Platelet-rich plasma versus microneedling effects in NB-UVB non-responder vitiligo patients

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Background
Narrow-band ultraviolet B (NB-UVB) is a crucial and effective line of treatment for nonsegmental vitiligo.
Objective
To compare the effect of adding platelet-rich plasma (PRP) injections versus microneedling sessions on the response to NB-UVB in patients who stopped giving response or did not give response from the start.
Patients and methods
An intrapatient randomized comparative study including 30 patients with stable, nonsegmental vitiligo was performed. Three lesions were assessed in each participant and randomly allocated to undergo PRP injections or microneedling every 2 weeks for four sessions. The third lesion was left as a control. Throughout the study, all lesions were subjected to NB-UVB three times a week. Photographic assessment by an independent dermatologist and a patient satisfaction questionnaire were used to assess repigmentation.
Results
PRP injection showed better results than microneedling in terms of repigmentation, complications, and patient satisfaction. The mean percentages of repigmentation in PRP, microneedling-treated, and control lesions were 58.17±21.52, 24.5±18.77, and 15.17±13.49, respectively ($P<0.001$). The onset of repigmentation was earlier in the PRP-injected lesions compared with microneedling (3.97±1.607 and 7.8 ±2.683 weeks, respectively; $P<0.001$). Follicular repigmentation was the predominant pattern in PRP sites (50%).
Conclusion
PRP therapy is a secure and effective procedure that helps patients with vitiligo and speeds up their reaction to NB-UVB as well as supports and encourages their recall response.

Keywords:
microneedling, narrow-band ultraviolet B, nonsegmental vitiligo, platelet-rich plasma

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Introduction

Vitiligo is a difficult condition to treat. Repigmentation is frequently partial, necessitating prolonged therapeutic phototherapy exposure and careful optimization of treatment procedures. Narrow-band ultraviolet B (NB-UVB) treatment is the most extensively used [1,2].

Various procedures have been attempted to wound the lesion to encourage the proliferation, migration, and repigmentation of the lesion's black hair follicles and peripheral melanocytes, for example, dermabrasion [3], cryosurgery[4], and microneedling [5,6].

Platelet-rich plasma (PRP) is an autologous preparation of enriched platelets in plasma. Vascular endothelial growth factor, platelet-derived growth factor, transforming growth factor, and insulin-like growth factor are among the growth factors that are secreted from concentrated platelets that have been triggered by aggregation inducers [7,8]. By binding to particular cell surface receptors, these substances are known to affect a variety of functions, such as cell motility, adhesion, proliferation, differentiation, and stimulating the formation of extracellular matrix [9,10]. PRP has been employed in a range of surgical procedures and therapeutic interventions because of the high concentration of these growth factors [11]. To improve response to NB-UVB in stable nonresponder patients with vitiligo, the study looked at the effect of PRP injection and microneedling.

Patients and methods

Patients

In this prospective intrapatient randomized comparative study, 30 patients were recruited from

the outpatient clinics of the Dermatology and Andrology department, Faculty of Medicine, Benha University, Egypt.

Ethical statement: The Benha Faculty of Medicine's human participants research ethics committee gave its approval to the study (RC 29.10.2022). The study was done following the ethical standards of the Helsinki Declaration 2013. Before the study started, all participants received comprehensive information about the procedures and gave their written, signed agreement.

Inclusion criteria: patients with stable nonsegmental vitiligo who either stopped responding to NB-UVB or did not respond at all, despite good compliance to phototherapy sessions were included. A nonresponder was considered after 72 regular UVB sessions with no response, according to the Vitiligo Working Group committee's guidelines [12].

However, patients with unstable vitiligo, segmental type, acral type, noncompliance with phototherapy sessions, having received topical or systemic treatments in the past 2 months, a history of bleeding tendency, or being uncooperative were excluded.

The absence of new lesions over the preceding 6 months, the growth of existing lesions, the Koebner's phenomenon, and lesions with ill-defined borders were all considered indicators of stability [13].

Methods

All patient details were recorded, including age, sex, skin Fitzpatrick type, location of lesions, and duration of illness. To randomly assign 90 patches into three study groups of lesions, three comparable lesions per patient (in terms of place and size) were chosen. Randomization was done through sealed envelopes. PRP injection was used to treat the first lesion, microneedling was used to treat the second, and the third was left untreated as a control. There were four treatment sessions, each separated by 2 weeks. All lesions received NB-UVB treatments over the course of the study. All of the individuals who were included were instructed not to take any topical or systemic medications throughout the research.

Narrow-band ultraviolet B therapy

A chamber with TL-01 lamps was used for NB-UVB phototherapy (Waldmann Medizintechnik, Villingen Schwenningen, Germany) with wavelengths from 310 to 315 nm. All patients received a standard 280 mJ/cm^2 first dose, which was given three times a week on different days. The least amount of erythema in the lesions signaled the achievement of the ideal constant dose. When a pink, asymptomatic erythema lasting 24 h (a targeted response) occurs, the dose is kept constant until the erythema goes away, at which point it is increased by 20% [14].

