

**Efficacy of Skin Microneedling in combination with Narrow Band
- Ultraviolet B Phototherapy in Vitiligo**

Abstract

Background: Vitiligo is a chronic cutaneous disease characterized by milky white depigmented patches that leave psychological impact on the patient's quality of life. New treatment modalities have been developed to shorten the duration of treatment of vitiligo with the least side effects.

Objective: To evaluate the safety & efficacy of microneedling in combination with narrow band-UVB in the treatment of vitiligo.

Patients and methods: This study included 20 patients with stable vitiligo. They were treated by microneedling (one session every 2 weeks) in combination with narrow band-UVB (3 sessions weekly) for 3 months.

Results: The studied patients reported statistically significant degree of clinical improvements as follow; 10% reported good improvement, 25% showed moderate improvement, 45% showed mild improvement and 20% showed no improvement, after 3 months therapy. The reported side effects were minimal and transient in the form of minor pain, burning sensation and erythema at site of microneedling that disappeared spontaneously within few hours.

Conclusion: Microneedling in combination with narrow band-UVB phototherapy could be considered as effective treatment of vitiligo. Microneedling is a tolerable technique, harmless with negligible side effects.

Keywords: Microneedling; narrow band-UVB; Vitiligo.

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Introduction

Vitiligo is an acquired cutaneous achromia characterized by milky white cutaneous patches of various sizes and shapes resulting from loss of epidermal melanocytes. Multiple mechanisms have been suggested to be involved in loss of melanocyte: genetic predisposition, environmental triggers, metabolic abnormalities, altered inflammatory and immune responses, the autoimmune theory is the leading hypothesis⁽¹⁾. The prevalence of the disease varies between 0.1- 4% of the world population of all skin types, races, and both sexes. There are several treatment modalities for vitiligo, such as topical corticosteroid, vitamin D3 analogue derivatives, calcineurn inhibitors, photochemotherapy and eximer laser⁽²⁾.

Microneedling is a relatively slightly invasive technique involving superficial and controlled puncturing of the skin by rolling with miniature fine needles⁽³⁾. It improves drug penetration through stratum corneum, which might potentiate their activity⁽⁴⁾. In addition, it induces processes similar to wound healing with production of cytokines and growth factor beneficial for repigmentation. Needling is used for treating localized vitiligo alone or in combination with narrow band-UVB with quite satisfying therapeutic results⁽⁵⁾.

The aim of our work is to evaluate the safety & efficacy of microneedling in combination with narrow band-UVB in the treatment of vitiligo, **in a trial to accelerate and augment the therapeutic response and shorten the duration of treatment.**

Patients and Methods:

This study is a preliminary clinical trial that was conducted on 20 vitiligo patients. They were collected from the Outpatient Clinic of Dermatology and Venereology Department, Tanta University Hospitals, Egypt. **Approval from Research Ethical Committee, Faculty of**

Medicine, Tanta University, was acquired and patients' informed consents were taken before joining this work.

Inclusion Criteria:

1. Patients with stable vitiligo for at least 1 year.
2. Patients with vitiligo who stopped receiving any treatment (systemic, topical, or phototherapy) for the last 3 months.
3. Patients with no other skin or systemic diseases.

Exclusion criteria:

1. Patients with active vitiligo.
2. Patients who have any other skin disease.
3. Patients suffering from acute or chronic diseases such as (kidney and liver disease, ischemic heart disease or oncological diseases).
4. Bleeding and coagulation disorders and anticoagulant users.
5. Pregnancy and lactation.

Therapeutic Procedure:

Each patient treated as follow; microneedling (one session every 2 weeks) in combination with narrow band-UVB (3 sessions weekly), for 3 months. Patients were photographed at the first visit and at the end of therapy.

