MAK HILL Publications International Journal of Tropical Medicine

Research Article
doi: 10.36478/makijtm.2024.4.86.91

Role of Topical 5 Fluorouracil with Microneedling in Stable Vitiligo

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ABSTRACT

The objective of this study was to determine the effectiveness of topical 5-Fluorouracil in combination with microneedling for the treatment of stable vitiligo in patients aged 18-60 years. A randomized study was conducted at Saraswati Institute of Medical College Hapur UP, India, involving 19 participants with stable vitiligo. The participants, aged <18 years, were included in the study. The study included Fitzpatrick skin types II-V and the absence of adverse condition for microneedling. Participants underwent microneedling sessions weekly, followed by the application of 5-FU solution on treated patches. Treatment responses were evaluated using a G score on a four-point scale. Data were analysed using SPSS software and the efficacy of treatment was assessed through descriptive statistics and Wilcoxon signed-rank tests. The study found that 52.5% of patients achieved an excellent response (G4) after treatment, with acral lesions showing the highest efficacy (42.1% achieving G4). Overall, 21% of patients exhibited poor outcomes (G1), indicating variability in treatment responses. The chronic nature of the disease was evident, with 36.8% of participants having had vitiligo for over ten years. The findings suggested that microneedling combined with 5-FU is an effective treatment for stable vitiligo, particularly in acral areas. The variability in responses highlights the necessity for personalized treatment plans tailored to individual patient characteristics and lesion locations. Continued research is essential to refine therapeutic strategies and improve management of vitiligo, ultimately enhancing the quality of life for affected individuals.

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Key Words

5-fluorouracil, microneedling, re-pigmentation, vitiligo, dermatology

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Received: 30 August 2024
Accepted: 05 October 2024
Published: 08 October 2024

Citation: Megha Sharma and Prashant Kumar Yadav, 2024. Role of Topical 5 Fluorouracil with Microneedling in Stable Vitiligo. Int. J. Trop. Med., 19: 86-91, doi: 10.36478/makijtm.2024.4.86.91

INTRODUCTION

Vitiligo is a skin disorder that affects many individuals over the course of their lives; however, it is more frequently acquired than inherited. The condition is characterized by patches of skin that lack pigmentation, a hallmark of the disorder. Its primary cause is the gradual depletion of melanocytes, which underlies the disease's mechanism [1]. Dermatologists are particularly concerned about vitiligo as it presents no obvious symptoms to the naked eye, despite only affecting a small percentage of the global population. Although the condition shows no bias based on age, gender, or race, it can significantly impact a person's social and psychological well-being[2]. Affected individuals may suffer from low self-esteem, discrimination, and depression, among other challenges. While vitiligo is closely associated with autoimmune thyroid disorders, its exact etiology remains unclear[3]. Three main hypotheses exist to explain the condition: neuronal, cytotoxic and autoimmune mechanisms, each offering a unique perspective[4]. Vitiligo treatments include photo therapy, topical immunomodulators and surgery. However, the effectiveness of treatment varies depending on the type and severity of the condition. Due to the persistence and resistance of vitiligo to traditional therapies, microneedling and autologous melanocyte transplantation have recently gained attention as promising surgical options[5]. Both procedures aim to restore pigmentation by promoting melanocyte recovery or transplantation. Microneedling, a minimally invasive technique, can facilitate re-pigmentation by enhancing melanocyte migration and other healing processes[6]. Despite the range of available treatments, vitiligo remains a significant challenge for the dermatological community. The appearance of skin macules, a symptom of this acquired depigmentary disorder caused by selective melanocyte destruction, can deeply affect a patient's self-image[7]. Treatment options include both non-invasive and surgical approaches. Non-surgical therapies such as topical corticosteroids, tacrolimus, PUVA and narrowband UVB (NB-UVB) are commonly used, while surgical techniques, including skin grafting and the transplantation of epidermal suspension or cultured melanocytes, are employed in more resistant cases. Nevertheless, no single treatment guarantees success for all patients, underscoring the need for new therapies to improve re-pigmentation outcomes and overall patient well-being[8]. Recent advancements in treatment have introduced microneedling as a viable option for patients seeking enhanced drug delivery and re-pigmentation. Microneedling, which involves creating tiny punctures in the skin, facilitates better absorption of topical medications. This process triggers localized inflammation, encouraging the migration of melanocytes and keratinocytes to the wound site, potentially aiding in re-pigmentation[9].