Platelet-rich plasma preparation

RegenLab kits (Regenlab, New York, New York, USA) were used. PRP was prepared under proper aseptic conditions. As an activator, calcium chloride at a 10 : 1 ratio (0.1 ml of $CaCl_2$ to each 1 cm of PRP) was added immediately before the injection. For superficial intradermal microinjections, a 30-G needle was employed [15].

Microneedling

Dermapen (My M Dermapen, China) was used for the procedure. The needle was inserted into the selected lesions at a depth of 0.5–1 mm, and numerous passes were made in different directions until pinpoint bleeding was noticed. After the session, a topical antibiotic cream was used for 3 days.

Outcome measurements

Time till repigmentation started, the kind of repigmentation (diffuse, marginal, or follicular) and the degree of repigmentation were all evaluated. Using a quartile grading scale (1: 25% repigmentation, no or minor improvement; 2: 25–49%, moderate; 3: 50–74%, marked; and 4: 75–99%, excellent), this was carried out by a different dermatologist who was unaware of the study [16]. Digital photography (Samsung Galaxy Note 10+, 12-16 megapixel cameras, Korea) was used to assess the lesions at baseline, each visit, and 2 weeks after the last one. Patient satisfaction was graded as unsatisfied, slightly satisfied, satisfied, and extremely satisfied. Patients were instructed to report any consequences, such as erythema, ecchymosis, infection, or expanding lesions.

Statistical analysis

The SPSS (Statistical Package for the Social Sciences) version 26 computer program was used to analyze the data (Armonk, NY, USA). Descriptive statistics were applied in the following formats: mean, SD, number, and percent. Numerical (parametric) data were compared between more than two groups using the analysis of variance, continuous nonparametric data were compared between groups using the Kruskal–Wallis test, and different parameters were correlated using the Pearson or Spearman correlation coefficient tests. *P* value less than 0.05 was considered statistically significant.

Results

In 30 patients with vitiligo, a total of 90 lesions were evaluated and studied. Vitiliginous lesions were identified on the trunk (n=6), face (n=5), upper limbs (n=7), and lower limbs (n=12). The mean age of the study patients was 23.73±3.83 years, with a range of 19–32 years. Males and females constituted 60 and 40% of all patients, respectively. The mean duration of disease was 2.9±1.58 years, ranging from 1 to 6 years. There was family history of similar disease in two (6.7%) patients. Skin phototype IV formed the majority of patients (n=18, 60%) followed by type III (n=10, 33.3%) (Table 1).

There was a statistically significant difference in percent and grade of repigmentation among the lesions investigated, with best improvement in PRP-treated lesions (P<0.001). However, microneedling-treated lesions versus control ones showed no statistical difference regarding percent and grade of repigmentation (P=0.123 and 0.056, respectively) (Table 2; Fig. 1).

PRP-treated lesions began to repigment considerably earlier than the other examined lesions did (P<0.001). However, there was no discernible difference between the microneedling and control lesions (P=0.539) (Table 2).

Pattern of repigmentation in PRP-treated lesions varied mainly between follicular and marginal types (50 and 36.6%, respectively), but microneedling and control lesions showed mainly marginal repigmentation pattern in 60 and 46.4% of lesions, respectively (Table 2, Fig. 2).

There were no significant correlations found between the percentage of repigmentation in lesions that had

Table 1 Basic data of the patients

Variables	
Age (years)	
Range	19–32
Mean±SD	23.73±3.83
Sex [*n* (%)]	
Male	18 (60)
Female	12 (40)
Skin Fitzpatrick type [*n* (%)]	
III	10 (33.3)
IV	18 (60)
V	2 (6.7)
Site of the lesions [*n* (%)]	
Face	5 (17)
Trunk	6 (20)
Upper limb	7 (23)
Lower limb	12 (40)
Duration of the disease (years)	
Range	1–6
Mean±SD	2.9±1.58