Phototherapy:

The patients treated by narrow band phototherapy (one session every other day for 3 months), using narrow band-UVB source (Philips TL 100 fluorescent tubes, Germany) with a spectrum of 310–315 nm installed in a Waldmann UV-100 unit. The dose of narrow band-

UVB was 0.33 J/cm² (we started with 0.2 J/cm² and increased gradually to achieve the dose inducing mild erythema) ⁽⁶⁾.

Microneedling:

The skin was cleaned by ethyl alcohol and local anesthetic cream was applied under occlusion for 0.5-1 hour. After that, microneedling was done by Dermapen (MYM microneedling, Korea), (Figure 1). Adaptor was plugged into the hand piece. Sterilized needle was put into the top of the hand piece and set at (01.5 to 2.0 mm) needle depth by turning the adjustment ring. Microneedling session was performed by perpendicular application of the dermapen over the lesion and moving it in both vertical and horizontal lines, till the development of erythema ⁽⁷⁾.

Evaluation of the treatment outcomes

The patients were examined carefully in the first visit and a certain depigmented lesion was selected for the clinical trial. Then, they were reviewed weekly for evaluation of the progress of therapy and the presence of any side effects. Photographs were taken for the selected lesions before starting therapy and at the end of the study, using 18.2 mega pixels digital camera (SONY CYBERSHOT DSC-WX300). The repigmentation response was evaluated by comparing pre- and post-treatment photographs and was expressed qualitatively as follows: No change (0%), mild (1 –25%), moderate (26–50%), good (51 –75%), excellent (76 –99%), complete regimentation (100%) ⁽⁵⁾.

Evaluation of patient's satisfaction

It is the degree of improvement according to the patient opinion. The patients were asked at the final visit about the overall satisfaction according to whether the patient not satisfied, satisfied or very satisfied.

Evaluation of patient's tolerability

Each patient was informed to observe any adverse effects related to therapeutic procedure such as; burning sensation, inflammation, infection, ecchymosis, or any allergic manifestations.

Follow-up of patients

All patients were followed-up monthly for 3 months after the end of the treatment sessions to detect any recurrence, complications or worsening of the lesions.

Statistical analysis

The data were collected, tabulated and statistically analyzed using SPSS software statistical computer package version 12. For quantitative data, the mean and standard deviation were calculated. For qualitative data, number and percent were calculated. P-value less than 0.05 was considered statistically significant.

Results

This study included 20 vitiligo patients. Regarding the gender of the patients; there were 8 males (40%) and 12 females (60%). The age of the patients ranged from 10 to 52 years. Two patients (10%) had positive family history of vitiligo while 18 patients (90%) had negative family history of the disease. Regarding the skin type of the patients, 15 patients (75%) were skin type III and 5 patients (25%) were of skin type IV. Regarding the site of vitiligo there were 10 patients (50%) with lesions on the extremities, 3 patients (15%) with lesion on the face, 3 patients (15%) on the trunk, two patients (10%) on the neck, 2 patients (10%) in acral parts. While regarding the duration of vitiligo; it ranged from 2.6 to 12 years (Table 1).

Treatment outcomes

The present study didn't report excellent improvement in any patient, only two patients (10%) reported good improvement (Figure 2), 5 patients (25%) showed moderate improvement, 9 patients (45%) showed mild improvement and 4 patients (20%) showed no improvement, (Table 2). Regarding the duration of vitiligo, patients with shorter duration showed better response than those with longer duration. Regarding the site of vitiligo lesions, face and neck showed the best response followed by trunk and then extremities while acral parts showed poor response.

Regarding patients' satisfaction with the treatment outcomes, 3 patients (15%) were very satisfied, 8 patients (40%) were satisfied, and 9 patients (45%) showed not satisfied, (Table 3).

All studied patients tolerated the treatment well. The adverse reactions were minimal and transient in the form of burning sensation, inflammation at site of microneedling that disappeared spontaneously within few hours. On the other hand, recurrence was observed in 15% of the studied patients (3 patients) after 3 month from last session.

