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Original Article

Comparison of effectiveness and safety of narrow band ultraviolet B with and without platelet rich plasma in the treatment of vitiligo

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Abstract

Objective To compare efficacy and safety of Narrow Band Ultraviolet B with and without platelet rich plasma in the treatment of vitiligo.

Methods A total of 74 patients took part in the trial who were randomly divided in two groups (37 in each group). Patients in Group-A were given NBUVB alone, whereas those in Group-B were given both NBUVB and PRP. The NB-UVB treatment protocol included twice-weekly sessions for up to three months, or until complete re-pigmentation had occurred. Patients in Group B had fortnightly PRP treatment for a total of 6 sessions over the course of 3 months. PRP was injected intradermally into the lesion. After the final session, the patients were followed up with for an additional month.

Results Vitiligo patients benefited more from the NBUVB+PRP combination than from NBUVB alone. The effectiveness was statistically significant in group B (Group A: 64.9% vs. Group B: 91.9%, p-value=0.005). 35.1% of Group-A patients and 59.5% of Group-B patients achieved excellent treatment outcomes, according to evaluation criteria for effectiveness. While 30 percent of Group-A patients and 32 percent of Group-B patients had good treatment outcome, 35 percent of patients in Group-A and 8 percent in Group-B experienced moderate outcome. Both the treatments were safe and no serious or long-term adverse effects were noted.

Conclusion This study's findings suggested that platelet-rich plasma (PRP) combined with narrowband ultraviolet B (NB-UVB) was a better therapy for vitiligo than NB-UVB alone. This treatment for vitiligo was cost-effective, risk-free, and well-tolerated. It reduced the time spent in NB-UVB treatment, which should improve adherence.

Key words
Effectiveness; Safety; Narrow Band Ultraviolet B; Platelet rich plasma; Vitiligo.

Introduction

Vitiligo is an acquired pigmentary disorder that affects a high percentage of the general population. It's characterized by patches of skin that have lost their pigment due to the depletion of melanocytes from the basal layer of epidermis.[1] Vitiligo manifests itself clinically as white or milky macules or patches because of the selective loss of melanocytes. The patches can appear anywhere on the skin and mucous membranes.[2] Cause of vitiligo is yet to be determined. Metabolic disarray, oxidative stress, inflammatory cytokine generation, cell separation, and immune responses are all potential contributors to pathogenesis.[3] Vitiligo

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is seen in 0.4% to 2.0% of the world's population.[4] Studies show that females have a somewhat higher incidence, and about 50% of cases start in infancy. Treatment for vitiligo depends on the patient's age, the severity of their condition, and the location of their lesions.[5] Traditional methods of therapy are laborious and inefficient.[6]

The vitiligo area severity index (VASI) is used to quantify the area of involvement. Various researches on vitiligo has included its application[7, 8]

Narrowband ultraviolet B (NBUVB) is widely acknowledged as a safe and effective therapy for vitiligo, although patients may be at risk of suffering undesirable side effects and may be less likely to keep to the treatment plan if it lasts too long.[8] In vitiligo, NB-UVB works by stabilizing the depigmentation process and stimulating the few remaining follicular melanocytes.[9] Nucleic acid bases absorb UVB, which then induces formation of numerous DNA photoproducts, most notably pyrimidine dimers, in nuclear DNA. Interleukin-10 induction, decreased natural killer cell activity, and lymphoproliferation are all immunomodulatory effects that NB-UVB has been found to cause. Additionally, NB-UVB may contribute to its immunomodulatory actions by inducing the isomerization of urocanic acid from the trans to the cis form.[9]

Platelet-rich plasma (PRP) is an autologous preparation of platelets in plasma used as a therapy in a variety of medical fields, including orthopaedics, plastic surgery, and several dermatological treatments, including skin rejuvenation, treatment of acne scars, and hair restoration.[10,11] Platelets release several protein growth factors (such as PDGF, TGF-β, etc.). Platelet activation triggers degranulation, which in turn switches the secretory proteins to their active forms.[12]

