

CLINICAL EVALUATION OF THE EFFICIENCY OF INTRALESIONAL INJECTION OF AUTOLOGOUS PLATELET RICH PLASMA IN TREATMENT OF EROSIIVE ORAL LICHEN PLANUS

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ABSTRACT

Oral lichen planus (OLP) could be a doubtless malignant autoimmune disease, characterized by burning and pain that reduces the standard of patient's life. Treatment of OLP remains a significant challenge despite the recent advances in understanding the immunopathogenesis. The properties of Platelet-rich plasma suggested its application in clinical practice for treatment of OLP patients that do not respond to conventional therapy. This study aims to evaluate the effectiveness of intralesional Platelet rich Plasma (PRP) in treatment of Erosive lichen planus.

Materials and methods: The study sample consisted of 10 patients of erosive OLP among which were given intralesional PRP. All the patients were given weekly injections for 4 weeks. The two fundamentals variables used for assessment of the patient is pain control and healing of the lesion. Each visit consists of measuring the target lesion size and pain evaluation by visual analogue scale (VAS) .

Results: No serious adverse reaction was obtained in patients during the 4 weeks of treatment. The result was satisfactory with a significant reduction in patient symptoms. Reduction in terms of size and inflammation was observed.

Conclusion: This methodology of using intralesional PRP showed to be effective in decreasing the symptoms and improvement in clinical signs of OLP, which was resistant to conventional therapy.

KEY WORDS: Intralesional PRP, Erosive OLP, potentially malignant

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INTRODUCTION

Oral lichen planus (OLP) is a persistent autoimmune disease with a predominance of 1-2% within the common population that most commonly influences middle-aged and elderly female^(1,2). It has been outlined as a potentially malignant disorder of the oral cavity⁽³⁾. According to the World Health Organization (WHO), the estimated malignant changes rate changes from 1.09 to 1.14%⁽⁴⁾. Despite of extensive studies, the etiology and pathological process of OLP remains obscure. Different variables such as genetic predisposition and psychological factors, may be included in the development of OLP^(5,6).

Whereas the etiology is not totally understood, a cell related immune reaction probably plays a serious role. Cytotoxic T cells (CD8-positive T cells) particularly cause apoptosis of keratinocytes at the basal membrane⁽⁷⁾.

OLP is a chronic, persisting disorder of immunologic background, treatment is principally targeted on pain reduction and healing of the lesion. It is significantly difficult and at risk of failure within the erosive OLP treatment is mainly focused on pain reduction and healing of the lesion. It is particularly challenging and prone to failure in the erosive OLP due to its high resistance and recurrence. Treatment of symptomatic OLP is challenging. Several drugs are used with varied efficacy. Specific treatment includes corticosteroids (topical or systemic), cyclosporine, tacrolimus, retinoids and dapsone⁽⁸⁾.

These immunosuppressants are limited in their application due to the adverse effects related to their long-term use. Erosive OLP may be refractory to all currently accessible therapies and new therapeutic agents require assessment⁽⁹⁾.

PRP is a new approach in tissue regeneration and a developing area for clinicians and researchers. It is used in various surgical fields, including oral and maxillofacial surgery. PRP is prepared from the patient's own blood and contains growth factors that influence wound healing. Example of these growth

factors are (platelet-derived growth factor, transforming growth factor, vascular endothelial growth factor, fibroblast growth factor insulin-like growth factor, and epidermal growth factor) which play a pivotal role in tissue repair mechanisms⁽¹⁰⁾.

Platelet related growth factors should have a beneficial role in enhancing numerous medical specialties, as dentistry, orthopedics, maxillofacial surgery, and cosmetic surgery for over three decades⁽¹¹⁾.

Bolanča, et al stated the benefit effect of using PRP injections in lichen planus resistant to intralesional corticosteroids. Another study reported significant clinical improvement of resistant oral erosions in patients with pemphigus vulgaris after intralesional injection of PRP^(12,13).

MATERIALS AND METHODS

The study group comprised of ten Patients diagnosed histopathologically with oral erosive Lichen Planus, with no extra oral lesions presenting to the Oral Medicine and Periodontology Department, Faculty of Dentistry, Mansoura University in Egypt. Among them were 7 females and 3 males. Age from 50 to 65 years. Those Patients were resistant to conventional therapy.