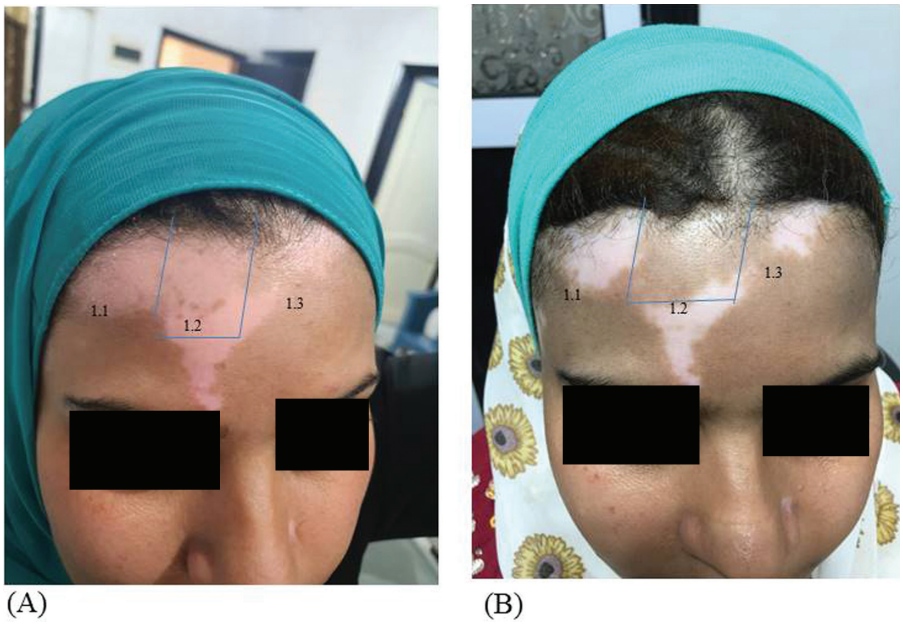
Table 2 Comparison of repigmentation response between the studied lesions at 8 weeks

Groups	Mean±SD	Test of significance	*P*	Post-hoc Tukey HSD (beta)*
Grade of repigmentation				
PRP	2.83±0.7466	f=57.5	<0.001*	P vs. M (P <0.00*) P vs. C (P<0.001*) M vs. C (P=0.056)
Microneedling	1.37±0.7184			
Control	0.93±0.6915			
Percent of repigmentation (%)				
PRP	58.17±21.52	f=46.2	<0.001	P vs. M (P <0.001*) P vs. C (P <0.001*) M vs. C (P=0.12254)
Microneedling	24.5±18.77			
Control	15.17±13.49			
Onset of repigmentation (weeks)				
PRP	3.97±1.6078	f=12.2	<0.001	P vs. M (P <0.001*) P vs. C (P <0.001*) M vs. C (P=0.539)
Microneedling	7.8±2.6833	χ^2=20.4	0.002*	
Control	6.93±4.4793			

Pattern of repigmentation	Follicular [*n* (%)]	Marginal [*n* (%)]	Diffuse [*n* (%)]	No response [*n* (%)]
PRP	15/30 (50)	11/30 (36.7)	4/30 (13.3)	0/30
Microneedling	6/30 (20)	18/30 (60)	6/30 (20)	0/30
Control	4/30 (13.3)	14/30 (46.7)	4/30 (13.3)	8/30 (26.7)

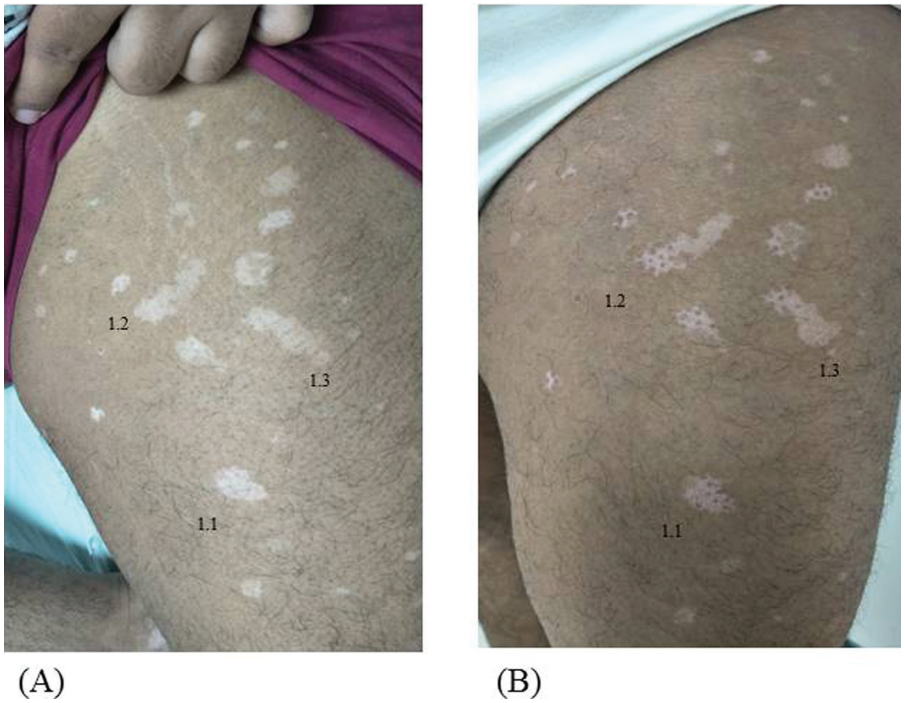
PRP, platelet-rich plasma. P, PRP; M, microneedling; C, control. Analysis of variance test. χ^2 test. *P values < 0.05 is considered statistically significant.

