Original Article

Enhancing Repigmentation in Vitiligo: A Comparative Clinical Trial of Microneedling with Topical 5-Fluorouracil, Fluocinolone, and Microneedling Alone

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ABSTRACT

Background: Vitiligo, a pigmentary skin disorder, poses therapeutic challenges due to its progressive nature and varied treatment responses. We aimed to investigate the efficacy of a novel approach, combining microneedling with topical 5-Fluorouracil (5-FU), compared with microneedling with Fluocinolone and microneedling alone for treating vitiligo lesions.

Methods: A single-blinded clinical trial was conducted from Aug 2022 to Feb 2023 at Ahvaz University of Medical Sciences, Ahvaz, Iran. Twenty patients with persistent vitiligo lesions were randomly assigned to three treatment groups. Microneedling was performed using Dermapen cartridge 36 once a week for 12 wk. In patch A, 5% 5-FU cream was applied immediately after microneedling; in patch B, patients used fluocinolone 0.025% cream twice daily; and in patch C, microneedling was performed alone. Clinical repigmentation was evaluated using the G-score scale, and treatment side effects were recorded.

Results: Microneedling combined with 5-FU demonstrated significantly higher repigmentation rates, with 70% of lesions showing moderate to excellent responses ($P<0.001$). In contrast, microneedling with Fluocinolone and microneedling alone exhibited lower response frequencies. Side effects were minimal, with only one patient experiencing burning and itching in the microneedling and 5-FU group. No corticosteroid-related complications were observed. Six months follow-up revealed sustained repigmentation in the microneedling and 5-FU group, contrasting with no response or recurrence in microneedling alone-treated lesions.

Conclusion: Microneedling combined with topical 5-FU presents a promising therapeutic strategy for vitiligo lesions, yielding superior repigmentation outcomes compared to other treatments.

KEYWORDS
Vitiligo; Microneedling; 5-Fluorouracil; Fluocinolone

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INTRODUCTION

Vitiligo is a pigmentation skin disorder characterized by macules and depigmented patches. This progressive condition leads to the destruction of some or all melanocytes in the skin [1]. On average, vitiligo affects half to two percent of the world's population, with an average age of onset at 20 years. While vitiligo may be more noticeable in individuals with darker skin, it does not exhibit ethnic or racial preferences [2]. Vitiligo is a multifactorial disorder involving genetic and non-genetic factors, leading to the progressive loss of melanocytes. The exact cause remains unknown, with proposed mechanisms including cytotoxic, autoimmune, intrinsic defects, neural, and oxidant-antioxidant processes [3]. The progression of the disease is frequently characterized by unpredictability and exhibits variability in its response to treatment. Depigmentation often leads to psychological distress, social stigmatization, and diminished self-esteem [4]. Vitiligo is treated using a range of topical and systemic medications, phototherapy, laser therapy, and surgical therapy. Topical therapy options encompass corticosteroids, calcineurin inhibitors, and vitamin D analogs. Surgical treatment options are restricted to segmental or localized vitiligo confined to a small area [5].

5-fluorouracil (5-FU), an antimitotic agent that stimulates melanocyte migration and proliferation, is being investigated topically and intradermally to treat vitiligo [6]. Studies have examined the effectiveness of 5-FU in conjunction with NB-UVB, dermabrasion, and Erbium: YAG laser ablation [7, 8]. Different topical corticosteroids like Fluocinolone were studied for vitiligo. Skin permeability, migration of residual melanocytes from uninvolved skin, melanocyte damage reversibility, and follicular reservoir preservation and density affect anatomic site-specific repigmentation rates [9]. Micro-needling, or collagen induction therapy, is a minimally invasive procedure using fine needles to create controlled scratches on the skin. Since 1995, it has been recognized for inducing trauma-induced inflammation, triggering the release of growth factors, and facilitating the penetration of drugs, making it potentially beneficial for treating conditions like vitiligo lesions [10-12].

Considering the diverse applications of topical corticosteroids, microneedling, and topical 5-FU in the treatment of vitiligo and limited studies in this area, the present study aimed to compare microneedling with topical fluocinolone, microneedling with 5-FU, and microneedling alone for improving vitiligo lesions.