Discussion

The aim of treatment in vitiligo is to restore the normal appearance, morphology, and function of the skin. Several treatment modalities are currently available for treatment of vitiligo that can be broadly classified under medical and surgical modalities; each having certain indications and limitations. A combination of traditional and newer treatments may work synergistically to provide additional improvement in patients' disease state, quality of life and reduce the potential side effects^(1,2). In this work we tried to evaluate the efficacy and safety of microneedling in association with narrow band-UVB in the treatment of vitiligo, in

a trial to accelerate and augment the therapeutic response and shorten the duration of treatment.

At the end of follow up period (3 months after last session), different grades of repigmentation were observed in 80% of patients with good improvement in 10%, moderate improvement in 25%, and mild improvement in 45%.

The results of Batool et al.,⁽⁸⁾ were superior to our result. They reported that patients with vitiliginous patches who were treated (three/week) by needling with insulin syringe, and then were given narrowband UVB sessions for at least six months, showed very good to excellent improvement in about 91% of patches.

In addition, El-Zeftawy et al.,⁽⁷⁾ conducted a study to compare the efficacy of narrow band-UVB phototherapy versus combined narrow band-UVB phototherapy and microneedling in treatment of vitiligo. They reported that, the mean percentage of improvement was significantly high in the group of patients (Group A) treated by combination of microneedling and narrow band-UVB phototherapy than the other group (Group B) treated by narrow band-UVB phototherapy alone. In Group A 20% showed mild improvement, 20% showed moderate improvement, (40%) showed good improvement and 20% showed excellent improvement. In Group B 30% showed no improvement, 50% showed mild improvement, 10% showed moderate improvement and 10% showed good improvement⁽⁷⁾.

Mohaghegh et al.,⁽⁹⁾ tried to assess the efficacy of narrow band -UVB therapy with and without needling by insulin syringe in the treatment of vitiligo. The patches included in their study were divided into A and B groups. Both groups received NB-UVB (three/week) for three months. In addition, the B side also received needling by insulin syringe. Side B had

statistically greater improvement in pigmentation with 41.5% achieving very good level of repigmentation.

Ahmad et al., ⁽⁵⁾ also concluded that, needling is a safe, effective and promising adjuvant treatment to narrow band-UVB for repigmentation of non- responding localized vitiligo, as 90% of treated patches showed good to excellent response after six months of needling with narrow band-UVB exposures without evident side effects.

Attwa et al., 2019 ⁽¹⁰⁾ in a study to assess the effectiveness of using microneedling prior to application of topical 5- FU in treatment of localized vitiligo and to compare its results with microneedling alone, microneedling performed with dermapen (Dr Pen Derma Pen Ultima M5®) with needle length (1- 2 mm according to the treated site). In patch A treated by microneedling alone, there was no excellent or very good grades of repigmentation, while one patient (3.7%) showed good grade, 4 patients (14.8%) showed satisfactory grade, and 22 patients (81.5%) showed poor grade of repigmentation. In addition, Sheikh ⁽¹¹⁾ conducted a study to evaluate the efficacy of combination of needling and narrow band-UVB for treatment of vitiligo. They reported that this combination regimen is very safe and effective against vitiligo as compared to UVB alone in all age groups.

In contrast to our result, Ebadi et al., ⁽¹²⁾ who used needling once per week and narrow band-UVB 3 times per week and the overall repigmentation was low about (15.57%). Therefore, they suggested that needling is not recommended.

Regarding the efficacy of microneedling on different body sites, our study showed good to moderate response on face and trunk, while extremities and acral parts showed less response. These finding agreed with Sheikh ⁽¹¹⁾ who conducted a study to evaluate the efficacy of combination of needling and narrow band-UVB for treatment of vitiligo. They

reported that best results were on the face, repigmentation after 12 week was 70 % in face, 60% in trunk area and 50% in arms.

