Efficacy and tolerability of needling as an adjuvant to narrowband ultraviolet B therapy in the treatment of vitiligo: a clinical trial

Atyeh Ebadi, MD [1]
Hamideh Moravvej, MD [1]
Somayeh Hejazi, MD [1]
Shima Younespour, MS [2]
Fariba Ghalamkarpour, MD [1]

1. *Skin Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
2. *Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran*

Corresponding Author:
Fariba Ghalamkarpour, MD
Skin Research Center, Shohada-e-Tajrish Hospital, Shahrdary St, Tehran, Iran
E-mail: fghalamkarpour@yahoo.com

Conflict of interest: none to declare

Received: 5 February 2013
Accepted: 10 September 2013

Background: Despite great advances in therapeutic regimens, complete repigmentation in vitiligo is still out of reach**.** The aim of this assay was to study the efficacy and tolerability of repeated needling combined with narrowband ultraviolet B (NBUVB) therapy in the treatment of generalized, stable, refractory vitiligo.

Method: Twenty-six patients with stable generalized intractable vitiligo were recruited in before/after clinical trial. The patients received needling for selected patches weekly for 12 weeks. All the patients received NBUVB phototherapy three times a week. Repigmentation improvement was assessed by two blinded investigators at weeks 4, 8 and 12. Tolerability was assessed by a 5-point scale.

Result: Twenty-two patients (16 women and 6 men) with a mean (SD) age of 34.41 (12.75) years completed the 12-week therapy period. In comparison with the baseline, improvement in the mean percentage of repigmentation was 7.10±10.15, 12.95±20.29, and 15.57±17.38 at week 4, 8 and 12 of therapy, respectively. A significant improvement was observed in repigmentation percentages in the three time points ($p<0.0001$).

Conclusion: Although our patients showed repigmentation improvement, the overall repigmentation was very low (about 15.57 %); therefore, we do not recommend needling as an alternative to other available surgery procedures that have more favorable efficacy and tolerability in contrast to this new procedure.

Keywords: needling, narrowband ultraviolet B, surgical treatment, vitiligo

Iran J Dermatol 2013; 16: 89-93

INTRODUCTION

Vitiligo is a chronic debilitating disorder with many cosmetic and psychological problems that affects 0.5-4% of the general population [1]. This multifactorial polygenic disorder is caused by the destruction of skin functioning melanocytes and characterized by white depigmented macules or patches anywhere on the body [1-3]. The course of vitiligo is unpredictable. Despite several hypotheses formulated, the etiology is yet unknown. This benign condition imposes serious emotional and psychological stress as well as social embarrassment on patients, mainly due to its lack of proper treatment and unpredictable course [1].

Treatment options for vitiligo include watchful waiting, tanning, active regimentation (by medical or surgical therapies) and depigmentation [1,4]. The limited use of medical treatments might be attributed to their side-effects, limited efficacy, and possible carcinogenicity [4]. Surgical methods for vitiligo are indicated when medical treatment is insufficient

and vitiligo is stable and recalcitrant [3,5]. Despite different therapeutic regimens recommended for vitiligo, many patients with this disease are unable to achieve satisfactory outcomes.

Given the limitations of current approaches in the treatment of vitiligo, search for effectual therapies that are also convenient, inexpensive, and affordable is continued. One of the newest therapies that could theoretically push or drag the melanocytes physically from the normal peripheral skin to white depigmented center is needling. Tahir claims that repigmentation of white patches during the needling process is primarily due to melanocytes dragged physically by the tip of the needle from the pigmented periphery or from the pigmented islands toward the depigmented areas so melanocytes may proliferate and settle in their new location. He explains that the islands may previously exist or form during needling and may serve as rich reservoirs of melanocytes available for further spread [6]. Based on the good to excellent results reported by this new modality and the positive anecdotal reports of its benefit for repigmentation of vitiliginous lesions, we conducted a prospective, single-center, randomized, before-after, clinical trial to determine the efficacy and tolerability of repeated needling combined with NBUVB therapy in the treatment of generalized, stable, refractory vitiligo.

