

Original Research Article

Effect of intralesional platelet rich plasma in chronic localized vitiligo

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ABSTRACT

Background: Vitiligo is a disease caused by destruction of melanocytes in lesional skin. It occurs worldwide in occurrence of 0.1 to 2.0 percent. It is a multifactorial polygenic disease with complex pathogenesis. Several treatments, old and new are advocated for such patients. The first line of treatment includes topical corticosteroids and calcineurin inhibitors, and phototherapy (NB-UVB, PUVA). The second line of treatment includes systemic corticosteroids, topical calcipotriol 0.005%, lasers such as excimer laser (308 nm). The aim of the study was to evaluate the efficacy of platelet rich plasma in 40 cases of stable vitiligo with less than or equal to 1% body surface area involvement.

Methods: 40 cases of stable vitiligo not responding to adequate topical therapy for more than 1 year were included in the study. They were subjected to intralesional injections of freshly prepared autologous platelet rich plasma (PRP) by double spin technique. Each patient was given injections every 2 weekly intervals for a total of 6 injections. Results were evaluated using the vitiligo area severity index (VASI) score.

Results: Out of 40 patients 15 Patients showed good response, 12 patients showed Average response and 13 patients showed no response to treatment according to VASI score.

Conclusions: PRP may be considered as an additional therapy in patients not responding adequately to traditional therapies. Our patients were not subjected to histopathology. It was also felt that patients might require more than 6 sittings for complete repigmentation.

Keywords: Vitiligo, PRP, VASI score

INTRODUCTION

Vitiligo is a disease that occurs due to destruction of melanocytes with a worldwide incidence of 0.1 to 0.2%. It is a disease with immense psychosocial impact though it is not life threatening.¹ Traditional therapies for repigmentation, including topical agents and phototherapy, remain mainstays of current treatment. Topical treatments include corticosteroids, calcineurin inhibitors, and vitamin D analogues. Phototherapy treatments include narrowband UVB (NB-UVB) or psoralen and UVA (PUVA).² However the search for new

and faster responding treatment in vitiligo either alone or in combination with other modalities is always on. Platelet rich plasma is a new break through in soft tissue healing. It contains platelets in a concentration of 7 times the normal blood level (about 1 million) by virtue of which several growth factors are made available to the tissue where it is used.

Aims of the study

- To evaluate the outcome of intralesional autologous platelet rich plasma in chronic patches of vitiligo

involving limited surface area of the body (<1% i.e. less than or equal to one hand unit)

- To study of safety profile of intralesional PRP therapy in vitiligo.

METHODS

A total of 40 patients of stable vitiligo attending the the outpatient clinic of dermatology and venereology department, Dhiraj General Hospital, Pipariya, Vadodara were screened. The patients with depigmented patches involving less than 1% body surface area with inadequate response to conventional line of treatment for over one year were enrolled in the study, after obtaining the approval of the research ethics committee of Sumandeep vidyapeeth. The study duration was one year (September 2016 to August 2017).

Patients who had stable lesions [absence of newer areas of depigmentation or enlargement of the pre-existing lesions for 12 months and absence of Koebner phenomenon during the same period] were included. Disease severity was assessed according to vitiligo area severity index (VASI). Those patients with VASI ranging from 90-100 on first visit with less than 1% body surface area were enrolled in the study. Pregnant or lactating females and young patients below 12 years were excluded from this study. Informed consent was taken from every patient in adults and from guardians in children. Clinical photographs were taken at every sitting. Using an insulin syringe, 5-10 units of PRP were injected intradermally into every depigmented patch, every 2 weeks for 12 weeks. Patients were counselled to apply Tacrolimus (0.03%) ointment in the night and Placental extract gel in the morning daily during the entire duration of the study. Multivitamin supplement was also started. Each patient was explained to expose the part to sunlight daily morning for 10 minutes. The patients were called back every 2 weeks for the subsequent injections till a total of 6 injections. The patients were followed up monthly for a period of 3 months after cessation of injections.

PRP preparation technique^{3,4}

10 ml of blood was withdrawn from ante cubital vein under aseptic conditions. PRP was prepared by the double spin technique. The initial centrifugation was done ("soft" spin) at 3000 rpm for 7 min to separate the plasma and platelets from the red and white cells. The resulting plasma supernatant, containing the suspended platelets (and may contain a portion of the white cell "buffy coat") was harvested and subjected to a second centrifugation step ("hard" spin) at 4000 rpm for 5 min, leading to separation of the plasma into 2 portions:- platelet-poor plasma (PPP) and PRP. Typically, the lower 1-2 cc of the plasma (10% of the initial volume of autologous blood), was yielded as PRP concentrate after centrifugation.

