International Journal of Research in Dermatology
Pandey AK et al. Int J Res Dermatol. 2023 Jul;9(4):175-181
http://www.ijord.com

DOI: https://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20231824

Original Research Article

A comparative study of narrowband-ultraviolet B plus intralesional normal saline versus narrowband-ultraviolet B with platelet rich plasma in treatment of vitiligo

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Received: 12 April 2023
Revised: 15 May 2023
Accepted: 02 June 2023

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ABSTRACT

Background: Treatment of vitiligo remains a challenge and there is no universal consensus about optimal treatment. Platelet rich plasma contains several growth factors and is being used as an effective treatment of several dermatological disorders. Now it is clear that along with melanocytes, keratinocytes and fibroblasts are also involved in pathogenesis of vitiligo. The aim of this study was to compare the effect of narrowband-ultraviolet B (NB-UVB) with platelet rich plasma versus NB-UVB and intralesional normal saline in treatment of vitiligo.
Methods: A prospective observational study was done between March 2016 to August 2017 on patients of vitiligo attending BRD Medical College, Gorakhpur. A total of 80 patients were enrolled with symmetrical lesions. For each patient one side was treated with NB-UVB along with intralesional platelet-rich plasma (PRP) and other side with NB-UVB plus intralesional normal saline was given. Intralesional PRP and intralesional normal saline was given on an interval of every 2 weeks for 4 months and patients were receiving NB-UVB therapy thrice weekly on alternate day.
Results: We found that combination of PRP with NB UVB had statistically significant improvement as compared to NB UVB alone with pigmentation detected in 60% patient in combined site versus 20% in NB UVB plus intralesional normal saline.
Conclusions: Intradermal PRP injections along with NB-UVB are efficacious, safe, cheap and easy technique in treatment of vitiligo it is more efficacious when compared to NB-UVB therapy. It also shortens the duration of NB-UVB therapy.

Keywords: Vitiligo, NB-UVB, Platelet rich plasma, Intralesional saline

INTRODUCTION

Vitiligo is a common acquired idiopathic and often, familial hypomelanosis, which is characterized by pale white macules that enlarges centrifugally over time.

Vitiligo alone involved 1-2% of the world's population. It causes cosmetic problems as well as socio-psychological disaster.[1] Prevalence of vitiligo figures from nearly 1–2% of the world population.[2]

In India, the incidence of vitiligo in dermatological outpatient is around 3% to 4%.[3] There are many cases of vitiligo who either fail to respond or only partially respond to medical line of treatment indicating melanocytes are targeted by multiple aggressions leading to marked reduction of pigment cells and eventually to their complete destruction.[4] The various medical therapeutic modalities used for treatment of vitiligo have certain limitations. "Stable vitiligo" is the term carried for such cases where, in addition, the disease is inactive and no new patch has

developed in past 1 year.[5] We decided to compare the effect of NB-UVB alone and along with platelet-rich plasma (PRP).

METHODS

A prospective observational study total of 80 stable vitiligo patients was done from March 2016 to December 2017 on patients of vitiligo attending BRD Medical College Gorakhpur after taking an informed consent. The equation below was used to include maximum number of vitiligo patient assuming prevalence to be 20% and drop out of 20%).

$$n = 4P \times q/d^2$$

A detailed clinical history with special reference to age, sex, marital status, occupation and place or residence was noted.

The criteria for selection was based on patients having non-progressive type of vitiligo not responding to systemic or topical PUVASOL therapy tried for minimum period of one year and the existing lesions have not increased in size. A wash of period of 3 months was considered prior to start of study. A complete clinical examination was done in good day light with special attention towards cutaneous lesions.

Inclusion criteria

Patients willing for treatment, patients not respond adequately to medical treatment, patients should be stable for 12 months (no new lesions, no expansion of old ones), and patients aged 5-6 years were included.

Exclusion criteria

Patients aged less than 05 years and patients receiving any concomitant medical treatment (systemic or topical), patients who are positive to infectious disease HIV, hepatitis C virus (HCV), hepatitis B virus (HBV), pregnancy and lactation, chronic kidney disease and malignancy; patients who have a history of koebnerization, Keloid tendency and bleeding disorders or patients on anticoagulant medications (aspirin, warfarin, heparin); and patients with active infection at local site or low pain threshold .