Basic fibroblast growth factor (b-FGF) promotes the movement of melanocytes and stimulates the multiplication of keratinocytes and fibroblasts.[13] The effectiveness of TGF-β is increased when vitiligo is in a stable state.[14] Furthermore, PRP activates dormant stem cells and increases the expression of cyclin Kinase-dependent 4, which is crucial for cell movement and reproduction.[15]

Various growth factors promote the proliferation of keratinocytes and fibroblasts while enhancing their interaction with melanocytes, leading to increased stability.[16] These multiple factors facilitate the movement of melanocytes from the surrounding skin, enabling repigmentation.[17-19] PRP demonstrates anti-inflammatory properties and can inhibit the secretion of cytokines (including interleukin-1, interferon-c, and tumor necrosis factor-α), thereby enhancing the interplay between melanocytes and keratinocytes.[20] Components of PRP, such as fibrin, fibronectin, and vitronectin, improve cell adhesion among keratinocytes, fibroblasts, and melanocytes, serving as a foundation for epithelial formation.[21,22]

The combination of intradermal PRP injection with NBUVB has recently been described as a feasible, inexpensive, and well-tolerated method for treating vitiligo. It decreases the time needed for NBUVB treatment, which should improve adherence.[11] in the PRP group 33 patients (55%) in published pilot research reported an excellent improvement, while 12 patients (20%) reported good response, 9 patients (15%) reported a moderate, and 6(10%) ha mild improvement.[11] Among those exposed to UVB alone, 11 patients (18.3%) showed no improvement, 75.0% showed mild improvement, and 6.7% showed moderate improvement. None of the patients had excellent response in this group.[11]

The novelty of our research lies in the fact that it will be the first to examine the effectiveness and safety of NB-UVB with and without PRP in the

treatment of vitiligo in our local community. There is a lack of relevant local data, and an international pilot trial found that PRP and NB-UVB combination was more effective than PRP alone.[14]

Based on the results of this research, PRP will be introduced to traditional NB-UVB therapy in the future in an effort to increase patient satisfaction and treatment effectiveness for vitiligo.

Methods

A comparative interventional pre-post study was conducted at the department of dermatology Unit-I, KEMU/Mayo hospital, Lahore from June 2022 to June 2023 after approval from institution ethical board (No. 21829/REG/KEMU/22, dated December 30th, 2022). Non-probability convenient sampling was used and sample size of 74 patients (37 in each group) was taken. Patients of either gender between the ages of 20 and 50 years with stable vitiligo were included in the study.

Patients with blood dyscrasias, or those who had systemic therapy (within the last two months) and topical therapy for vitiligo (within the last month), patients with hepatitis B and C and HIV, patients with platelets count below 100,000, immunosuppression with other photo-aggravated dermatoses, patients who could not stand in the UV chamber and pregnant women were excluded from the study.

Patients meeting the inclusion criteria were recruited from the dermatology outpatient clinic at KEMU/Mayo Hospital in Lahore after approval from the institution's ethics committee. After receiving written informed consent from each patient, pre-treatment photographs were taken. The NB-UVB therapy was administered twice weekly to all the patients. Every other week, PRP was intradermally injected to two pre-determined patches. Before beginning therapy, a blood sample was taken from the patient and PRP collected after centrifugation. All patients were treated with NB-UVB twice weekly for up to three months, or until full re-pigmentation had occurred. Starting at 0.33 mJ/cm^2, the UVB exposure was raised by 20% for each subsequent session until the lowest erythema dose was reached. PRP was injected intradermally into the lesion using an insulin syringe. Injection sites were separated by 2 centimeters, and 0.1 cc of PRP was administered at each site. Group B patients received this therapy over the course of 3 months, with sessions spaced out every 2 weeks. After the final session, the patients were followed up for an additional month. Results were evaluated by two dermatologists. Effectiveness and safety were recorded on the predesigned proforma. Vitiligo Area Severity Index (VASI) was calculated to measure the treatment response.

