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Original Research Article

Comparative evaluation of autologous platelet rich plasma and triamcinolone acetonide injection in the management of erosive lichen planus and oral submucous fibrosis: a clinical study

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ABSTRACT

Background: It is need of an hour to establish an effective and efficient treatment modality for OLP and OSMF with lesser or no adverse effects. Platelet rich plasma can be used in mucosal lesions as it has a high concentration of various growth factors and anti-inflammatory properties. It could be a better novel substitute to the corticosteroid without any side effects. The present study is an effort to evaluate the therapeutic effects of intralesional injection of PRP in oral erosive lichen planus and OSMF compared to intralesional corticosteroids in the same patient.

Methods: It was a randomized controlled clinical study consisting of 40 patients between the age groups of 18-60 years visiting dental OPD diagnosed clinically with either erosive lichen planus or OSMF. Triamcinolone 40 mg(1mg/ml) mixed with 2% (1:80,000) lignocaine hydrochloride was injected into the lesion on one side in case of erosive lichen planus and into the submucosal plane and fibrous bands in case of OSMF patients. Autologous PRP was prepared and injected on the other side in same patients. At every visit, all the patients were evaluated for pain and burning sensations, size, and severity of the lesion, and interincisal mouth opening (mm). The parameters were measured and recorded during the patient's every visit. All the results were obtained and statically analyzed.

Results: Intralesional injections of triamcinolone acetonide and PRP are effective in reducing pain and burning sensation in OSMF, but PRP is less effective in improving cheek flexibility as compared to triamcinolone acetonide. In OLP, both triamcinolone acetonide and PRP are almost equally effective in reducing the size of the lesion. However, PRP shows slightly better results in reducing the severity of the lesion and in pain and burning sensation in the patients of OLP as compared to intralesional triamcinolone acetonide.

Conclusions: Thus, PRP is an effective modality in treating both OSMF and oral erosive lichen planus with no adverse effects.

Keywords: Platelet rich plasma, OSMF, Erosive OLP, Triamcinolone acetonide, Intralesional injections

INTRODUCTION

Platelet-rich plasma (PRP) is a simple, efficient, and minimally invasive method of obtaining a natural concentration of autologous growth factors (GFs). Generation of PRP involves centrifugation of autologous blood to separate and extract the plasma and buffy coat

portion of the blood, which contain high concentrations of platelets. PRP has established use in the fields of dentistry, dermatology, plastic and maxillofacial surgery, acute trauma, cosmetic surgery, and veterinary medicine. The rationale for the widespread use of PRP in the healing process of such varied tissue types resides in the fact that platelets represent an easily accessible reservoir of critical

GFs and other signaling molecules, including leukocyte-derived catabolic cytokines and fibrinogen, which may govern and regulate the tissue-healing process. This milieu of bioactive molecules contributes to a well-orchestrated tissue-healing response to injury, which proceeds sequentially through the inflammatory, reparative, and remodeling phases of wound healing.¹⁻⁴ Very few studies have used this PRP in the treatment of potentially malignant disorders like Oral submucous fibrosis (OSMF) and Oral erosive lichen planus (OELP) which are difficult to treat.⁴ The main diagnostic clinical features of OSMF include blanching, mucosal stiffness, and limited mouth opening. On other end, Lichen planus is a chronic mucocutaneous inflammatory disease that frequently affects the oral mucosa, with predominance towards the middle age female patients. It has the tendency to be more chronic and more resistant to treatment. The most predominant type of OLP is the reticular type, which can be characterized by the presence of Wickham striae followed by the erosive type which is symptomatic and is associated with desquamative gingivitis.^{5,6}