METHODS

Participants and study design

This study was conducted as a single-blinded clinical trial from Aug 2022 to Feb 2023 at the Dermatology Clinic of Ahvaz University of Medical Sciences, Ahvaz, Iran. The study population consisted of patients with persistent vitiligo lesions. Twenty patients with vitiligo were enrolled in the study based on inclusion and exclusion criteria. Inclusion criteria included patients older than ten with persistent vitiligo lesions and informed consent of the patient to participate in the study. Exclusion criteria include pregnant women and lactating mothers, vitiligo lesions on the face, genitalia, and wrinkled areas, active Koebner phenomenon, coagulopathy, active systemic or dermal infections, patient with a high risk of keloid and previous history of keloid and hypersensitivity to 5-fluorouracil or Fluocinolone. In each patient, three patches were randomly selected to conduct the study. The patients were unaware of how to allocate the treatment to the patches, but the therapist was aware.

Procedures

Before performing the process of all three patches, the lesion site was anesthetized locally after sterilizing with 70% alcohol using lidocaine cream for 20 min. Microneedling was performed once a week for 12 wk using Dermapen cartridge 36 (Dr. Pen brand) with a thickness of 1.5 mm until Pinpoint Bleeding occurred. In patch A, immediately after performing microneedling, 5% 5-FU cream was applied on the lesion's surface as a thick layer. Then, the lesion was covered with a closed dressing for 24 h. After opening the dressing, the target area was washed and cleaned. Moreover, the patient used 5-FU cream topically once daily on the lesion every other day. In patch B, microneedling is performed, and after that, the patient uses fluocinolone 0.025% cream twice a day. In patch C, microneedling was performed alone.

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Variables and outcomes

Demographic characteristics of patients, including age, gender, family history, skin phenotype, previous treatments, and affected areas, were recorded. Photographs of all included lesions before and after treatments were taken. The primary outcome in this study included the clinical repigmentation, which dermatologists evaluated using the G-score (Grading of repigmentation) based on before and three months after initial treatment lesion photographs (Table 1). The secondary outcome included treatment side effects.

Statistical analysis

SPSS program (ver. 28, IBM Corp., Armonk, NY, USA) was used for statistical data analysis. The chi-square test was used to compare qualitative data. In all analyses, *P*-value less than 0.05 is considered significant.

RESULTS

Twenty patients were examined. The demographic and clinical characteristics of patients are shown in Table 2. The frequency of patients in terms of response to treatment based on the grading of repigmentation three months after the start of the study in each treatment group is shown in Table 3.
As mentioned in Table 3, in patches treated with microneedling and 5-FU, moderate, good, and excellent response frequencies were significantly higher than in other treatment methods ($P<0.001$)

Table 1: Grading of repigmentation.

Repigmentation(%)	Grade	Response
<25	G1	Poor
25–50	G2	Moderate
51–75	G3	Good
76-100	G4	Excellent

Table 2: Clinical data of the studied patients.

Variables	n (%)
Age (yr):	
Less than 15	3 (15)
16 to 39	15 (75)
40 and more	2 (10)
Gender:	
Male	3 (15)
Female	17 (85)
Skin phenotypes:	
Fair	5 (25)
Darker White	7 (35)
Light Brown	7 (35)
Brown	1 (5)
Previous treatments:	
Topical	2 (10)
Topical + Phototherapy	10 (50)
Systemic	1 (5)
No Treatment	7 (35)
Vitiligo family history:	
Positive	8 (40)
Negative	12 (60)
Lesions sites:	
Acral	3 (15)
Upper extremity	6 (30)
Lower extremity	3 (15)
Trunk	8 (40)

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(Figures 1-3). Only moderate and poor responses to treatments were found in the microneedling and Fluocinolone and microneedling alone treatment groups. Moreover, the frequency of moderate repose was significantly higher in microneedling and Fluocinolone than in the microneedling alone group (P<0.001) (Figures 4-6).

Regarding side effects, only one patient out of 20 studied patients had burning and itching as well as vesicles at the lesion site after using the microneedling and 5-FU. No side effects were seen in other patients using the other two treatment methods. Corticosteroid-related complications such as telangiectasia, hypertrichosis, atrophy, or hypopigmentation were not seen in the lesions that were treated with microneedling and topical fluocinolone. After 6 months of follow-up after treatment, none of the patients responded to microneedling and 5-FU, and no recurrence of lesions was observed.