The level of residual depigmentation was reported as a percentage (10%, 25%, 50%, 75%, 90%, or 100%).

Assessment criteria using percentage reduction in VASI at the end of the study was used with improvement recorded as Excellent (75 - 100%), Good (50 - 74%), Moderate (26 - 49%), Mild (< 25%).

The data was entered using SPSS-26. Quantitative variables i.e., age, duration of disease, VASI score at baseline and after 4 months were summarized as means and standard deviation. Frequencies and percentages were used for presentation of qualitative variables like gender, site of lesion and effectiveness and safety. Data was stratified for age, gender, site of lesion and duration of vitiligo. Chi square test was applied to compare effectiveness and safety in both groups and for post stratifications keeping p-value of ≤ 0.05 as significant.

Results

In this study, mean age of patients in Group-A and Group-B was 28.86±6.95 and 29.62±4.18 years. Minimum and maximum age of patients in both groups ranges between 21 to 42 years respectively. In Group-A 12(32.4%) patients were male and 25(67.6%) were female while in Group-B 14(37.8%) were male and 23(62.2%) were female. Mean duration of disease for patients in Group-A and Group-B was 7.43±1.77 and 9.95±3.05 months respectively. In Group-A 18(48.6%) patients had lesion on extremities, 7(18.9%) patients had lesion on face and 12(32.4%) patients had lesion on trunk while in Group-B 26(70.3%) patients had lesion on extremities, 8(21.6%) had on face and 3(8.1%) patients had lesion on trunk. At baseline and 2nd and 3rd month no significant difference was seen for VASI score between groups. At 4th month mean VASI score was significantly higher in Group-A and compared to Group-B patients. i.e. p-value<0.001 **(Table 1)**. Mean percent reduction in VASI score form baseline till last follow up showed statistically significant difference between groups. Percentage reduction in VASI score from baseline till last follow up was significantly higher in Group-B patients. i.e. p-value=0.002 **(Table 2)**.

Table 1 VASI score in study groups.

	Group-A (n=37)	*Group-B (n=37)*	*p-value*
Baseline	16.13±4.23	16.55±4.28	0.672
1st Month	12.84±2.52	14.44±4.34	0.056
2nd Month	10.33±1.88	11.00±3.71	0.325
3rd Month	8.90±2.48	8.17±4.09	0.353
4th Month	6.93±2.1	5.03±2.17	<0.001

Group-A: NBUVB alone
Group-B: NBUVB alone+ PRP

Table 2 Mean Percentage difference in VASI score between study groups.

	Group-A (n=37)	*Group-B (n=37)*
Mean	57.04	69.69
SD	19.76	13.32
p-value 0.002		

Table 3 Effectiveness in study groups.

	Group-A	*Group-B*	*Total*
Yes	24 (64.9%)	34 (91.9%)	58
No	13 (35.1%)	3 (81%)	16
Total	37	37	74
p-value 0.005			

Table 4 Effectiveness of treatment Based on assessment criteria

	Group-A	*Group-B*	*Total*
Excellent	13 (35.1%)	22 (59.5%)	35
Good	11 (29.7%)	12 (32.4%)	23
Moderate	13 (35.1%)	3 (8.1%)	16
Total	37	37	74
p-value 0.014			

Group-A: NBUVB alone
Group-B: NBUVB alone+ PRP

In Group-A 24(64.9%) patients and in Group-B 34(91.9%) patients showed treatment effectiveness. Treatment effectiveness was significantly higher in Group-B patients. i.e. p-value=0.005 **(Table 3)**. In Group-B excellent treatment outcome was observed in 59.5% patients while in Group-A 35.1% patients had excellent treatment outcome. (p-value=0.014) **(Table 4, Figures 1,2)**. The adverse effects were also recorded during the study. The frequency of erythema and pain was significantly higher in Group-B patients than that of Group-A patients. However, at 4th month none of the patients had erythema in both treatment groups. At 1st and 2nd month frequency of itching and bruising was significantly higher in Group-A patients as compared to Group-B patients. But at 3rd and 4th month no patients in both treatment groups experienced itching and bruising.