Calculation of VASI (vitiligo area severity index) score.^{5,6}

The percentage of vitiligo involvement is calculated in terms of hand units. One hand unit (which encompasses the palm plus the volar surface of all digits) is approximately equivalent to 1% of the total body surface area. The degree of pigmentation is estimated to the nearest of one of the following percentages: 100% - complete depigmentation, no pigment is present; 90% - specks of pigment present; 75% - depigmented area exceeds the pigmented area; 50% - pigmented and depigmented areas are equal; 25% - pigmented area exceeds depigmented area; and 10% - only specks of depigmentation present. The VASI for each body region is determined by the product of the area of vitiligo in hand units and the extent of depigmentation within each hand unit measured patch.

Total body VASI = \sum all body sites [hand units] \times [residual depigmentation]

Clinical evaluation

The patients were examined in the first visit and were reviewed fortnightly for the response of therapy and the presence of any side effects. Evaluation of pigmentation was done by VASI score. The repigmentation response was expressed as reduction in VASI score. Based on improvement in VASI score after 6 treatments the response was graded as, good response (VASI 10-25), average response (VASI 50-75), poor response (VASI 90-100).

Safety evaluation

The patients were informed to report any complications like erythema, pain, ulceration, burning sensation, ecchymosis, infection, post-inflammatory hyperpigmentation, or any allergic manifestations.

Statistical method

Friedman test, which is a non-parametric test was used based on the changes in the VASI score. The mean rank was calculated in all patients, based on which the p value and chi square value was determined.

RESULTS

This study included 40 patients with localized stable vitiligo, 18 males (45%) and 22 females (55%). Their ages ranged from 12 to 40 years. Out of 40 patients, 15 patients showed good response, 12 patients showed Average response and 13 patients showed no-response to treatment (Table 1). The average improvement in vitiligo area severity index ranged from 100 to 10. Visible signs of improvement were after the 3rd injection. (6 weeks). Facial lesions responded very well with complete clearance of smaller lesions (Figure 1). Lesions over the

neck showed complete repigmentation (Figure 2). Lip vitiligo showed poor response. Lesions over bony prominences responded poorly (knees, retroauricular region, dorsum of feet). Long standing lesions of greater than 4 years duration also had inadequate response. The improvement in these cases was visible as a decrease in size of the lesions with pigmentation starting from the periphery and gradually extending towards the centre of the lesion, (Figure 3 and 4) rather than a perifollicular pigmentation commonly seen in other topical therapies.

Therefore, the larger lesions (>5 cm diameter) showed an incomplete response. Children tend to show faster improvement. Side effects were minimal which included pain at the site of injection & ecchymosis. Patients with injection in periorbital region reported severe burning sensation. One patient with lesions on lip developed swelling of lower lip within one hour of injection, probably due to accidental deep dermal injection, however she recovered within one day with cold compress and antibiotics.

Table 1: Consecutive VASI scores during treatment.

| Sr. no | Site | VASI score | | | Response |
|--------|-------------------|----------------|--------------------------|--------------------------|----------|
| | | At first visit | At 3 rd visit | At 6 th visit | |
| 1. | Axilla | 90 | 75 | 25 | Good |
| 2. | Lip | 100 | 100 | 100 | Poor |
| 3. | Dorsum of hand | 90 | 90 | 90 | Poor |
| 4. | Neck | 90 | 50 | 10 | Good |
| 5. | Behind ears | 100 | 90 | 50 | Average |
| 6. | Shoulder | 100 | 75 | 50 | Average |
| 7. | Cheek | 90 | 50 | 10 | Good |
| 8. | Forehead & arm | 100 | 50 | 25 | Good |
| 9. | Finger & axilla | 100 | 100 | 100 | Poor |
| 10. | Lower leg | 100 | 100 | 90 | Poor |
| 11. | Neck & chest | 90 | 90 | 90 | Poor |
| 12. | Axillae | 100 | 90 | 50 | Average |
| 13. | Fingers | 90 | 90 | 90 | Poor |
| 14. | Dorsum of leg | 100 | 100 | 100 | Poor |
| 15. | Lip | 90 | 90 | 90 | Poor |
| 16. | Neck | 90 | 50 | 10 | Good |
| 17. | Eyelid | 100 | 90 | 50 | Average |
| 18. | Axilla | 100 | 75 | 50 | Average |
| 19. | cheek | 90 | 50 | 10 | Good |
| 20. | Forehead | 100 | 50 | 25 | Good |
| 21. | Shoulder | 100 | 75 | 25 | Good |
| 22. | Fingers | 100 | 100 | 100 | Poor |
| 23. | Back | 90 | 90 | 90 | Poor |
| 24. | Fingers | 100 | 90 | 50 | Average |
| 25. | Forearm | 90 | 75 | 25 | Good |
| 26. | Shin of tibia | 100 | 100 | 100 | Poor |
| 27. | Dosum of feet | 90 | 90 | 90 | Poor |
| 28. | Neck | 90 | 50 | 10 | Good |
| 29. | Shoulder | 100 | 90 | 50 | Average |
| 30. | Perioral area | 100 | 75 | 50 | Average |
| 31. | Chin | 90 | 50 | 10 | Good |
| 32. | Fingers | 100 | 50 | 25 | Good |
| 33. | Preauricular area | 100 | 75 | 25 | Good |
| 34. | Back | 100 | 50 | 50 | Average |
| 35. | Elbow | 90 | 90 | 50 | Average |
| 36. | Lower leg | 100 | 90 | 50 | Average |
| 37. | Dorsum of hand | 100 | 100 | 100 | Poor |
| 38. | Forehead | 100 | 50 | 25 | Good |
| 39. | Lip | 90 | 90 | 90 | Poor |
| 40. | Eyelid | 90 | 75 | 50 | Average |