Method

A total of 80 patients with almost symmetrical lesions with respect to size, site and disease activity (i.e. perifollicular pigmentation, and margins) were included in the study. In each patient patches were randomly given either PRP treatment or normal saline.

Platelet rich plasma

Collect 10-20 ml of patient blood and mix it with anticoagulant such as acid citrate dextrose (ACD). Platelet rich plasma prepared by two stage of centrifugation process. After centrifugation platelet and other growth factors are raised at the top of the tube. Before injecting platelet rich plasma, it is activated by mixing calcium gluconate (1 part of calcium gluconate in 9 part of PRP) as an activator. Under topical anesthesia activated and highly concentrated PRP injected into the lesion with the help of insulin syringe (round 1 unit in 1 cm^2 area). A maximum of 5 ml was injected at a time. Similarly, normal saline (equal quantity as PRP) was injected in same patient but different patch (control). Therefore, in same patient with similar vitiligo patch one site was treated with PRP and the corresponding site was injected with normal saline. The process was repeated and each lesion received one kind of treatment either normal saline or PRP throughout the treatment.

NB-UVB phototherapy

A NB-UVB machine will be used to provide NB-UVB radiation over the lesion. Initial dose of radiation will be 250 mj/cm^2 in adult and 150 mj/cm^2, dose will be increased 20% on each next sitting, it will be increased until minimal erythema dose is reached. The dose just prior to MED will be final dose for patient and it will be kept stable for rest period of study. The patient will receive NB-UVB radiation on alternate day.

Method of evaluation

The patients were followed up for a period of nine months. The result of study has been evaluated on the basis of clinical assessment and photographic assessment and response was classified as shown in Table 1.

Table 1: Type of response.

Type of response	% of improvement
Excellent	100-75
Good	74-50
Fair	49-25
Poor	<25

Statistical significance of the result and p value was calculated using Chi square test.

RESULTS

In the present study as seen in Table 2, 52 patients were females (65%), 28 patients were males (35%), with male female ratio 1: 2. Majority of the patients were 16 to 30 years age, with maximum age being 60 years and minimum 5 years. 60% of cases had vitiligo of 6 to 10 years, with 17 years recorded as the maximum duration and one year as the minimum year of disease (Table 3). Table 4 shows maximum number of patients 25 (31.25%) had lesions on the lower extremities followed by trunk.

Table 2: Distribution of patients according to sex.

Sex	No. of patients	Percentage
Male	28	35
Female	52	65
Total	80	100

Table 3: Duration of vitiligo in patients.

Duration (in years)	No. of patients	Percentage
1-5	20	25
6-10	48	60
>11	12	15
Total	80	100

Table 4: Site of vitiligo involved in order of frequency.

Site	No. of patients	Percentage
Lower extremities	25	31.25
Trunk	24	30
Face and neck	09	11.25
Upper extremities	22	27.50
Total	80	100

Patients were divided in two broad groups, first group constituting 80 patients with 80 lesions (50%) underwent treatment with NB UVB plus normal saline while second group constituting 80 lesions (50%) underwent NBUVB plus PRP.

In group 1, 80 lesions received NB UVB plus intralesional normal saline while in group 2, another 80 lesions received NB UVB plus intralesional platelet rich plasma. A maximum of twelve such sittings were given and the response was noted at each sitting. The patients were followed for a total of one year.

In group 1 as per Figure 1 that is patient receiving NB UVB plus intralesional normal saline at the end of study duration a very good response was seen in 58.75% while poor response where seen in 11.75%.

In group 2 as per Figure 2 that is NB UVB intralesional PRP at the end of study very good response was seen in 78.75% while poor response is seen in 3.75%.

The comparison of the results can be seen in Figure 3.

The most common side effects in both the groups were pain at the site of injection, which was seen in almost all the patients followed by erythema/burning/discomfort at site of infection seen in 35% of patients in group 2 while 10% of patient in group 1 as depicted in Figure 4.