DISCUSSION

We attempted to investigate the effectiveness of a new treatment method, which combines microneedling and topical 5-Fluorouracil (5-FU) drug. For simultaneous comparison, the combination of microneedling and topical Fluocinolone and microneedling alone was used for similar lesions. These results have been evaluated according to the G-Score scale, which shows the percentage of repigmentation and healing of the lesion in 4 levels. None of the 20 lesions treated with microneedling (alone) responded to the treatment, and all were reported as G1 (0-25% repigmentation). However, the response in the lesion treated with microneedling and 5-FU was different, and among 20 lesions, 14 (70%) showed different degrees of repigmentation, and 6 (30%) did not respond to this treatment or responded poorly. Among these 14 lesions, 11 (55%) showed a moderate response (G2), 2 (10%) showed a

Table 3: Grading of repigmentation three months after the first intervention

Variable	n (%)			
G-score/Groups	Microneedling + 5-FU	Microneedling + F	Microneedling	*P*-value*
G1	6 (30)	18 (90)	20 (100)	
G2	11 (55)	2 (10)	0 (0)	
G3	2 (10)	0 (0)	0 (0)	<0.001
G4	1 (5)	0 (0)	0 (0)	
Total	20 (100)	20 (100)	20 (100)	

*: Chi-square test, 5-FU: 5-fluorouracil, F: Fluocinolone.

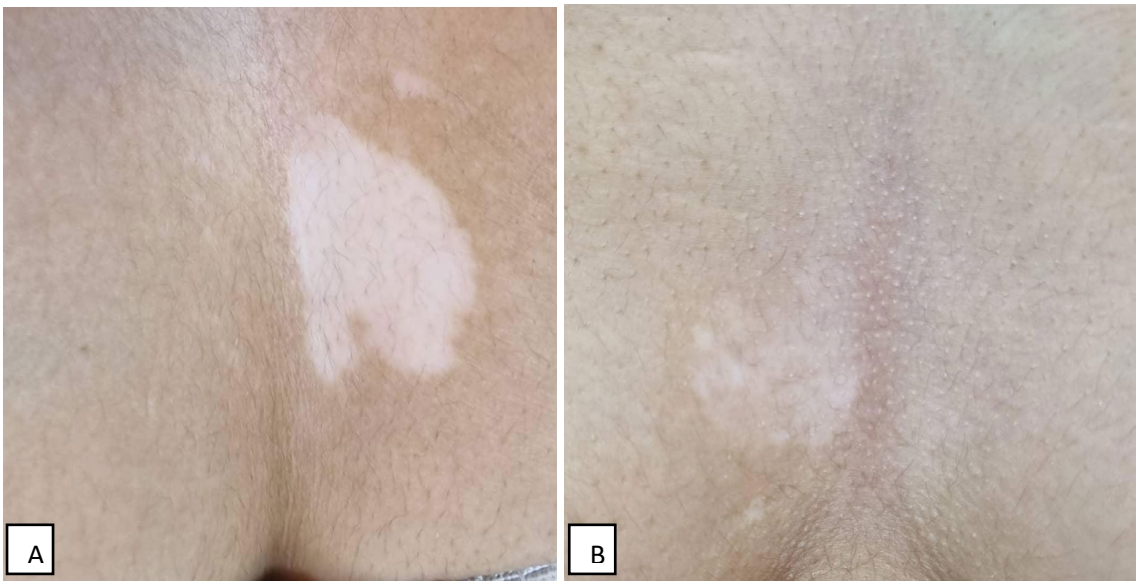

Figure 1: Patient 1. A: Before the intervention with 5-FU and microneedling, B: After the intervention with 5-FU and microneedling

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good response (G3), and 1 (5%) showed an excellent response (G4). The response to treatment based on repigmentation grading was significantly better in the microneedling and topical 5-FU treatment group.

In the same context [13], out of 25 patients, 18 patients (72%) had a good response (more than 25% repigmentation) to treatment with microneedling and 5-FU for vitiligo which is consistent with the