Corticosteroids have been considered the first-choice agent for the management of both OLP and OSMF. Corticosteroids are especially helpful in the management of OLP and OSMF in view of their anti-inflammatory effect and anti-immunological properties. They are administered topically, systemically, or through intralesional injections.⁸ Intralesional steroid injections have been proposed as an effective and simple method with the aim of attaining sufficiently high drug concentration locally for an enhanced immune-suppressing effect but less systemic toxicity. The intralesional injection of Triamcinolone acetonide and dexamethasone has shown successful results in both OSMF and oral erosive lichen planus.⁹ However, continuous and prolonged use is associated with many systemic adverse effects such as bad taste, nausea, facial swellings, dryness, mucosal atrophy, candidal infection, granuloma formation, hypersensitivity reactions, delayed wound healing and in later stages; hypothalamus pituitary adrenal suppression.^{9,10} Therefore, it is the need of an hour to establish an effective and efficient treatment modality for OLP and OSMF with lesser or no adverse effects. PRP can be used in mucosal lesions as it has a high concentration of various growth factors and anti-inflammatory properties. It could be a better novel substitute to the corticosteroid without any side effects.

The emergence of PRP as a vehicle for localized delivery is supported by its simplicity, safety, availability, and potential cost-effectiveness. Unfortunately, despite the widespread use of PRP in so many areas, research on its clinical efficacy is still in its infancy. Although several animal studies have offered promising results, well-controlled human studies are lacking.^{10,11} Hence, the present study is an effort to evaluate the therapeutic effects of intralesional injection of PRP in oral erosive lichen planus and OSMF compared to intralesional corticosteroids in the same patient.

METHODS

It was a randomized controlled clinical study consisting of 40 patients between the age groups of 18-60 years visiting dental OPD diagnosed clinically with either erosive lichen planus or OSMF. Pain and burning sensation were evaluated using visual analog scale (VAS) graded on a point scale from 0-10 where 0 represents no burning sensation and 10 represents the worst burning sensation. All 40 patients were divided into group A and B according to the diagnosis. Group A consisted of 20 patients diagnosed with erosive lichen planus. In these 20 patients, on one side intralesional injection of triamcinolone mixed with 2% of local anesthesia was given and on the other side, freshly prepared intralesional injections of PRP were given. All the patients were given a weekly injection for 1 month and followed up for 4 months for assessing the parameters such as pain and burning, severity, and size of the lesion. Group B consisted of 20 patients diagnosed with OSMF. In these 20 patients, on one side intralesional injection of triamcinolone and other side intralesional injections of PRP were given. All the patients were given a weekly injection for 3 months and were followed up for 4 months for assessing the parameters such as pain and burning, cheek flexibility, and interincisal mouth opening. The interincisal distance was recorded in millimeters from the mesio-incisal angle of the maxillary central incisor to the mesio-incisal angle of the mandibular incisor using a vernier caliper or graduated measuring scale. The cheek flexibility was measured by drawing a line from the corner of the mouth to the point where it intersects with another line that was drawn vertically downward from the outer canthus of the eye. Aggressive physiotherapy was done for mouth opening with the help of a heister mouth gag for 30 minutes bilaterally at every visit after the intralesional injections were given. All 20 patients were trained to do mouth-opening exercises at home. Triamcinolone 40 mg(1mg/ml) mixed with 2% (1:80,000) lignocaine hydrochloride was injected into the lesion in case of erosive lichen planus and into the submucosal plane and fibrous bands in case of OSMF patients. Autologous PRP was prepared from the patient's blood using the centrifugal machine, working on 220V AC, 50 Hz with a built-in 5-speed regulator and maximum speed regulator and a maximum speed of 3500 rpm and then injected on opposite side. At every visit, all the patients were evaluated for pain and burning sensations, size, and severity of the lesion, and interincisal mouth opening (mm). The parameters were measured and recorded during the patient's every visit. All the results were obtained and statically analyzed.