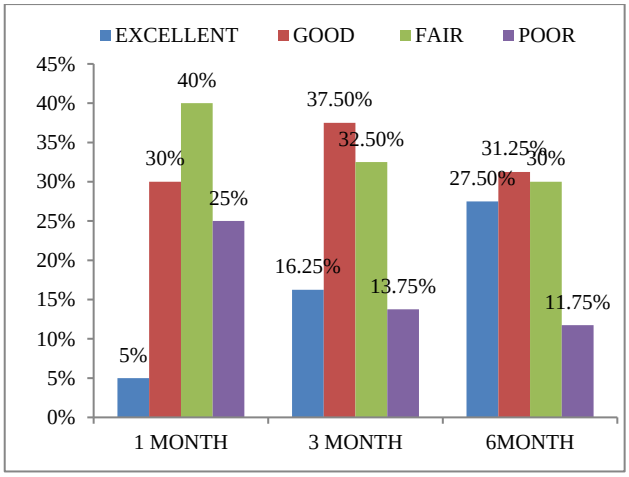

Figure 1: Comparison of result of NBUVB plus intralesional normal saline after 1 month, 3 month and 6 month (performed in 80 lesions).

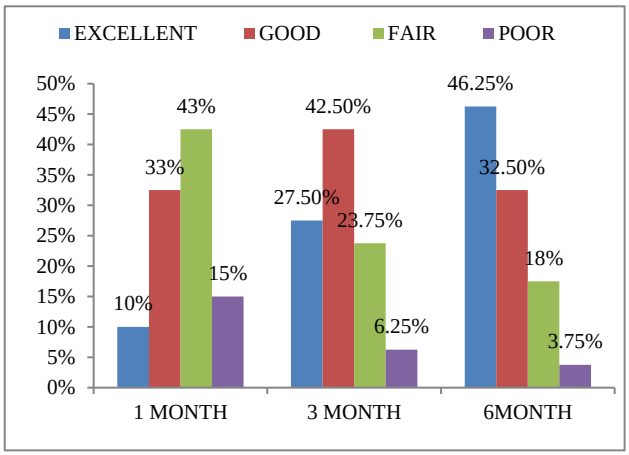

Figure 2: Comparison of result of NBUVB plus intralesional PRP after 1 month, 3 month and 6 month (performed in 80 lesions).

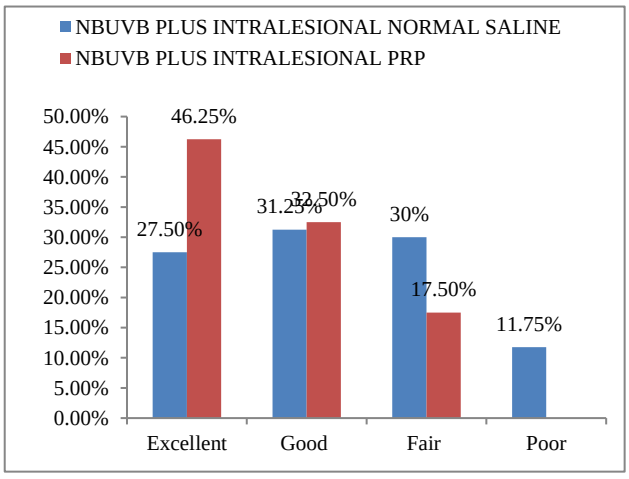

Figure 3: Comparisons between final result of NBUVB plus intralesional normal saline and NBUVB plus intralesional PRP after 6 months of duration.