PATIENTS AND METHODS

Before initiating any study-related procedure, ethical approval was obtained from the Ethics Committee of Shahid Beheshti University, Tehran, Iran. The procedure was explained to the participants and written informed consent was obtained from them.

This 12-week, randomized, before-after single-center, clinical trial was conducted at Shohada-e-Tajrish Hospital to evaluate the clinical efficacy and tolerability of needling as an adjuvant to narrowband ultraviolet B (NBUVB) therapy for the treatment of stable generalized intractable vitiligo.

Twenty-six known cases of generalized intractable vitiligo who were visited at the Dermatology Outpatient Clinic of Shohada-e-Tajrish hospital from September to December 2010 were included in this study. The patients had stable vitiligo for at least 2 years. The exclusion criteria were as follows: age < 18 years old, history of pregnancy, breastfeeding, photosensitivity, phototoxic drug use, allergy to lidocaine, history of skin cancer or other cancers, immunosuppression, cutaneous atrophy or infection, and tendency to form keloid or hypertrophic scar. In addition, patients with a history of systemic diseases including xeroderma pigmentosum, systemic lupus erythematosus, porphyries, autoimmune disorders, cardiovascular and hematologic diseases, and coagulopathies were also excluded.

The washout period for prior vitiligo therapies was 4 weeks for topical therapy with corticosteroids, vitamin D analogues or tacrolimus and 8 weeks for phototherapy (NBUVB or PUVA) and any systemic, laser, or surgical therapy. Other concomitant vitiligo therapies at any location were not permitted during this study.

To evaluate the occurrence of Koebner's phenomenon and confirm the stability of vitiligo, needling was tested in a small area near the reference patch 2 months before the surgery. To minimize the pain of needle insertion, local administration of lidocaine was performed 15 min before the procedure for each patch [7-11]. Briefly, the normal skin nearly 5 mm out of the circumscription of the lesion and near the dermo-epidermal junction was pricked with a 30 G needle. Then, the needle was moved through the pigmented areas toward the depigmented patch to push melanocytes forward, such movements were made repetitively through all the periphery of each patch. Finally, the needled patch was covered by a thin dressing.

The patients received needling for selected patches at baseline (week 0) followed by once a week for 12 weeks. All the patients received additive NBUVB (311 ± 2 nm) therapy with an initial dose of 50mj/cm^2 three times a week. The NBUVB dose increased 50mj/cm^2 per session until the maximum dose reached 2000mj/cm^2; then, the same dose was continued.

For each participant, sex, age, race, duration of the disease, body surface area (BSA) of the disease, primary size and site of the patches (at four anatomical sites: head and neck, proximal extremities, trunk and distal extremities), prior treatment, and medical and family history were recorded. Tolerability assessments were also performed by recording adverse events (erythema, pain, pruritus, scaling/dryness, erosion/crusting,

scar, Koebner's phenomenon, post inflammatory hyper/hypo pigmentation) on a 5-point scale from 0 (none) to 4 (severe) by the investigator at each visit.

For all patients, professional photography with a professional camera (SLR 40 D, Lens Eos 18-200) was performed 4, 8 and 12 weeks after the baseline visit. Calculation of the percentage of the repigmentation (0%-100%) of the treated areas was done with AutoCAD (Autodesk Inc., San Rafael, CA, USA) and ImageJ (National Institute of Health, USA) software via analyzing patients' photographs at weeks 4, 8 and 12 in comparison with baseline.

The Friedman test was used to evaluate the differences of repigmentation percentages among the three time-points (weeks 4, 8 and 12) and Wilcoxon signed rank tests with bonferroni corrections were conducted to test the pair-wise comparisons. Statistical analysis was performed using the statistical software SPSS 16.0.0. (SPSS Inc. Chicago, IL, USA). P-values (P) less than 0.05 were considered significant.