None of the patients experienced folliculitis, hyperpigmentation, atrophy/scarring in both treatment groups. Frequency of xerosis was significantly higher in Group-A patients as that of Group-B patients.

Discussion

Numerous treatment techniques have been used for treating vitiligo in the light of its complicated

Figure 1

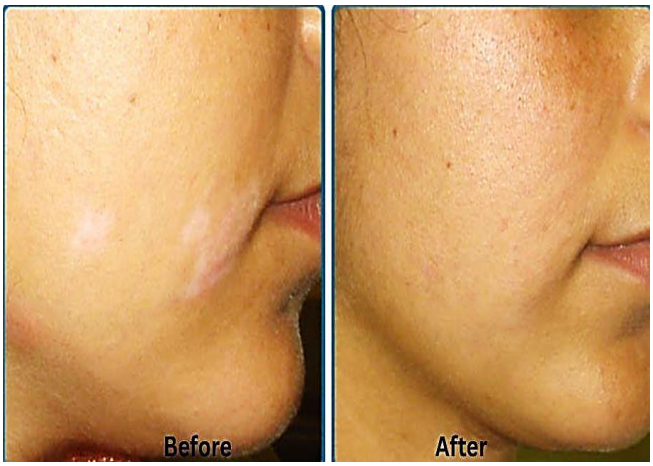

Figure 2

Figures 1 and **2** Treatment response of patients in patients treated with NBUVB plus PRP.

pathophysiology. Since each modality has its own implications and treatment durations, it is still debatable which one is the best option. Given the multifactorial and polygenic nature of vitiligo, it may be better to use certain parameters allow for combination treatment to get greater response than monotherapy. Topical and systemic immune-modulators, corticosteroids, topical calcineurin inhibitors, calcipotriol, phototherapy, excimer laser, and surgical techniques like cellular or tissue transplantation are currently used to halt disease progression, stabilize the progressive lesion, and reactivate the melanocytes for repigmentation.[23]

Our study aimed to evaluate the effectiveness and safety of NB UVB therapy for the treatment of vitiligo, comparing it to PRP alone. Patients' ages were found to be evenly distributed between the ages of 20 and 50, with a mean age of 29 years. Patients in the research by Tawfik *et al.* and Kale *et al*. had a mean age of 30 years (range: 18–66 years old).[24,25] Ibrahim *et al.* found that the average age of their patients was 28 years, with a range of ages from 18 to 35 years.[11] When compared to the research by Ibrahim *et al*. and the study by Tawifk *et al*., the age range of patients in our study is much wider and evenly distributed between the ages of 20 and 50, with a mean age of 29 years.

The number of female patients in our study was significantly greater than that of male patients. These findings are congruent with those of Ibrahim *et al.*, who also reported that female patients outnumbered male patients in their study.[11] Another research, found that more women were affected than men with vitiligo. i.e. 59% vs. 40%.[26] According to Tawfik *et al.* female patients outnumbered male ones. i.e. 57% vs. 42%.[24]

In our study, the average length of illness was 8 months in both therapy groups. Similar to this research, Tawfik *et al*. reported a mean duration of illness of 8 months.[24] A study by Elsaadany *et al*. showed a lower mean duration of disease of 3 months.[26] This difference could be due to different inclusion criteria used in our study.

The VASI score was used to determine the success of therapy. According to the evaluation criteria, the treatment effectiveness for patients in Group-B was higher than that for patients in Group-A.

In a study by Abdelghani *et al*., eighty adults with vitiligo were included and evaluated the effectiveness of a combination of Fractional CO2 laser and PRP to laser and NBUVB combination, laser monotherapy, NB-UVB

alone, and PRP monotherapy. On average, 63% of patients in the laser and PRP combination group, 39% of patients in the laser and NB-UVB group, 31% of patients in the laser monotherapy group, and 27% of patients in the PRP alone group achieved pigmentation following treatment.[27] These results are in line with the results of this study combination of PRP+ NBUVB treatment groups as compared to NBUVB alone. However, in this study we used VASI score for calculation of treatment effectiveness.