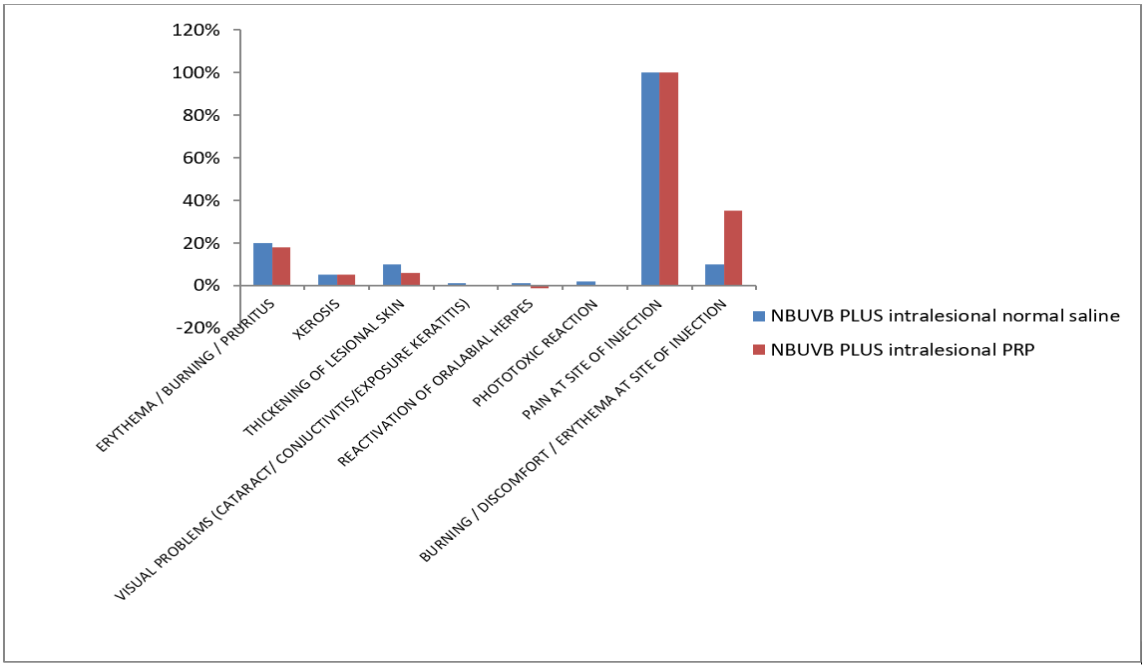

Figure 4: Adverse effects of treatment.

Figure 5: Before PRP and after 6 months after PRP +NBUVB.

Figure 6: Before and after 6 months of PRP +NBUVB.

Figure 7: Before NS + NBUVB and 6 months after NS + NBUVB.

Figure 8: Before NS + NBUVB and 6months after NS + NBUVB.

DISCUSSION

Vitiligo is a depigmentary disorder with marked social stigma requiring proper management. There are various medical and surgical method for treatment. NB UVB therapy is a widely accepted treatment but prolonged course and partial or non-responsiveness of treatment in stable vitiligo lesions is a limiting factor. Stable vitiligo lesions are relatively refractory requiring surgical therapies like skin grafting or grafting of invitro cultured and non-cultured melanocytes or 5 fluorouracil cream with microneedling or platelet rich plasma.

In the present study as seen in Table 2 and Figure 1, out of 80 case, female patients 65% outnumbered male patients 35%. Male to female ratio was 1:2 as compared to Singh et al observed male to female ratio of 3:5.[6] Savant reported 17 males and 45 females in his study.[7] Das reported 60 patients out of which 21 were males and 39 were females.[8] So, in our study also females outnumbered males.

In the present study, age of the patients ranged from 5 years to 60 years. Maximum number of patients 42 (52.5%) was of the age group 16 to 30 years (Table 3). Second largest group was constituted by patients aging 31 to 45 years.

Vitiligo is known to occur in any age group with maximum incidence between ages 16 to 30 years. Similar to our study Jha et al reported that most of the cases were in the range of 15 to 30 years.[9]

In the present study maximum duration of vitiligo was 17 years and minimum was 1 year. But in most of the patients 60% it was of 6 to 10 years duration as seen in Table 4 and Figure 3. Shah et al in a series of 20 patients reported 1 to 5 years duration of vitiligo in most of the cases.[10]

In present study, as seen in table 4 and fig. 4, nine cases i.e. 11.25% had vitiligo lesions on face and neck. Twenty-five patients (31.25%) had lesions on lower extremities. Twenty-two (27.50%) patients have vitiligo on upper extremities. Twenty-four patients (30%) have involvement of trunk. Similar to our study, lower extremities were found to be common site of involvement, in the studies of Sarin and Rathi et al.[11,12]