This study explores the combination of microneedling with 5-fluorouracil (5-FU) as a treatment for localized and stable vitiligo, with the goal of improving re-pigmentation outcomes and patient response to therapy. By investigating this integrated approach, the research aims to contribute to the development of more effective and reliable treatment options for vitiligo, ultimately enhancing the management of the disorder and improving the quality of life for those affected.

Aim of the Study: The study evaluated the role of topical 5-Fluorouracil (5-FU) in combination with microneedling in patients with stable vitiligo.

Objectives: To determine the effectiveness of topical 5-Fluorouracil (5-FU) with microneedling in patients with stable vitiligo.

MATERIALS AND METHODS

The randomized study was conducted at Saraswati Institute of Medical College Hapur UP , India involving 19 participants with stable vitiligo. The participants, aged <18 years, were included in the study. The study included individuals with Fitzpatrick skin types II-V and those with contraindications to microneedling. Participants received weekly microneedling sessions, followed by the topical application of 5-fluorouracil (5-FU) solution on the affected skin areas.

Inclusion Criteria: The study involved participants aged, <18 years with stable vitiligo, Fitzpatrick skin types II-V with microneedling contraindications and healthy participants without skin concerns, who consented and followed the study procedure.

Exclusion Criteria: The following criteria were used to exclude patients from the study:

- Pregnant or breast-feeding women
- Patients with unstable or rapidly progressing vitiligo
- History of allergic reaction to 5 Fluorouracil or other topical treatments used in the study.
- Patients at high risk of developing keloids.
- Patients receiving anticoagulant therapy.

Data Collection: In this study, patients diagnosed with vitiligo were assessed using a Wood's lamp to confirm their condition. Key demographic information was documented, including age, gender, family history of vitiligo, prior treatments received, history of re-pigmentation, duration of the disease and lesion locations. A total of 19 patients participated in the study. Each patient had two symmetrical patches selected for treatment. A randomization method was

employed to allocate the treatment, using double random blocks for assignment to left and right patches. Patients underwent a treatment regimen where microneedling was performed weekly. Each treatment session involved using a Derma pen with a cartridge that had a maximum thickness of 1.5mm to create micro-injuries to the skin. After the microneedling procedure, a 5-fluorouracil (5-FU) solution was applied to the treated patch. The lesions were bandaged for 24 hours and the patients continued to apply the same concentration of 5-FU every other day for three months. Patients were advised to avoid irritants and to use sunscreen in the postoperative phase. Any adverse effects, such as erythema, discomfort, or allergic reactions, were documented throughout the treatment period. Clinical images were captured pre- and post-treatment for evaluation.

Data Analysis: Data analysis was conducted using the SPSS software version 16 for descriptive statistics. The efficacy of microneedling treatment was assessed through a G score that categorized responses to treatment on a four-point scale: 0-25% (Poor response), 25-50% (Moderate response), 50-75% (Good response) and 75-100% (Excellent response). A Wilcoxon signed-rank test was employed to determine statistical differences between treatment responses. The analysis included frequency distributions and mean and standard deviation calculations, with p-values below 0.05 considered significant.

RESULTS AND DISCUSSIONS

(Table 1) summarizes the duration of the disease among the study participants and their history of previous treatments. Most patients (36.8%) had the disease for more than 10 years, while only 10.5% had it for less than a year. As for previous treatments, most patients (57.9%) had undergone both topical and phototherapy treatments. A smaller percentage (5.3%) had not received any treatment prior to the study.

