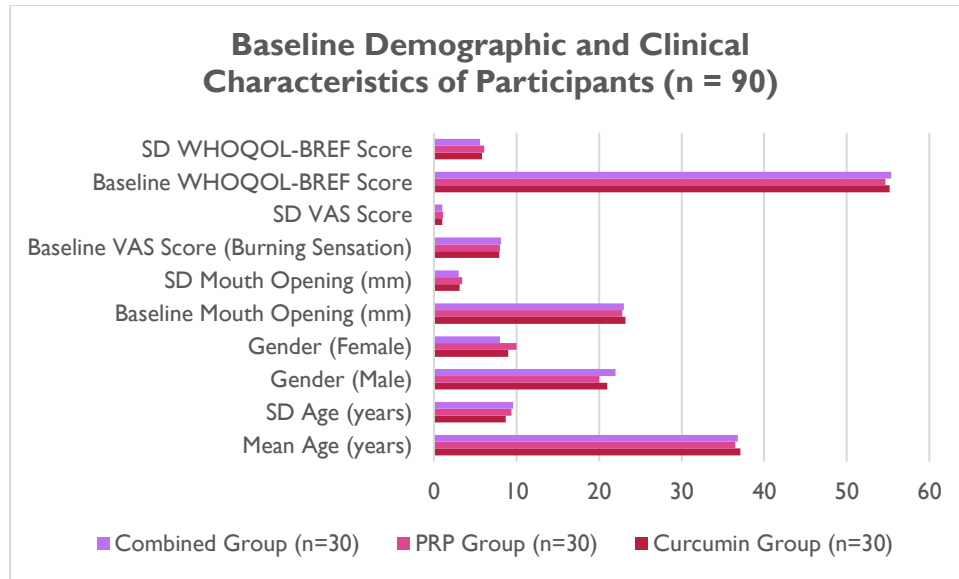


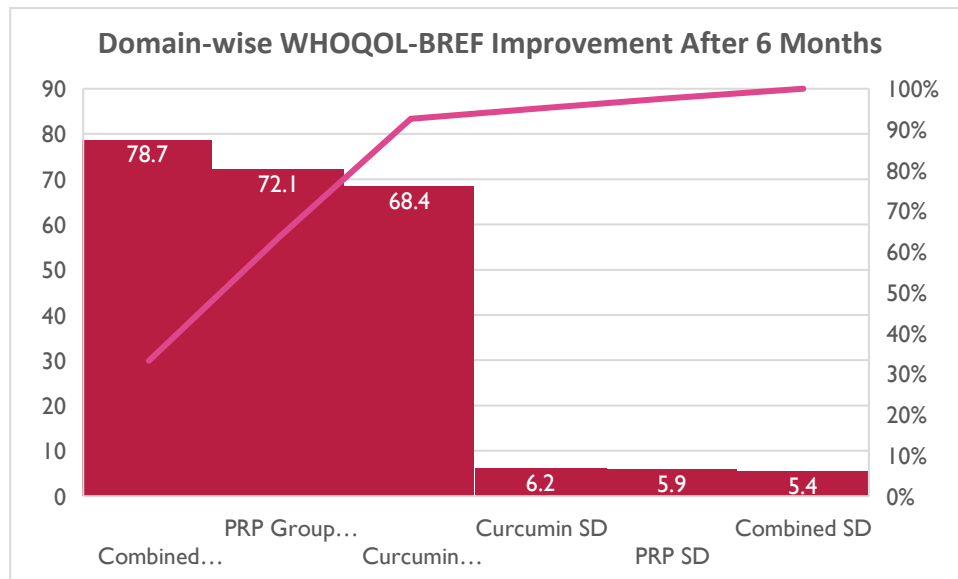
Table 2. Comparison of Clinical Outcomes at 6-Month Follow-up

Outcome Measure	Curcumin Group	PRP Group	Combined Group	p-value
Mean Increase in Mouth Opening (mm)	5.6 ± 1.8	6.8 ± 1.9	9.4 ± 2.1	<0.001
Mean Reduction in VAS Score	6.5 ± 1.1	6.9 ± 1.2	7.8 ± 1.3	<0.001
Mean Improvement in WHOQOL-BREF Score	14.6 ± 4.3	17.9 ± 5.1	23.8 ± 5.6	<0.001

Table 3. Domain-wise WHOQOL-BREF Improvement After 6 Months

Domain	Curcumin Group	PRP Group	Combined Group	p-value
Physical Health	68.4 ± 6.2	72.1 ± 5.9	78.7 ± 5.4	<0.001
Psychological Well-being	67.3 ± 6.8	71.2 ± 6.1	77.5 ± 6.0	<0.001
Social Relationships	66.5 ± 7.1	70.8 ± 6.7	76.9 ± 6.3	<0.001
Environmental Health	69.0 ± 5.9	72.4 ± 5.8	77.6 ± 5.5	<0.001

Figure: 2



The treatment of Curcumin and PRP together was noted to show statistically and clinically significant superiority in all of the outcomes measured. The synergistic effect was reflected in the improvement of the mucosal elasticity, pain reduction, and a considerable improvement in the quality of life scores of patients.