RESULTS

Age and sex distribution of OSMF and Lichen Planus

Out of the total of 40 patients, 20 patients were of oral submucous fibrosis and 20 patients were of oral lichen planus. The 20 patients with oral submucous fibrosis included 19 (95%) males and 1 (5%) female in the age range from 18 to 60 years with a main age of 32.5 years

and a standard deviation of ± 6.765 (Table 1, Figure 1). The 20 patients with oral erosive lichen planus included 5 (25%) males and 15 (75%) females in the age range from 18 to 60 years with a mean age of 35.75 years and a standard deviation of ± 8.746 .

Interincisal mouth opening in oral submucous fibrosis

The mean interincisal opening preoperatively was 22.75 ± 2.807 and at the end of the treatment, mean interincisal distance was 36.65 ± 3.631 . The mean difference is 13.90 ± 3.007 . Thus, by performing the combined 't' test the subjects showed a highly significant difference in the interincisal opening which was highly significant with a p value < 0.001 (Figure 1-2).

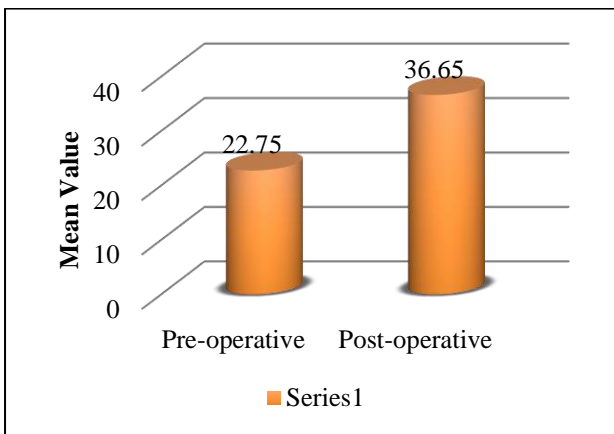


Figure 1: Difference in interincisal mouth opening pre and post-operative after intralesional injections in OSMF patients.



Figure 2: difference in pre and post-operative interincisal mouth opening.

Cheek flexibility in oral submucous fibrosis

In 20 subjects the cheek flexibility increased significantly on the side of triamcinolone acetonide injection as compared PRP side. On the triamcinolone side, 65% of patients showed 2-4mm improvement in cheek flexibility and 30% of the patients showed 4-6 mm improvement in cheek flexibility which was highly significant as compared to the PRP side with p value < 0.001 (Figure 3-4).

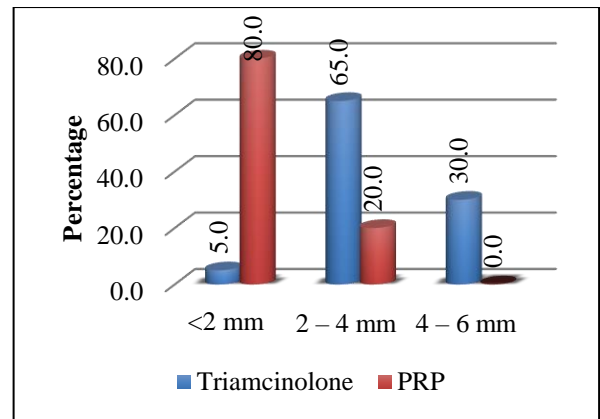


Figure 3: The difference in cheek flexibility post-operatively after intralesional Triamcinolone and PRP injection in OSMF patients.



Figure 4: The difference between the cheek flexibility when the patient inflates his cheeks.

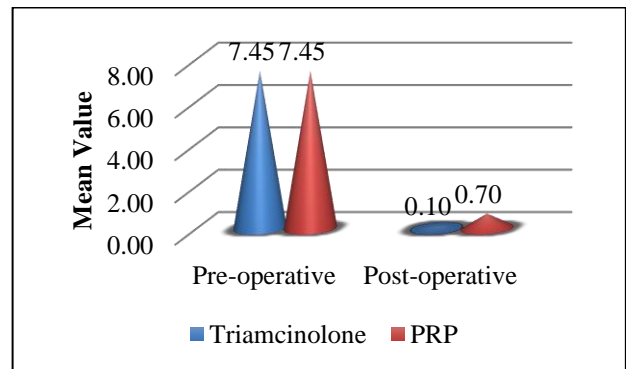


Figure 5: The mean difference in pain and burning sensation score pre and post-operatively after intralesional Triamcinolone and PRP injection in OSMF patients.