Figure 1: Improvement in the facial lesion.



Figure 2: improvement in neck lesion.

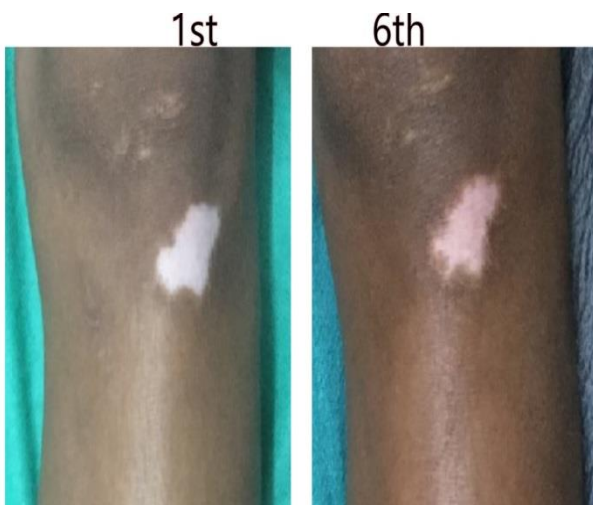


Figure 3: Lesion on the knee, pigmentation commencing on the periphery.



Figure 4: Improvement in lesions over arms and popliteal fossa.

Table 2: The table depicting mean rank, chi square value and p value.

| Visit schedule | N | Mean rank | Chi square value | p value |
|----------------|----|-----------|------------------|---------|
| At first visit | 40 | 2.65 | 52.51 | 0.0001 |
| At 3rd visit | 40 | 2.01 | | |
| At 6th visit | 40 | 1.34 | | |

P value was 0.0001 and chi square value was 52.51 which was significant (Table 2).

DISCUSSION

PRP is an effective concentration of multiple fundamental growth factors (GFs) by virtue of platelets alone (stored as -granules in platelets) and plasma proteins, namely fibrin, fibronectin and vitronectin. This mixture of GFs is pivotal in modulation of tissue repair and regeneration.⁷⁻⁹ The following is the table depicting the various growth factors in PRP.⁹

Table 3: Various growth factors in PRP.

| Growth factors | |
|--|--|
| PDGF-$\alpha\alpha$, $\alpha\beta$, $\beta\beta$ | Chemotactic for fibroblasts and macrophages. Mitogenic for fibroblasts, smooth muscle cells and endothelial cells |
| TGF*- β1, β2 | Mediates angiogenesis, chemotactic for fibroblasts, keratinocytes and macrophages, mitogenic for fibroblasts, smooth muscle cells, inhibits endothelial cells, keratinocytes and lymphocytes. Regulates matrix proteins including collagen. Proteoglycans, fibronectin and matrix-degrading proteins |
| VEGF¹ | Chemotactic and mitogenic for endothelial cells. Mediates angiogenesis |
| EGF² | Mediates angiogenesis. Mitogenic for fibroblasts, endothelial cells and keratinocytes |
| HGF³ | Mediates regeneration |
| FGF⁴ | Mediates tissue organization and regeneration |
| FGF-9 | Aids regeneration of new follicles |

TGF: Transforming growth factor, VEGF: Vascular Endothelial growth factor, EGF: Epidermal growth factor, HGF: Hepatocyte growth factor, FGF: Fibroblast growth factor.

The beneficial effect of platelet rich plasma in vitiligo could be suggested through these growth factors which stimulate keratinocytes and fibroblasts proliferation with subsequent improvement of their interaction with melanocytes leading to the stabilization of melanocytes, it was also found that platelet rich plasma treatment induced accelerated proliferation and migration of fibroblasts through up-regulation of cyclin E and cyclin-dependent kinase 4, which is important in cell migration and proliferation.¹⁰

There are several scoring systems in vitiligo.