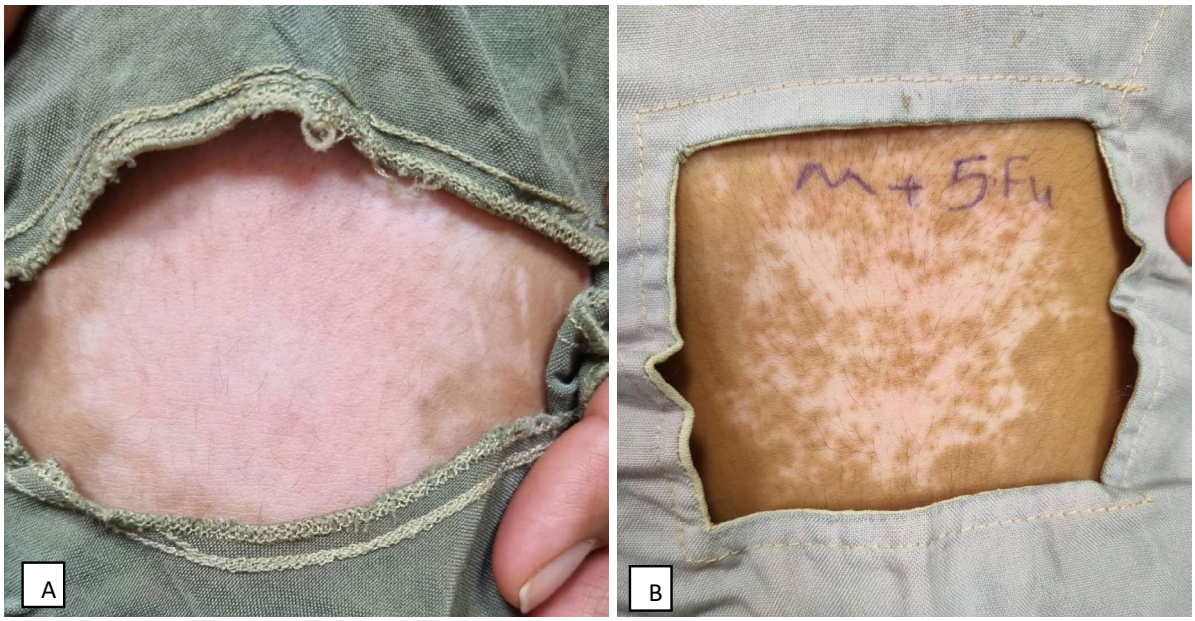

Figure 2: Patient2. A: Before the intervention with 5-FU and microneedling, B: After the intervention with 5-FU and microneedling