Pain and burning sensation in oral submucous fibrosis

In 20 subjects, the VAS score significantly decreased i.e., from 7.45 ± 1.191 to 0.10 ± 0.308 for pain and burning sensation on the side of triamcinolone acetonide injections compared with VAS score reduction on the side of platelet-rich plasma injections which was from 7.45 ± 1.191 to 0.70 ± 0.865 at the completion of 10 weeks. By performing

the Wilcoxon signed rank test, the 'Z' value is 2.588 postoperatively which was significant with the p value 0.010 (Figure 5).

Size of the lesion in oral erosive lichen planus

In 20 subjects, there was a significant decrease in the size of the lesion on both the sides. At the first visit, on the side of triamcinolone acetonide injections, 100% of the patients lesion size was more than 1cm² and on the side of platelet-rich plasma injections, 85% of the patient have >1cm². Then after the 2nd and 3rd visits, a significant decrease was seen on both the sides. After 4th visit on both the sides almost the same result was obtained i.e., in 75% of the patients the size of the lesion was completely resolved with the P value 0.008 which was significant. (Figure 6-10).



Figure 8: Post-operative images of oral erosive lichen planus patient on the side of PRP injection.

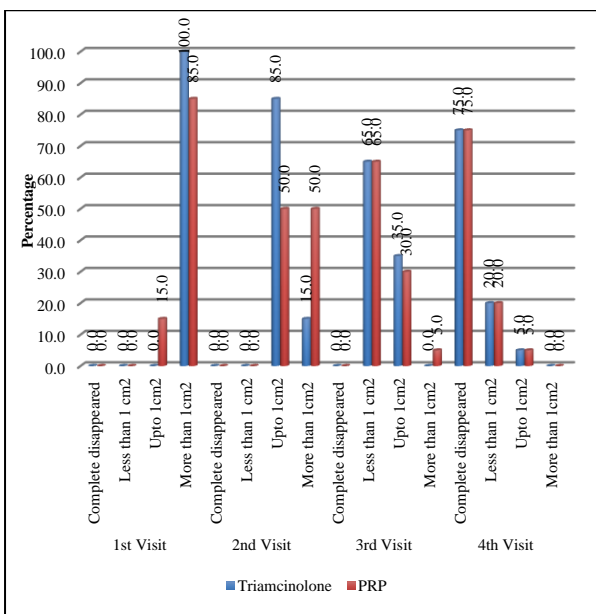


Figure 6: Decrease in the size of the lesion in different groups at different intervals of time during weekly visits in lichen planus patients.



Figure 9: Preoperative images of oral erosive lichen planus patient on the side of triamcinolone acetonide injections.



Figure 7: Preoperative images of oral erosive lichen planus patient on the side of PRP injections.



Figure 10: Post-operative images of oral erosive lichen planus patient on the side of triamcinolone acetonide injections.

The severity of the lesion in oral erosive lichen planus

In 20 subjects, at the first visit, the severity of the lesion on both the sides was almost equal that is 80% of the patients showed moderate erythema. The p value at the first visit was 0.046. After the second and 3rd visits, a significant result can be seen in the patients on both the sides. On the side of triamcinolone acetonide injections, 75% of the patients showed only keratosis and on the side of platelet-rich plasma injections, 65% of the patients showed only keratosis and the lesion almost healed completely. At the end of 4th visit, on the side of triamcinolone acetonide injections around 25% of the patients showed complete resolution of the lesion and on the side of platelet-rich plasma injections around 70% of the patients showed complete resolution of the lesion (Figure 11).