All patients were diagnostic for erosive oral lichen planus made based on clinical findings such as grayish white lesion with reticular pattern with varying degrees of ulceration present on the cheek mucosa, dorsum surface of the tongue and lips. One case had the lesion on the hard palate as well as on the cheek mucosa. These symptoms were all accompanied by pain, difficulty in eating and rough sensation.

The protocol was approved by the Ethics Committee of the faculty of Dentistry Mansoura University with no (A01111120).

All the selected patients were educated about all the procedures that will be done and signed the consent form of Ethical committee in the faculty of Dentistry Mansoura University.

The inclusion criteria for the study were:

1. Lack of response to conventional therapies for erosive lichen planus.
2. All patients participating in the study had discontinued any medication for the lesion six months before starting the study.

Patients with history of renal disease, malignancy, hematological diseases, cardiovascular diseases, and Diabetes were excluded and also patients who took any drugs which may cause lichenoid reaction.

Socio demographic data, such as age, gender and job status were recorded as well as oral symptoms, oral clinical features, and oral localizations of the lesions.

Digital photographs were taken of the target site using digital camera.

They were repeated on each clinical visit (once weekly) for four weeks to evaluate clinical outcome or response. Patients were followed up for two months after the stoppage of the treatment.

Subjective index or outcome variable:

The two fundamentals variables used for assessment of the patient is pain control and healing of the lesion. Each visit consists of measuring the target lesion size and pain evaluation by visual analogue scale (VAS) ⁽¹⁴⁾.

The lesions were measured on their longest dimension. The symptomatology score was obtained using the VAS which consists of a 10 cm horizontal line marked 0 to 10 (0=no pain; 10=most severe pain). This measurement was done at each visit.

Total resolution of the clinical signs (complete response) was characterized by the disappearance of the lesions. Scores were either 0 or 1.

Total resolution of the symptoms (no symptoms) was outlined as the absence of discomfort corresponding to a VAS score of 0 partial response or getting worse or persistence of the patient's

condition meant a decrease or increase or no modification respectively in patients score. The distinction between baseline and endpoint scores numerically outline the clinical and symptomatic improvement.

Preparation and Application of PRP:

Each patient was withdrawn 10 cm. of blood intravenous, then the blood is drawn into a tube containing an anticoagulant to avoid platelet activation and degranulation. The first centrifugation is termed soft spin, Separation into three layers, namely bottom – most RBC layer (55% of total volume), top-most a cellular plasma layer called PPP (40% of total volume) called the buffy coat.

Using a sterile syringe, Platelet poor plasma (PPP), PRP and some RBCs were transferred into another tube without an anticoagulant. This tube undergone a second centrifugation, which is longer and faster than the first, termed ‘ hard spin’. This permits the platelets (PRP) to settle at the bottom of the tube with a very few RBCs. The acellular plasma, PPP (80 % of the volume), is found at the top. Most of the PPP is removed with a syringe and discarded, and the remaining PRP is shaken well.

Each patient was injected with 0.5 ml of autologous PRP per 1cm² of the ulcerated mucosa using a 25-gauge needle once weekly for 4 weeks, total of 4 injections has been injected for each patient. Patients were recalled after 2 weeks of the last injection to obtain the end point measures. Patients were followed up for 2 months and were told to return to the clinic to report any flare episodes of the disease.

Statistical analysis

The data were analyzed using SPSS® software version 22 (SPSS Inc., Chicago, IL, USA). The data was non-parametric and violated the normal distribution. To detect significant differences between observation times, Friedman test was used followed by Wilcoxon signed ranks test to compare between two times. P-values <0.05 were significant.