Table 1. Patients' demographic data at baseline

Sex, no. (%)	
Female	18 (69.23%)
Male	8 (30.77%)
Age, years	
Mean (SD)	35.38 (13.65)
Range	(18-60 years)
Fitzpatrick, no. (%)	
Type II	2 (7.69%)
Type III	15 (57.70%)
Type IV	9 (34.61%)
Years since first sign of depigmentation	
Mean (SD)	10.96 (7.42%)
Median (Range)	10 (1.5-36)
Body surface area affected (%)	
< 25%	17 (65.38%)
25-50%	8 (30.77%)
51-75%	1 (3.85%)
>75%	-
Location of patch	
Hands	16 (61.54%)
Feet	7 (26.92%)
Arms	1 (3.85%)
Neck	1 (3.85%)
Genital area	1 (3.85%)
Diameter patch, cm	
Mean (SD)	5.36 (3.13%)
Median (Range)	5 (2-13.5)

RESULTS

Twenty-six patients (8 men, 18 women) with previous diagnosis of generalized recalcitrant vitiligo were enrolled in this study. After one week of therapy, three patients discontinued the study (1 due to the pain of the procedure and 2 due to personal reasons). Four weeks after the beginning of the therapy, one patient (male) withdrew due to difficulty attending the follow-up visits. Finally, a total of 22 patients (16 women and 6 men) completed the 12-week therapy period. Table 1 shows the patients' demographic and baseline characteristics. In comparison with the baseline, improvement in the mean percentage of repigmentation was 7.10 ±10.15, 12.95±20.29, and 15.57±17.38 at week 4, 8 and 12 of therapy, respectively (Figure 1). There was a significant difference in the repigmentation percentage among these three time-points (weeks 4, 8 and 12) ($p<0.0001$). Also, pair-wise comparisons showed a significant increase in the percentage of skin repigmentation in each therapy visit as compared to week 4 and the previous visit (p-values at most 0.0015) (Figure 2a, 2b).

Approximately, 28% of the patients had mild to moderate scaling over therapy visits and one patient suffered from severe scaling in this period. About 41% of the patients at week 4, 27% of the patients at week 8 and 36% of the patients at week 12 experienced mild to moderate erythema. Five patients had moderate pain at week 4 and approximately 58% of the patients had mild to moderate pain at weeks 8 and 12. Twenty seven percent of the patients at week 4, 32% of the patients at week 8 and 36% of the patients at week

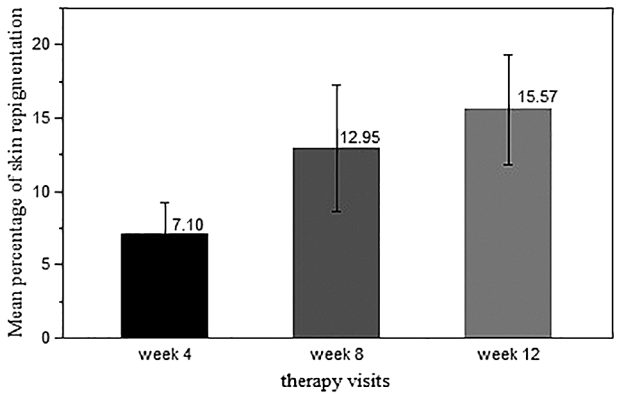

Figure 1. Mean percentage of skin repigmentation at 4, 8 and 12 weeks after beginning the therapy.