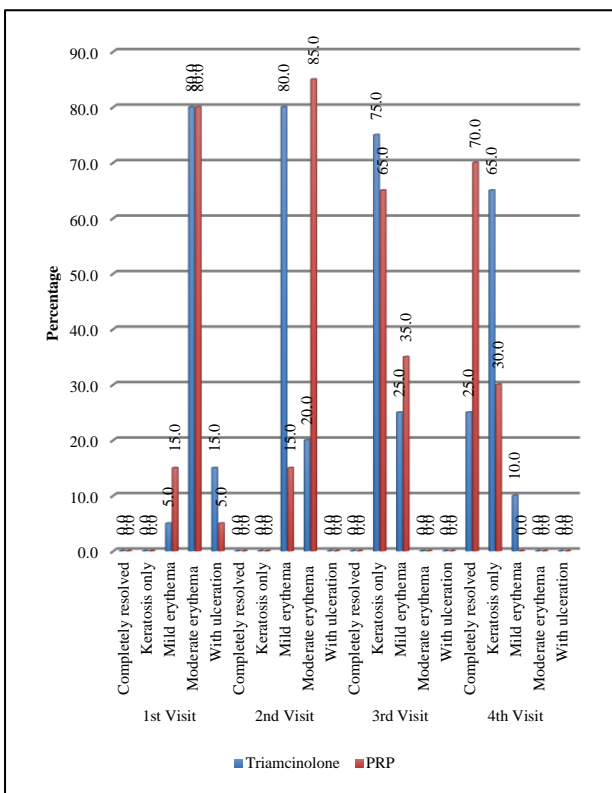


Figure 11: Decrease in the severity of the lesion in different groups at different intervals of time during weekly visits in lichen planus patients.

Pain and burning sensation in lichen planus

In 20 subjects, the VAS score significantly decreased i.e., from 8.60 ± 0.883 to 0.25 ± 0.716 for pain and burning sensation on the side of platelet-rich plasma injections compared with VAS score reduction on the side of triamcinolone acetonide injections which was from 8.65 ± 0.813 to 0.55 ± 0.999 at the completion of 4 weeks. By performing the Wilcoxon signed rank test, the 'Z' value is 1.511 postoperatively. The p value was 0.131 which was not significant (Figure 12).

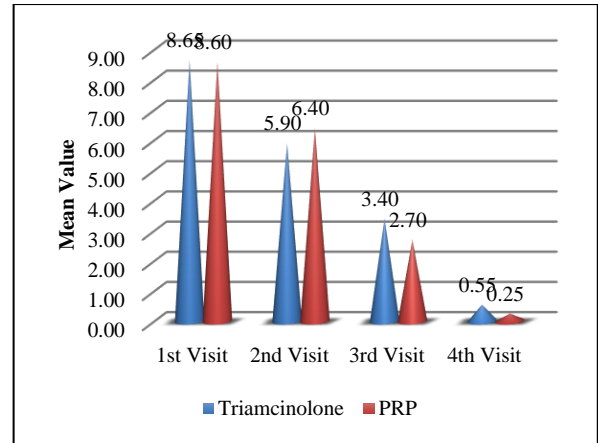


Figure 12: Mean difference in pain and burning sensation score at different time intervals after intralesional triamcinolone and PRP injection in lichen planus patients.

DISCUSSION

Due to the several side effects of the current treatments, there is a need to establish an effective and efficient treatment modality for erosive OLP and OSMF with lesser or no adverse effects. Platelet-rich plasma (PRP) is the concentrated plasma of the patient's blood that contains a high concentration of platelets along with increased growth factors (GFs). PRP is emerging as an increasingly demanding clinical application as an alternative source of GFs for several dental procedures and oral mucosal lesions.² Activated platelets release various GFs, such as platelet-derived GFs, transforming GF, fibroblast GF, and vascular endothelial GFs; these are the main contributing and leading factors for cell proliferation, differentiation, neo-angiogenesis, toxins withdrawal, and cellular regeneration. PRP decreases the associated morbidity and promotes wound healing with anti-inflammatory action. On the other hand, no adverse effects had been linked to PRP application and because it is usually prepared using the patient's blood it does not elicit any immunological or allergic reactions.¹⁻³ The rationale for conducting this study was to provide a safe alternative treatment for patients suffering from OSMF and resistant erosive OLP, which had proved a promising regenerative potential in the management of several refractory skin and mucosal lesions. Hence, the present study was done to evaluate the therapeutic effects of intralesional injection of PRP in oral erosive lichen planus and OSMF compared to intralesional corticosteroids in the same patient.