Figure 1



Face one site divided into three tested lesions: (1.1) control, (1.2) PRP injected, and (1.3) microneedling treated (A) before and (B) 8 weeks after. (1.1) Control (repigmentation grade 1, <25%), (1.2) PRP injected (grade 4, 75–99%), and (1.3) microneedling treated (grade 2, 25–49). PRP, platelet-rich plasma.

Figure 2



Thigh: three tested patches one the same side: (1.1) Control, (1.2) PRP injected, and (1.3) microneedling treated (A) before and (B) follicular repigmentation after 4 weeks. (1.1) control (grade 1, <25%), (1.2) PRP injected (grade 2, 26–49%), and (1.3) microneedling treated (grade 1, <25%). PRP, platelet-rich plasma.

undergone PRP treatment and any of the following factors: patient age, skin type, or duration of disease (Table 3).

Patient satisfaction was better with PRP-treated lesions (15/30 satisfied and 8/30 very satisfied). On the contrary, unsatisfactory response was more with

Table 3 Correlations between percent of repigmentation with platelet-rich plasma and different variables

	r	*P*
Age (years)	0.224	0.234
Duration of disease	–0.041	0.83
Skin type	–0.069	0.717

Pearson correlation. *P* value less than 0.05 is considered statistically insignificant.

microneedling and control lesions (20/30 and 25/30, respectively). There were just a few minor adverse effects, including ecchymosis with PRP (3/30), crustations and expansion of the microneedling treated lesions (5/30, 2/30, respectively).

Discussion

The therapy of vitiligo has been attempted using several therapeutic modalities. For the treatment of moderate to severe vitiligo, NB-UVB is thought to be the most efficient and secure initial treatment [17]. The response to NB-UVB, however, could be slow and delayed [18].

Aside from the distance to go, the financial burden, and the time lost in attending the hospital, the main cause for noncompliance is the protracted period of NB-UVB therapy. This clearly emphasizes the importance of combining therapy with NB-UVB to decrease the duration.

In this study, we assessed the effectiveness and acceptability of two straightforward approaches used as adjuvant treatments to restore or obtain a repigmentation response with NB-UVB. The effects of individual characteristics were mitigated using an intrapatient comparative design.

In the PRP-injected areas, the repigmentary response occurred more quickly, to a greater extent, and the follicular pattern predominated. This is in line with those reported by Ibrahim *et al.* [19] and Parambath *et al.* [20]. In contrast, Lim *et al.* [21] claimed that PRP was ineffective in the treatment of vitiligo after administering intradermal injections once a week for 10 weeks to 20 individuals with the condition.

It is still unclear how PRP works to treat vitiligo. According to various reports, keratinocytes and fibroblasts as well as melanocytes play some roles in the etiology of vitiligo [8]. The positive effects of PRP on vitiligo could be attributable to growth factors that encourage keratinocyte and fibroblast proliferation, improving their interactions with melanocytes and upregulating cyclin E and CDK4, which are crucial for cell migration and proliferation [22].

While UVB increases melanogenesis and inhibits the immune system, PRP improves the environment for melanocytes to grow and be well attached to keratinocytes. To improve the outcomes, all of the mechanisms work together. The rise in melanocyte count in lesions treated with PRP was confirmed by histological examination [19].

Stanimirovic *et al.* [5] and Ebadi *et al.* [23] did not find any further advantages and did not suggest combining microneedling and NB-UVB. This is consistent with what we discovered. However, some studies have revealed that needling is useful for curing vitiligo [24,25]. In 70% of patients with acrofacial vitiligo, Elshafy Khashaba *et al.* [26] found that combination microneedling and NB-UVB produced good repigmentation.

According to Wassef *et al.* [27], the fundamental mechanism of needling-induced repigmentation is the transfer of melanocytes from pigmented to depigmented areas. By injuring the basal cell layer, microtrauma can also promote cutaneous melanophages and hyperpigmentation. These all support melanogenesis [28].

According to Fabbrocini *et al.* [29], the mechanism by which microneedling functions is based on the formation of microchannels, which results in the creation of a zone of bleeding that serves as a potent stimulus for the release of numerous growth factors, including platelet-derived growth factor, transforming growth factor alpha and beta, and fibroblast growth factor.

Limitations of the study: the small sample size and short follow-up were the main drawbacks of this work.

Conclusion

In nonresponder patients with vitiligo of the nonsegmental form, PRP injection is preferable than microneedling and more tolerated for achieving an optimum response with NB-UVB. PRP may reduce the duration of UVB exposure, making it more convenient for many patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the

patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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