A recent study carried out in Pakistan showed significantly better treatment response in patients treated with Fractional CO2 laser combined with PRP compared to Laser treatment alone. Our study differs from this study in the treatment modality used i.e., Fractional CO2 laser whereas we used NBUVB therapy in combination with PRP.[28]

Ibrahim *et al*. conducted a study on whether or not PRP injection would enhance the outcomes of short-term NB-UVB therapy for those with stable vitiligo. Their research showed that the re-pigmentation rate was much higher in the PRP with NB-UVB group compared to the NB-UVB group. Effectiveness was seen in 43.3% of patients in the combination Group (PRP with NB-UVB) compared to 10% in the Control Group (p-value=0.001).[11] These results are also in line with our study showing higher effectiveness with combination of NBUVB and PRP as compared to NBUVB alone.

Excellent response rate of 55% was reported by Ibrahim *et al*.[11] Similarly, our study showed excellent response in 59% of patients in group B. Khattab *et al*. also reported better outcome in the patients treated with Excimer laser in combination with PRP than Laser monotherapy.[15] Pandey *et al*. reported that the PRP with NBUVB therapy (60%) had a statistically significant improvement in comparison with NBUVB with intralesional saline (20%).[29] Fawzi *et al*. also found combination therapy effective and long lasting.[30]

However, recent double-blind randomized controlled trial by Kale *et al*. conducted in India found no significant improvement in treatment outcomes when PRP was added to NBUVB therapy. The difference could be due to different assessment scoring system (PGA scoring) in this study.[25]

Regarding adverse effects, our research found erythema, itching/bruising, xerosis, and pain to be more frequent side effects of therapy. However, after 4 months of therapy, the majority of individuals did not experience these adverse effects anymore. Patients treated with combination treatment reported considerably more frequent erythema and pain, whereas those treated with NBUVB monotherapy complained of itching and xerosis. Similar side effects were reported by Mahajan *et al*.[31]

This side effect profile is in line with the study by Ibrahim *et al*. in which 50% of patients had discomfort during injection and 15% of patients developed ecchymosis. Minor adverse events were noted by all patients in the PRP group.[11] According to Kale *et al*, both PRP and control group patients reported pain as their most common adverse effect. Three (9.37%) of patients treated with PRP and two (6.25% of cases) treated with NB-UVB alone (control group) showed ecchymosis.[25]

Injecting your own platelet-rich plasma (PRP) under the skin to cure vitiligo has the potential to be a safe, effective, and side-effect-free alternative therapy. As there is no risk of development of antibodies in PRP, which improves its acceptability among patients. The majority of patients may expect good to

exceptional outcomes at a reasonable cost. It has been hypothesized that combining PRP with NB-UVB, which stabilizes melanocytes and encourages their proliferation, enhances the result of re-pigmentation in a shorter period of time.

Limitations of the study were small sample size as it was a time bound study and it was a single center study.

Conclusion

This study's findings suggest that platelet-rich plasma (PRP) combined with narrowband ultraviolet B (NB-UVB) is a better therapy for vitiligo than NB-UVB alone. This treatment for vitiligo is simple, risk-free, and well-tolerated. It reduces the time spent in NB-UVB treatment, which should improve adherence.

Declaration of patient consent The authors certify that they have obtained all appropriate patient consent.

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Conflict of interest Authors declared no conflict of interest.

Authors' contribution

TR: Substantial contribution to study design, acquisition of data, analysis and interpretation of data, manuscript writing, has given final approval of the version to be published.

SS: Substantial contribution to study conception and study design, interpretation of data, manuscript writing, has given final approval of the version to be published.

MS,AA,SAAG,GB,IH: Substantial contribution to concepts and study design, critical review, has given final approval of the version to be published.

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