All participants in the present study were free from any systemic disease that compromise the diagnosis of idiopathic OLP and OSMF, nor taking drugs that affected platelet function. A review of the medical literature reveals that there is no significant published study either documenting the use of PRP in managing OSMF or comparing its effect with intralesional steroids. Yet they took an idea of improvement in Maximal inter incisal distance by comparing the results of different studies.

Regarding PRP, in dentistry, several studies have been done for the treatment of chronic inflammatory diseases and those which aid in bone regeneration in postoperative cases of alveolar or jaw diseases. In otorhinolaryngology, the use of PRP as a biological graft material for the repair of tympanic membrane perforation was used which gave a 100% success rate. Hence, our study was selected so that we can show the significant result of PRP in treating OSMF. In patients of OSMF, results revealed that administration of PRP injection at the fibrosis site of OSMF proved to be more significant in subsiding the symptoms in younger male patients. This might be due to the production of one of the growth factors i.e., PDGF by platelets, which is recognized as an important protein for hard- and soft-tissue healing.

In addition, platelets serve as the greatest source of specific growth factors, which enhance the healing of injuries by enhancing granulation tissue development and subsequent mitosis division, vascular synthesis, macrophage activation, and concomitant activation of other growth factors. At the injury site, PDGF has been observed to be stimulated the accumulation and migration of stem cells. Consequently, leads to the synthesis of matrix bone formation and angiogenesis by stimulating increased levels of VEGF. This might lead to activated soft-tissue healing just because of the neovascularisation process taking place. In a study conducted in Karachi Pakistan, male to female ratio in patients of OSMF was found to be 7:1 showing the male preponderance in this group of the Pakistani population. This is in accordance with the findings of our study thus indicating a similar pattern in the Indian population. Recently, Hydri compared the effect of triamcinolone versus platelet rich plasma (PRP) injection intraorally for improving trismus in oral submucous fibrosis (OSMF).¹² There was a male preponderance in the study group with a male-to-female ratio of 5.1:1. In group 'A', the mean pre-treatment MIID was 2.3 ± 0.7 cms, while in group 'B', it was 2.2 ± 0.5 cms. After the completion of 6 weeks of treatment, the mean MIID improved in group 'A' to 3.08 ± 0.8 cms, and in group 'B' to 3.22 ± 0.5 cms. The mean improvement in MIID in group 'A' was 0.783 ± 0.25 cms compared to 1.01 ± 0.05 cm in group 'B' ($p < 0.05$). Thus, the results of intralesional PRP were better in this study. This is in contrast to our study where we found that triamcinolone intralesional injections showed better results in improving cheek flexibility and burning sensation in comparison with PRP.

Lichen planus is a chronic, potentially malignant, mucocutaneous, inflammatory, immunological disease having preponderance towards middle-aged females, that frequently affects the oral mucosa and it usually tends to be more persistent and immune to treatment. Oral erosive lichen planus (OELP) has been estimated to affect 0.5%–2% of the general population. The present study also shows that oral Lichen Planus is more prevalent in middle-aged females. Erosive forms of Oral erosive lichen planus were selected in our study. In the patients of oral erosive lichen planus, our study showed that pain, burning sensation, and

severity of the lesion improved better on the side where intralesional PRP was administered as compared to the side where intralesional triamcinolone injections were administered. Sobhy et al applied intralesional PRP injections for five sessions with 2 weeks intervals with no side effects or lesion recurrence; Sethi Ahuja et al reported significant lesion size reduction with no recurrence on the eighth week of treatment with intralesional PRP injections when selecting a treatment plan of weekly injections for 4 weeks which is consistent with the present study as no recurrence of lesions were seen on the side of intralesional PRP administration.¹³