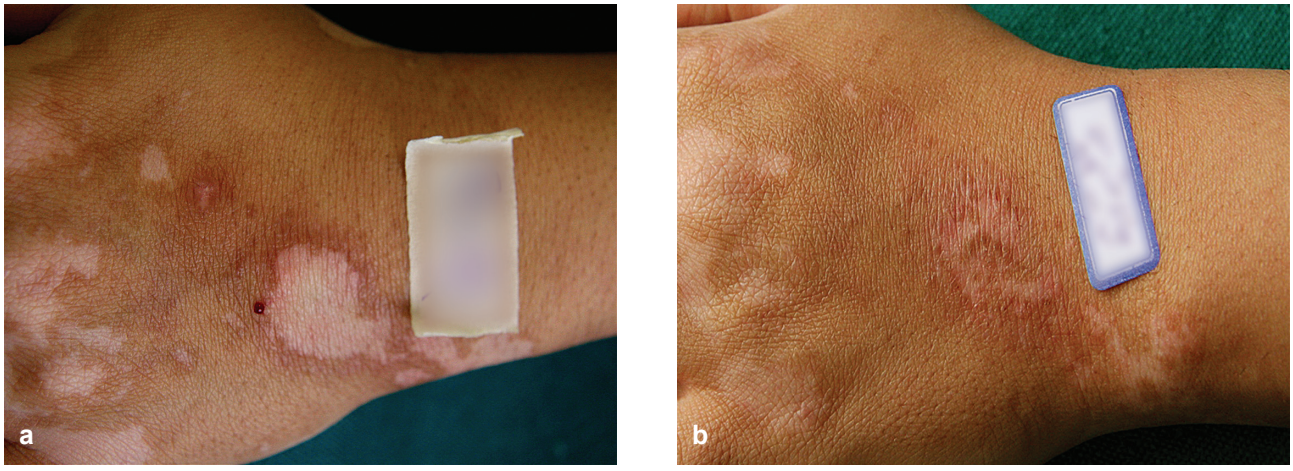

Figure 2. a) Vitiligo on the dorsal aspect of a 26-year-old patient at week 4; b) the same lesion after 12 weeks.

12 experienced mild to moderate erosions. Mild to moderate post inflammatory hyperpigmentation was observed in approximately 23% of the patients during the study period at the peripheral normal skin of the patches. Other complications such as pruritus, post inflammatory hypopigmentation and scar were not observed during the therapy sessions.

DISCUSSION

Our results showed gradual repigmentation of the patches in the three time-points (weeks 4, 8 and 12) which was statistically significant compared to the baseline. However, despite this gradual improvement, the overall improvement in repigmentation was only 15.57 % at the end of the study in comparison to the baseline; therefore, our patients responded poorly to needling plus NBUVB treatment. Needling was tolerable for our patients and no significant or permanent complications such as scarring or Koebner's phenomenon were observed. Erythema was the most common objective complication and pain was the most expressed complaint even between sessions.

The needling protocol was first introduced by Tahir Jamil Ahmad as a simple effective therapy for stable vitiligo [6]. Furthermore, using the needle for the treatment of vitiligo was also mentioned in some anecdotal articles prior to Tahir [7-11] but there was no previous record of needling in our country; so, we planned a protocol based on our patients' compliance as well as our center limitations and ethics. The trial was composed of weekly sessions of needling plus three times a week NBUVB therapy for three months so we could provide our patients with more mental relief and a longer recovery period following each needling procedure. At the end of the twelfth session, we reviewed the results but the achieved repigmentation was not considerable; therefore, our center refused to extend the study period.

Tahir [6] reported good to excellent repigmentation (above 50%) in almost all needled patches while in our study, repigmentation was only about 15.7 % which was far from expectations and lower than the results reported by Tahir.

In conclusion, the protocol of our study can be considered as an ineffective method in the treatment of intractable stable vitiligo patches. Although the procedure is quite simple and practical, it is very time consuming and hard for patients to adhere to their treatment protocol. Complications are temporary and almost mild to moderate but exposure to multiple microtraumas by the needle should be considered. Physicians need be cautious about its long term side effects, especially in darkly pigmented patients. To sum up, we do not recommend needling as an alternative to other surgical methods such as various techniques of dermoepidermal graft in the treatment of intractable stable vitiligo.

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