One of the remarkable finding in our study was that, the reported side effects of microneedling were few and minor, and all patients tolerated the procedure well. Pain occurred in all cases during microneedling session, and reduced when local anesthesia was applied. Erythema occurred in all cases and also disappeared within 24 hours. This may indicate that microneedling could be considered safe and tolerable technique for treatment of vitiligo, consistent with our results, previous studies done by Ahmad et al.,⁽⁵⁾.

Microneedling instruments are devised of rows of fine needles, which are stamped over the skin to create rapidly healing punctures, resulting in a wound-healing response and subsequent collagen and elastin production. This technique is also used to augment transdermal drug delivery through pores created through the stratum corneum⁽¹³⁾. It is an evolving treatment modality for a growing number of dermatologic conditions⁽¹⁴⁾.

To understand the mechanism by which microneedles increase skin permeability and enhance drug delivery through the skin by increasing skin blood perfusion, A Laser Doppler Perfusion Monitor was used to record maximum blood flow and the time needed to reach maximum blood flow in the treatment areas. Sections treated with microneedles showed a higher maximum blood flow and reached maximum blood flow faster than sites not treated with microneedles⁽¹⁵⁾.

Microneedling expand the scope of transdermal delivery by creating microscopic channels that enhance the delivery of therapeutic agents ranging in size from small molecules (including drug-loaded nanoparticles) to macromolecules such as proteins across the skin⁽¹⁶⁾.

Small and very sharp microneedles have sufficient length and strength to penetrate the stratum corneum and epidermis but do not stimulate the nerve fibers and blood vessels ⁽¹⁷⁾. These microchannels are reversible in nature and close within a few hours of microporation; the time frame being dependent on the length of the microneedles. This reversible nature of microchannels is very advantageous for the controlled delivery of cosmetic agents/therapeutic compounds ⁽¹⁸⁾.

Microneedling does not target specific chromophores in the skin or use thermal energy, and therefore has minimal effect on pigmentation ⁽¹⁹⁾. It is also suggested that repigmentation of white patches with needling occurs mainly from melanocytes which are physically dragged or pushed by the tip of the needle from colored margins of the patch or islands of pigment present within the patch. These islands are either already present or are produced during needling and serve as a source of melanocytes available for further spread ⁽¹¹⁾.

Conclusion

Skin microneedling in combination with narrow band-UVB is an easy procedure, cost-effective, safe with minimal side effects, and therapeutically promising in the treatment of stable vitiligo. Further studies with larger number of cases, greater number of treatment sessions, longer periods of follow up could be helpful to determine whether increasing the duration of therapy may result in better response and to determine the stability of repigmentation and long term safety of the treatment.

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Tables:

Table (1): Distribution of the studied cases according to different parameters (n= 20)

	No. (%)
Age	
≤20	10 (50%)
>20	10 (50%)
Sex	
Male	8 (40%)
Female	12 (60%)
Type of vitiligo	
Ns localized	9 (45%)
Ns generalized	11 (55%)
Duration of disease by years	
≤5	14 (70%)
>5	6 (30%)
Site of lesion	
Face	3 (15%)
Neck	2 (10%)
Trunk	3 (15%)
Extremities	10 (50%)
Acral	2 (10%)
Skin type	
I	0 (0%)
II	0 (0%)
III	15 (75%)
IV	5 (25%)
Family history	
Negative	18 (90%)
Positive	2 (10%)

Table (2): The degree of clinical improvement in the studied patients (n= 20)

	No.	%
Degree of clinical improvement		
No	4	20.0
Mild	9	45.0
Moderate	5	25.0
Good	2	10.0
Excellent	0	0.0

Table (3): The degree of patient satisfaction in the studied patients (n= 20)

Patient satisfaction	No.	%
Not satisfied	9	45.0
Satisfied	8	40.0
Very satisfied	3	15.0



Figure (1): Dermapen and its disposable needle ((MY M microneedling, korea)).

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Figure (2): A 26-years-old male with vitiligo in extremities (A); Before treatment (B); Immediately after treatment session (C); 3 months after last session with good improvement.

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