More recently, Bennardo et al, reported no statistically significant difference in pain scores after 8 weeks of intralesional injections of injectable platelet-rich fibrin (i-PRF) compared to intralesional injections of TA for the treatment of symptomatic OLP which is in contrast to our study.¹⁴ Our results had shown a significant reduction in pain scores in both groups after 2 months of follow-up after treatment. In addition, there was a statistical difference between both the sides in the same patient at 4 weeks period in terms of pain reduction and extent of the lesion. These findings are in accordance with the previous work of Sobhy et al who used PRP intralesional injections for recalcitrant OELP patients.¹³

To assess pain and burning, the VAS scale was used in the present study. Ahuja, et al compared intralesional PRP and triamcinolone acetamide applications in OELP lesions by measuring changes in VAS-pain values during 4 months of follow-up.¹³ They reported that both applications were successful and had similar effectiveness. Likewise, Bennardo, et al compared the 4-week results of PRF and triamcinolone acetamide injected therapies in patients with OLP patients in a split-mouth study.¹⁴ The authors reported a mean decrease of 47.6% in the VAS score for PRF-treated sites; the decrease in the score for the triamcinolone acetamide-treated sites was 40%. The study reported no statistically significant difference between the groups; however, the authors stated that PRF is as effective as triamcinolone acetamide at reducing VAS-pain values for OLP lesions. Our study showed that baseline VAS-pain levels were high and that VAS-pain values decreased significantly on the 2nd, 3rd, and 4th visit.^{13,14} Extensive past research has proven the effectiveness of intralesional steroids in the treatment of Oral Lichen planus as seen in studies conducted by Chuanxia et al, Chan et al, Xia et al.¹⁴⁻¹⁵ In the present study also intralesional triamcinolone has shown good results on the side of its administration. On comparing both the groups, no statistically significant differences were observed on both the sides in reducing the size of the lesion. However, statistically significant differences were observed in relation to pain and burning sensation and severity of lesion where PRP showed significantly better result.

The success of our research was that PRP significantly showed improvements in symptoms of OSMF & OLP without any adverse effects. The small sample size and

relatively short follow-up period are the main limitations of the current study. Moreover, challenges in standardization of baseline measurements such as lesion site, size, and pain score were also found during patients' recruitment. These limitations may have affected the overall estimation of the PRP injections' healing effect. Further studies with a larger sample size would allow for stronger prediction related to effectiveness of PRP in OLP and OSMF. In the present study, the blood was collected every week for fresh PRP preparation. For some patients, it might be a concern to provide blood samples every week for PRP preparation. Thus, in the future, some methodology that can allow collected blood to be used multiple times for preparing PRP could prove to be more beneficial. In the future, we recommend further studies on PRP in treating OSMF and Oral erosive lichen planus on a larger sample size.

CONCLUSION

Intralesional injections of triamcinolone acetonide and PRP are effective in reducing pain and burning sensation in OSMF, but PRP is less effective in improving cheek flexibility as compared to triamcinolone acetonide. In OLP both triamcinolone acetonide and PRP are almost equally effective in reducing the size of the lesion. However, PRP shows slightly better results in reducing the severity of the lesion and in pain and burning sensation in the patients of OLP as compared to intralesional triamcinolone acetonide. One of the major highlights of using intralesional PRP is that there is no adverse effects or recurrence of lesions at the side of its administration. However, lesions recurrence was seen on the side of intralesional triamcinolone acetonide administration in lichen planus. Thus, PRP is an effective modality in treating both OSMF and oral erosive lichen planus with no adverse effects.

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Conflict of interest: None declared

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

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