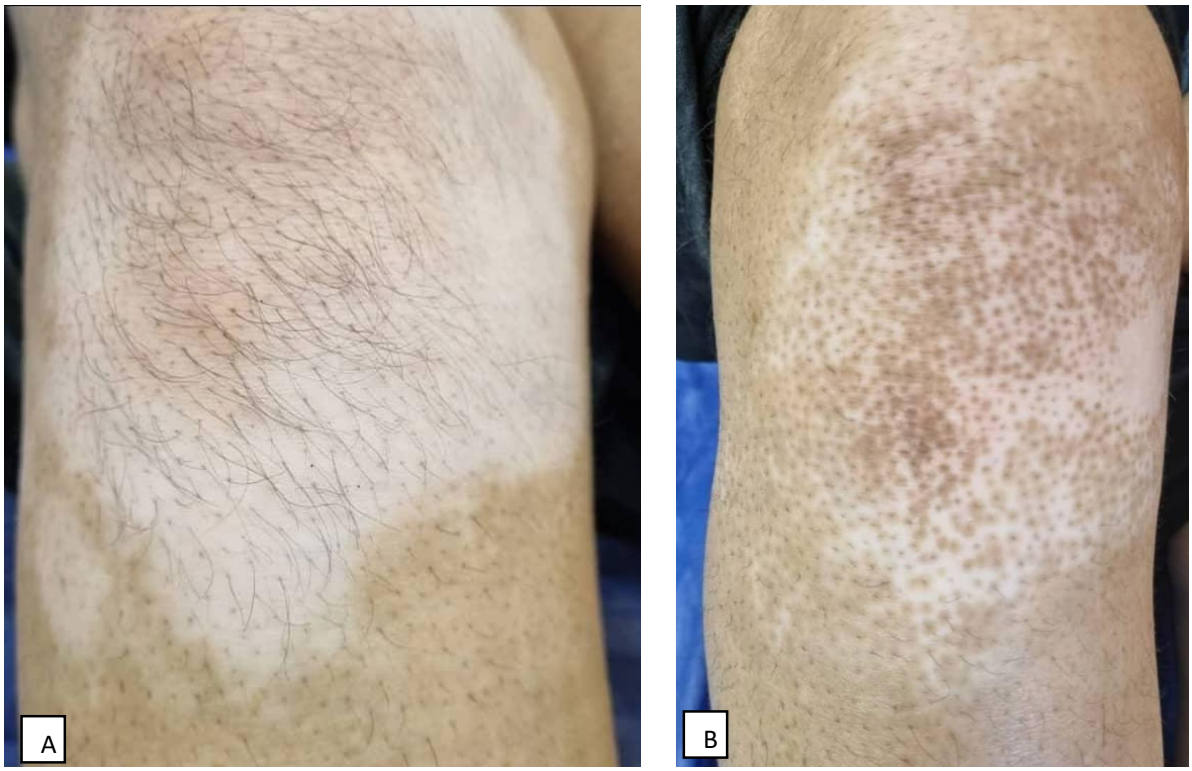

Figure 3: Patient3. A: Before the intervention with 5-FU and microneedling, B: After the intervention with 5-FU and microneedling

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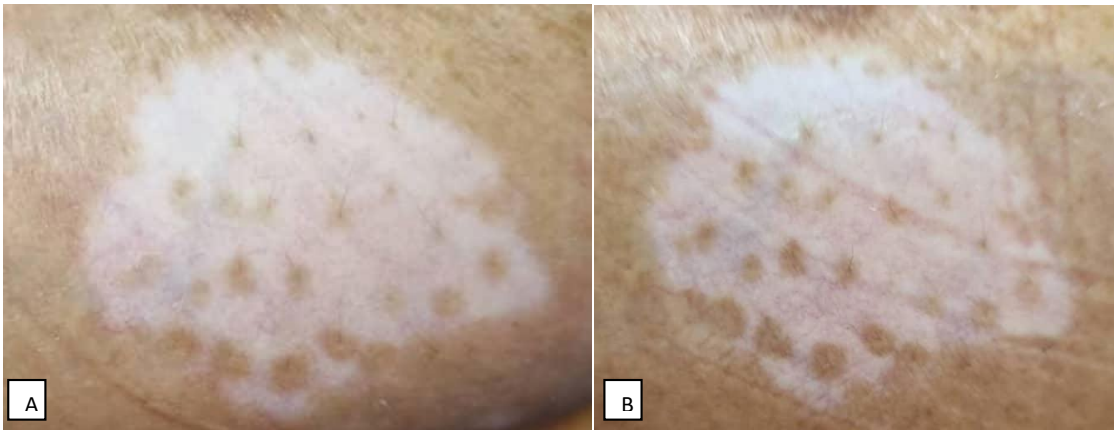

Figure 4: Patient 1. A: Before the intervention with Fluocinoloneand microneedling, B: After the intervention with Fluocinolone and microneedling

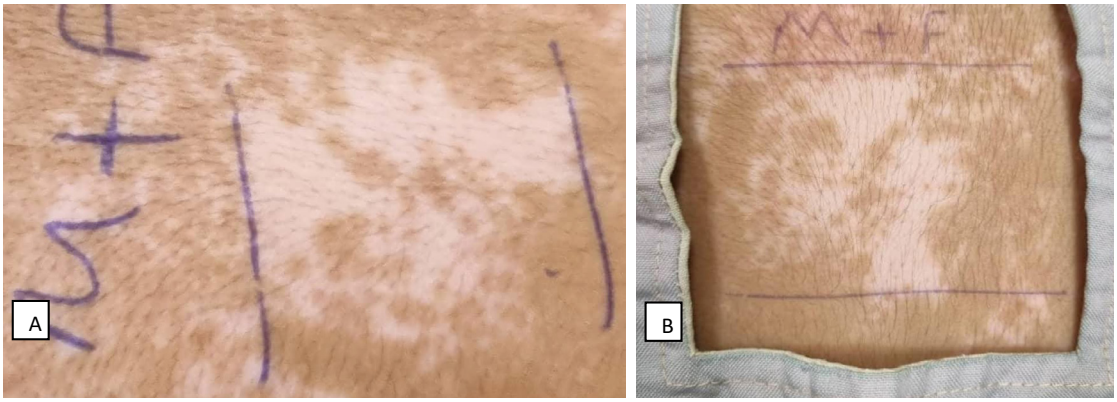

Figure 5: Patient2. A: Before the intervention with Fluocinoloneand microneedling, B: After the intervention with Fluocinolone and microneedling