Vitiligo extent tensity index (VETI)¹¹

VETI score is a new treatment evaluation criteria and severity assessment method for vitiligo. VETI score helps in clinical research on vitiligo patients by producing a constant and reproducible number, as by the PASI score in psoriasis.

Vitiligo disease activity score (VIDA)⁵

The VIDA is a six-point scale for assessing vitiligo activity. Scoring is based on the individual's own opinion of the present disease activity over time. Active vitiligo involves either expansion of existing lesions or appearance of new lesions.

Vitiligo area severity index (VASI)⁵

The VASI for each body region is determined by the product of the area of vitiligo in hand units and the extent of depigmentation within each hand unit measured patch.

There was only one study about the role of PRP in vitiligo. It was done in 2011, by Lim et al.⁷ They treated 20 patients with vitiligo by intradermal injections of PRP weekly for 10 weeks and they suggested that PRP was

not effective in the treatment of vitiligo. However in our study 67.5% of patients had visible repigmentation.

In a study done in Egypt in 2015 by Ibrahim et al.¹⁰, the effect of platelet-rich plasma on the outcome of short-term narrowband-ultraviolet B phototherapy in the treatment of vitiligo was evaluated with regard to body site and it was found that vitiligo of the face, trunk and extremities showed the best results. However in our study facial lesions showed a better response than truncal lesions and extremities showed a poor response.

In the study conducted by Ibrahim, 55% of patients in the PRP group achieved excellent repigmentation and 20% achieved good repigmentation in a 4-month duration compared to NB-UVB side. In our study 37.5% patients showed good response and 30% showed average response. The reported side effects in their study were minor and all patients tolerated the procedure well. Pain occurred in 50% of the patients which was mild and tolerable. Ecchymosis at the site of injection occurred in 15%. In our study, adverse effects were minimal as well, which included pain at the site of injection and ecchymosis. Patients with injection in periorbital region reported severe burning sensation. One patient with lesions on lip developed swelling of lower lip within one hour of injection. A total of 4 patients had side effects which account for 10% of cases, which however recovered in 24 hours.

CONCLUSION

Vitiligo has a profound effect on quality of life of a patient; hence newer efficacious treatments are always sought by patients and dermatologists alike. PRP offers a simple, minimally invasive, inexpensive treatment for vitiligo. It may be combined with topical therapies, surgical modalities and phototherapy. The results of our study are encouraging and large scale studies are required for further validation of results.

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Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee (SVIEC/UN/Medi/5RP/17048)

REFERENCES

1. Prasad D, Kumaran SM. Depigmentary and hypopigmentary Disorders. IADVL Textbook of Dermatology. 4th ed. 2016: 1308-1309.
2. Bleehen SS, Anstey AV. Disorders of skin colours. Rook's Textbook of Dermatology. 7th ed. 2004;39:55-6.
3. Kim DH, Je YJ, Kim CD, Lee YH, Seo YJ, Lee JH, et al. Can platelet-rich plasma be used for skin rejuvenation? Evaluation of effects of platelet-rich plasma on human dermal fibroblast. *Ann Dermatol*. 2011;23:424–31.
4. Faghihi G, Keyvan S, Asillian A, Nouraei S, Behfar S, Nilforoushzadeh MA. Efficacy of autologous platelet-rich plasma combined with fractional ablative carbon dioxide resurfacing laser in treatment of facial atrophic acne scar: A split-face randomized clinical trial. *Indian J Dermatol Venereol Leprol*. 2016;82:162-8.
5. Bhor U, Pande S. Scoring systems in dermatology. *Indian J Dermatol Venereol Leprol*. 2006;72:315-21.
6. Singh A, Kanwar AJ, Prasad D, Mahajan R. Randomized controlled study to evaluate the effectiveness of dexamethasone oral minipulse therapy versus oral minocycline in patients with active vitiligo vulgaris. *Indian J Dermatol Venereol Leprol*. 2014;80:29-35.
7. Lim HK, Sh MK, Lee MH. Clinical application of PRP in vitiligo: a pilot study. Official 1st International Pigment Cell Conference. 2011.
8. Steed DL. The role of growth factors in wound healing. *Surg Clin North Am*. 1997;77:575-86.
9. Arshdeep, Kumaran MS. Platelet-rich plasma in dermatology: Boon or a bane? *Indian J Dermatol Venereol Leprol*. 2014;80:5-14.
10. Ibrahim ZA, El-Ashmawy AA, El-Tatawy RA, Sallam FA. The effect of platelet-rich plasma on the outcome of short-term narrowband-ultraviolet B phototherapy in the treatment of vitiligo: a pilot study. *J Cosmetic Dermatol*. 2016;15:108-16.
11. Feily A. Vitiligo Extent Tensity Index (VETI) Score: A New Definition, Assessment and Treatment Evaluation Criteria in Vitiligo. *Dermatol Practical Concep*. 2014;4(4):81–4.

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