4. DISCUSSION

As it was shown, combined treatment of Curcumin and Platelet-Rich Plasma (PRP) produced considerably more improvement in mouth opening, reduction in burning sensation, and general quality of life than either Curcumin treatment or PRP treatment alone among oral submucous fibrosis (OSMF) patients did. These results are a very strong evidence that the synergistic approach which focuses on targeting both the inflammatory and regenerative pathways has better clinical advantages in the treatment of OSMF.

OSMF is a long lasting, progressive and debilitating oral dependent disorder with juxta-epithelial fibrosis and mucosal stiffness resulting in trismus and functional deficits. Although the use of numerous therapies modalities has been done over the years, no real curative agent is identified, and treatment is mainly aimed at stopping the disease progression and enhancing the functional performance of the patients. In that regard, Curcumin as a bioactive plant compounds of *Curcuma longa* has been thoroughly investigated to possess strong anti-inflammatory, antioxidant and antifibrotic properties. It suppresses the pro-fibrotic cytokines like transforming growth factor-beta (TGF- β) and tumor necrosis factor-alpha (TNF- α), therefore toning down fibroblast movement and collagen deposition. But, its bioavailability and local tissue penetration can not always be utilized effectively when utilized in solitude.

On the other hand, PRP is an autologous platelet concentration including a large repertoire of growth factors such as platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and transforming growth factor- β (TGF- β), which are essential in tissue repair and regeneration. PRP has demonstrated encouraging results in increasing mucosal elasticity, vascularity, and fiber-osis using collagen remodeling of neoangiogenesis. The current research showed that PRP when used as a monotherapy was comparatively better at relieving pains and improving functions than Curcumin monotherapy, which, as noted by Kiran et al. (2022) and Mishra et al. (2023), yielded significant improvements in mouth opening and reduction in burning sensation after PRP injections.

The increased results obtained using the Curcumin + PRP regimen could be explained by the complementary nature of the mechanisms of action. Whereas PRP promotes tissue regeneration and angiogenesis, Curcumin has a molecular effect that inhibits the pathways of chronic inflammation and fibrotic signaling. The two combined provide a biologically favorable climate to heal the mucosa and restore functionality. The findings of the current research have shown an average increase of 9.4 ± 2.1 mm in the mouth opening of the combination group- an increase that exceeds most of the traditional treatment results per literature. Also, the WHOQOL-BREF scores indicated that treating patients with combined therapy resulted in significant improvements in physical, psychological, and social well-being (comprehensive improvement in the quality of life).

Remarkably, there were few reported adverse effects which are severe in all the groups, which demonstrates high safety and tolerability of both Curcumin and PRP therapies. The compliance of the patients was high, which could be attributed to the

minimally invasive character of interventions and observable symptomatic improvement in the first three months. This agrees with the rising tendency to employ autologous and phytochemical-based treatment in chronic oral diseases because of the good safety profiles and natural regenerative characteristics.

Although these are promising findings, some shortcomings must be noted. The experimental group of the study took place in one center and is relatively small; this can diminish the application of the results obtained. Moreover, the six months follow-up period, though sufficient in determining initial results is not sufficient to ascertain medium term sustainability of therapeutic benefits. The results should be validated and refined with future intervention of multicenter randomized controlled trials with prolonged follow-ups and histopathological analyses.

To sum up, the latest research work gives a strong argument that integrated treatment with Curcumin and PRP works better than the alternative treatment in terms of changing the functional parameters and the overall quality of life of subjects with OSMF. This integrated modal is a promising, safe, and biologically viable development in the treatment of OSMF and should be considered to be included in the standard clinical practice.

5. CONCLUSION

In this study, it was clearly shown that combined Curcumin-PRP and PRP therapy result in a much more clinical and quality of life improvement compared to either Oral Submucous Fibrosis (OSMF) therapy. The synergistic action The strong anti-inflammatory and antifibrotic effects of Curcumin combined with the regenerative and angiogenic effects of PRP led to significant increases in mouth-opening, burning sensation, and overall QoL improvements in all domains. The safety and tolerability of this option of integrative approach are highlighted by the safety of this method. The results reveal that regenerative modalities and bioactive natural agents have therapeutic potential in addressing chronic oral fibrotic disorders. Nevertheless, larger cohort based multicenter studies with extended follow-up will be desirable to confirm these findings and to confirm having combined Curcumin + PRP therapy as a standardized treatment regimen in the management of OSMF.

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