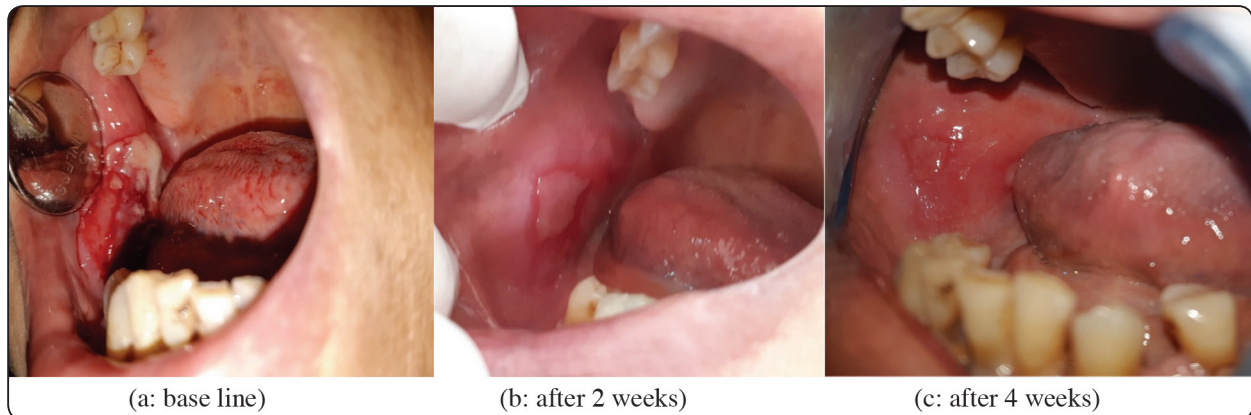


Fig. (1) A case with erosive Lichen planus at base line until 4 weeks after treatment.

RESULTS

Ten patients with erosive OLP were enrolled in the study. All patients were symptomatic and had only oral lesions without any skin lesions. Duration of the lesion ranged from six months to one year. All patients included in the study were free from any systemic disease.

The lesions were mostly on the cheek mucosa and the tongue. One case had the lesion on both the cheek mucosa and the hard palate. Another case had the lesion on the tongue and the lower lip.

Patient's complaints were described as severe pain or burning sensation with difficulty to eat and drink.

No serious adverse reaction was obtained in patients during the 4 weeks of treatment. The result was satisfactory with a significant reduction in patient symptoms. Reduction in terms of size and inflammation was observed (Fig 1).

Comparison of VAS between observation times is presented in table 1. There was a significant difference in median scores of VAS between observation times. The VAS decreased significantly with advance of time ($p < .001$). The VAS decreased from 1st day to 1st week, but the difference was not significant. Also, no significant difference in VAS scores

between 1st and 2nd weeks was observed. However, a significant decrease in VAS from base line to the 2nd week, to the 3rd week, and to the 4th week was noted. Also, the decrease in VAS between 2nd week and 3rd/4th weeks was significant. However, the difference between 3rd and 4th weeks was not significant. Multiple comparison between each 2 observation times is presented in the same table. Errors bars representing the change in median scores of VAS with advance of time are presented in fig (2).

TABLE (1) Comparison of VAS between the Base line time and 4 weeks intervals

	M	Min	Max	X	SD
Baseline day	10.00a	9.00	10.00	9.80	.42
1st week	8.00a, b	7.00	8.00	7.80	.42
2nd week	6.50b	3.00	7.00	6.00	1.41
3rd week	2.50c	1.00	3.00	2.40	.70
4th week	1.00c	1.00	2.00	1.30	.48
Freidman test	$<.001^*$				

M: median, Min: minimum, Max: maximum X: mean, SD: Standard Deviation. Different letters indicate a significant difference between median of evaluation times (Wilcoxon signed ranks test).

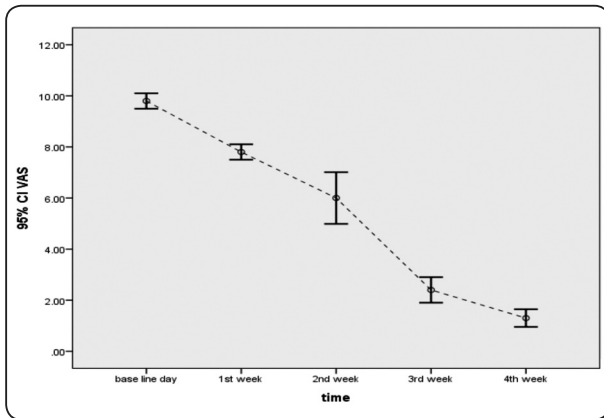


Fig. (2) Errors bar representing the change in median scores of VAS with advance of time

Thongprasom scale

Comparison of Thongprasom scale between observation times is presented in table 2. There was a significant difference in median scores of Thongprasom scale between observation times. The scale decreased significantly with advance of time ($p < .001$). The scale decreased from 1st day to 1st week, but the difference was not significant. Also, no significant difference in scale scores between 1st and 2nd weeks was observed. However, a significant decrease in scale from base line to the 2nd week, to the 3rd week, and to the 4th week was noted. Also, the decrease in Thongprasom scale between 2nd week and 3rd/4th weeks was significant. However, the difference between 3rd and 4th weeks was not significant. Multiple comparison between each 2 observation times is presented in the same table. Errors bars representing the change in median scores of Thongprasom scale with advance of time are presented in fig (3)