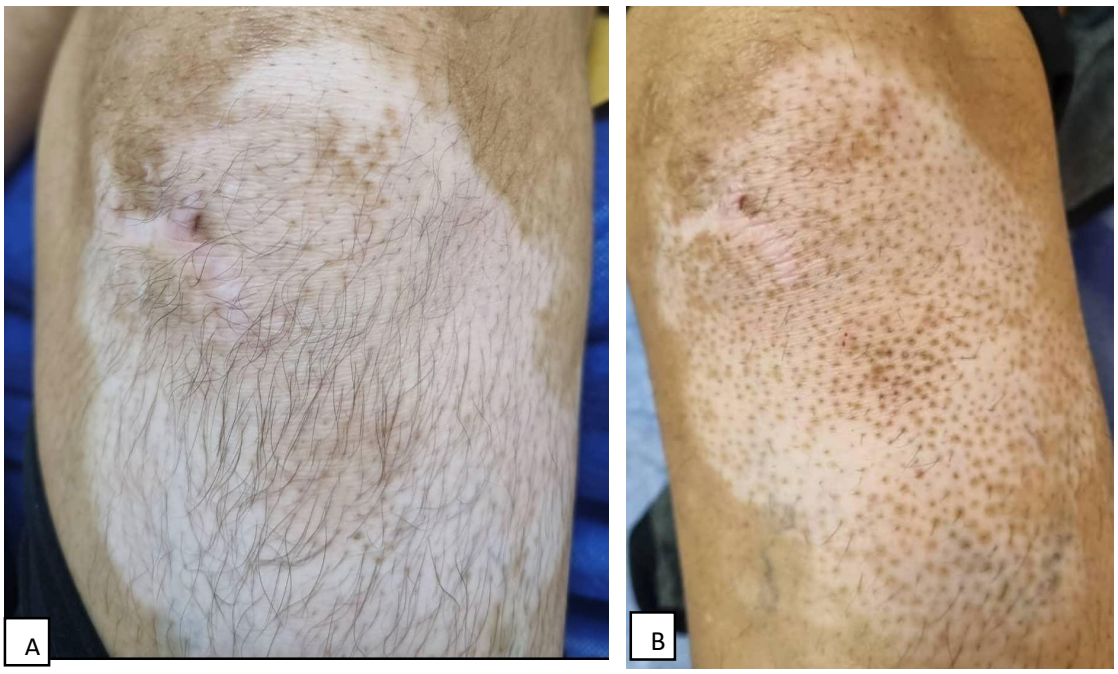

Figure 6: Patient3. A: Before the intervention with Fluocinoloneand microneedling, B: After the intervention with Fluocinolone and microneedling

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findings of the present study. Besides, in Attawa et al.'s study [14], among the 27 patients studied, the combination of microneedling and 5-FU had better results than microneedling alone. The present study also showed that microneedling and 5-FU can be more effective in treating vitiligo lesions than microneedling alone. In the study of El Fakahany et al. [15], twenty patients with vitiligo were studied with the combination of microneedling and 5-FU, observed in 16 patients (80%) with different percentages of repigmentation, which is in line with our findings. Similar results were reported in the study of Shashikiran et al. (68%), who investigated the effect of topical 5-FU and microneedling on vitiligo. Finally, 49% of the patches showed more than 75% Repigmentation, and 26% had between 50 and 75% Repigmentation.

Strengths of this study include its novel exploration of combining microneedling with topical 5-Fluorouracil for vitiligo treatment, providing valuable insights into an emerging therapeutic approach. The comparative design involving microneedling with Fluocinolone and microneedling alone enhances the study's comprehensiveness. However, limitations such as the small sample size and single-center setting may impact the generalizability of findings. Future research should prioritize larger, multicenter studies with diverse participant pools for broader applicability. Long-term follow-ups and comparative assessments against alternative vitiligo treatments would contribute to a more comprehensive understanding of the efficacy and sustainability of microneedling combined with topical 5-FU in vitiligo management.

CONCLUSION

This comparative clinical trial suggests that microneedling combined with topical 5-FU may offer a more favorable outcome for vitiligo lesions than microneedling alone. The results indicate promising repigmentation rates and minimal side effects, emphasizing the potential of this combined treatment approach. While the study has limitations, including a small sample size, the findings contribute to the evolving landscape of vitiligo management. Further research with larger cohorts and diverse populations must validate and build upon these initial observations.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests.

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