UVB phototherapy was introduced by in 1978 to psoriasis and uremic pruritus.[13] In 1988 van Weelden et al and Green et al introduced NB-UVB phototherapy was for the treatment of psoriasis by.[14,15]

Westerhof and Nieuweboers-Krobotovafirst in 1997 introduced NB-UVB phototherapy for the treatment of vitiligo.[16]

As we all know NBUVB therapy is more effective, less dangerous and superior to PUVA therapy for treatment of vitligo.[17-19]

A potential advance in UVB-based phototherapy has been the introduction of fluorescent bulbs (Phillips model TL-01) that deliver UVB in the range of 310 to 315 nm, with a peak at 312 nm.

NBUVB therapy is the preferred treatment for generalized vitiligo, pregnant women and children because of the high safety profile.[20,21] Determination of minimal erythema doses (MED) is essential and as reported by Serish and Srinivas mean MED for NBUVB is 300 mJ/cm^2 for the Indian skin.[22] In study conducted by Kumar et al, NBUVB therapy was started with an initial dose of 250 mJ/cm^2.[23]

In our study the starting dose was 250 mJ/cm^2 in adults and 150 mJ/cm^2 in children, with 20% dose increments at each subsequent visit given for a maximum period of 1 year. Patients were given intralesional PRP on one side while intralesional normal saline was given on opposite site every 2 weeks in same sitting.

In a recently published study, NB-UVB was reported to be effective and safe in childhood vitiligo.[24] In this open trial, 51 children with generalized vitiligo were treated twice weekly with NB-UVB radiation therapy for a maximum period of 1 year, resulting in more than 75% overall repigmentation in 53% of patients. Scherschun et al retrospectively analyzed their experience of treating vitiligo with NB-UVB administered as monotherapy 3 times a week.[25] Five of their seven patients achieved more than 75% repigmentation with a mean of 19 treatments, whereas the remaining two patients had 50% and 40% repigmentation after 46 and 48 treatments respectively. In a recent meta-analysis of non-surgical therapies in generalized vitiligo by Njoo et al, higher success rates were observed with NB-UVB (63%).[26] NB-UVB phototherapy produces a cosmetically good color match in Indian patients.[27] In our study we observed that in group 1 that is patient receiving NB UVB plus intralesional normal saline at the end of study duration a very good response was seen in 58.75% while poor response where seen in 11.75% which is very similar to results obtained to NB UVB monotherapy as discussed previously.

In group 2 that is NB UVB intralesional PRP at the end of study very good response was seen in 78.75% while poor response is seen in 3.75%. these results are in accordance to study conducted by Ibrahim et al to explore the effect of PRP injection on the outcome of short-term NB-UVB therapy for the patients with stable vitiligo which was done on 60 patients and it showed 43.3% regimentation in NBUVB PRP group while 10% in NB UVB alone.[28]

Chronic NB-UVB exposure is likely to increase photoaging and the risk of carcinogenesis.[29] Study conducted by Njoo et al recommend that responsive patients can be given NBUVB for a maximum of 24 months.[30] After the first course of one year, they recommend a resting period of three months to minimize the annual cumulative dose of UVB. In children, the maximum duration allowed is 12 months. Subsequently, if

required, only limited areas should be exposed. If no response is observed after six months, further therapy should be discouraged. In our study we observed that major side effect included Pain at site of injection which was seen in almost all the patients but was tolerable. The second major side effect included burning/discomfort/erythema at site of injection mainly seen in PRP group. Rest of the side effects were common in both the groups.

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.

Limitations

Presently there is insufficient human data available to provide recommendations regarding the safe maximum NB-UVB dose. The small sample size is also a limitation for the present study.

CONCLUSION

Intradermal PRP injections along with NB-UVB are efficacious, safe, cheap and easy technique in treatment of vitiligo. It also shortens the duration of NB-UVB therapy.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Pandey AK, Mohan A, Satyaraj P. A comparative study of narrowband-ultraviolet B plus intralesional normal saline versus narrowband-ultraviolet B with platelet rich plasma in treatment of vitiligo. Int J Res Dermatol 2023;9:175-81.