TABLE (2) Comparison of Thongprasom scale between observation times

	M	Min	Max	X	SD
Baseline day	5.00a	.00	5.00	5.00	5.00
1 st week	4.10a, b	.57	4.00	3.00	5.00
2 nd week	3.10b	.99	3.00	1.00	4.00
3 rd week	1.70c	.67	2.00	1.00	3.00
4 th week	1.10c	.32	1.00	1.00	2.00
Freidman test	$<.001^*$				

M: median, Min: minimum, Max: maximum X: mean, SD: Standard Deviation. Different letters indicate a significant difference between median of evaluation times (Wilcoxon signed ranks test).

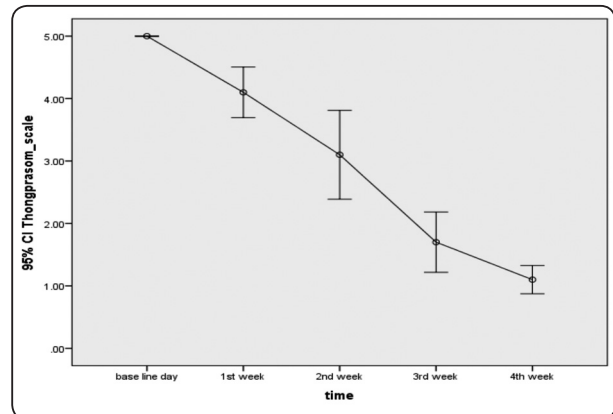


Fig. (3) Errors bar representing the change in median scores of Thongprasom scale with advance of time

DISCUSSION

Treatment of erosive OLP is challenging. Different treatment modalities are reported aiming at controlling the disease rather than inducing remission. Erosive OLP typically persists for long periods of time and rather simply relapse after treatment. OLP tends to have a chronic course, hence there is require for more viable and more secure treatments for symptomatic OLP⁽¹⁵⁾.

Topical steroids considered as initial alternative for severe cases, systemic steroids are considered as treatment of choice, however prolonged use ought to be avoided due to its adverse effects like mucosal atrophy, candidiasis, hypertension, and hyperglycemia⁽¹⁶⁾. Immunosuppressive agents influence the severity and progression of OLP but however in theory they may conjointly trigger malignant transformation. Despite several different treatment modalities as well as natural agents like curcumin, aloe vera, vitamin A, still OLP tends to be resistant and recurrence is common^(17,18).

In our study, we have selected a group of recurrent erosive OLP, whose oral symptoms were not responding to conventional therapies of OLP. Interestingly, all the ten patients in the study reported a complete remission of oral discomfort as well as a good response rate on their quality of life at the end of the study. There were no reported relapse or recurrence of the lesion after cessation of therapy up to three months.

A case study of non-responding Lichen Planus was treated by rinses of PRP and showed a relived symptom after PRP therapy, however the use of conventional method as steroids and laser was with no value in providing comfort and relief, Thus PRP could be an effective treatment in patients resistant to conventional therapies in OLP⁽⁸⁾.

Lore et al.⁽¹⁹⁾ in a pilot study compared the effect of PRP gel with cyclosporine mouthwash and retinoic acid lotion in different OLP phenotypes. They concluded that PRP is to be used in erosive type, which proved to be effective when applied once weekly.

Mehdat EL-Komy et al, in their pilot study on a resistant oral erosion of pemphigus vulgaris treated with weekly injections of PRP, an improvement was reported in healing of oral lesions and decrease in pain and discomfort associated with oral ulcers and erosions.⁽¹³⁾

Our results are with coincides with the study⁽²⁰⁾ that utilize of PRP in erosive OLP was found to be comparative and identical in its effectiveness to corticosteroids.

The growing use of blood-derived products is directly related to their combination of potency and safety for various wound-healing processes. In a systematic review, Martínez-Zapata et al. described the efficacy of autologous PRP in randomized controlled trials (RCTs) on oral and maxillofacial applications, chronic skin ulcers, and wound healing after surgery& analyzed the safety profile for PRP concluding that there is no proof for any reflection between PRP and unfavorable events.⁽²¹⁾

CONCLUSIONS

PRP showed to be safe and effective in improvement of clinical signs and symptoms of erosive OLP, which was resistant to conventional therapy. Further investigations by larger sample and longer follow up are required to approve this method as a standard treatment modality for patients with resistant erosive OLP

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