Table 1: Duration of Disease and Previous Treatments

Variable	Frequency N (%)
Duration of disease (years)	
Under 1	2 (10.5%)
1-5	4 (21.1%)
5-10	6 (31.6%)
More than 10	7 (36.8%)
Previous treatments	
Topical	5 (26.3%)
Phototherapy	2 (10.5%)

(Table 2) highlights the family history of vitiligo among patients and their previous history of re-pigmentation. A positive family history was reported by 26.3% of the patients, while 73.7% did not have a family history of vitiligo. More than half (52.6%) had experienced re-pigmentation in the past, indicating a history of some degree of treatment response, while 47.4% had not experienced re-pigmentation.

Table 2: Family History and Previous History of Re-pigmentation

Variable	Frequency N (%)
Family history	
Positive	5 (26.3%)
Negative	14 (73.7%)
Previous history of re-pigmentation	
Yes	10 (52.6%)

(Table 3) focuses on the location of vitiligo lesions among the patients. The most common location was the acral areas (52.6%), which include hands and feet. Lesions were less frequently observed on the upper extremities (15.8%), lower extremities (21.1%), and the trunk (10.5%). The distribution of lesions provides insight into the affected areas, which is important for understanding treatment responses and challenges.

Table 3: Lesion Location

Variable	Frequency N (%)
Lesion location	
Acral	10 (52.6%)
Upper extremity	3 (15.8%)
Lower extremity	4 (21.1%)
Trunk	2 (10.5%)

(Table 4) summarizes the efficacy of the microneedling treatment combined with 5-FU in patients with stable vitiligo, categorized by the G score indicating the level of re-pigmentation observed. Among the patients treated, a significant portion (52.5%) achieved an excellent response (G4), suggesting that this combination therapy is effective in promoting significant re-pigmentation. In contrast, poor response (G1) was recorded in 21% of cases, indicating that a minority of patients did not benefit from the treatment. Furthermore, moderate (G2) and good responses (G3) were observed in 16% and 10.5% of the participants, respectively. This distribution highlights the variability in treatment outcomes, emphasizing the need for individualized approaches when treating vitiligo.

Table 4: Response Rate to Treatment with Microneedling Plus Topical 5-FU

Variable	G1-Poor Response (0-25%) N (%)
Topical Tacrolimus	
G1-Poor Response (0-25%)	4 (21%)
G2-Moderate Response (25%-50%)	3 (16%)
G3-Good Response (50%-75%)	2 (10.5%)
G4-Excellent Response (75%-100%)	10 (52.5%)
Total	19 (100%)

(Table 5) details the treatment responses of microneedling combined with 5-FU in relation to the location of vitiligo lesions. In terms of lesion location, the acral area exhibited the highest efficacy with 42.1% of patients achieving an excellent response (G4). This responsive to this treatment regimen. suggests that acral lesions may be particularly.

Table 5: Response Rate by Lesion Location

Lesion Location	G1-Poor Response (0-25%) N (%)	G2-Moderate Response (25%-50%) N (%)	G3-Good Response (50%-75%) N (%)	G4-Excellent Response (75%-100%) N (%)	Total N (%)
Acral	1 (5.3%)	0	1 (5.3%)	8 (42.1%)	10 (52.6%)
Upper Extremity	2 (10.5%)	1 (5.3%)	0	2 (10.5%)	5 (26.3%)
Lower Extremity	1 (5.3%)	1 (5.3%)	1 (5.3%)	0	3 (15.8%)
Trunk	0	1 (5.3%)	0	0	1 (5.3%)

The upper extremities showed a varied response with 10.5% reaching an excellent score and a moderate response noted in 5.3% of cases. For lower extremity lesions, the response was more modest, with no patients achieving an excellent response, though some displayed moderate to poor outcomes. Finally, lesions located on the trunk had the least favourable results, with only one case achieving a moderate response. The findings presented in this study offer significant insights into the characteristics of vitiligo among the participants, including disease duration, treatment history, family history, lesion locations, and the efficacy of the combined microneedling and 5-fluorouracil (5-FU) treatment. Understanding these factors is essential for tailoring effective treatment strategies for individuals affected by vitiligo. A notable proportion of participants (36.8%) reported having vitiligo for more than ten years, which emphasizes the chronic nature of this condition. Conversely, only a small fraction (10.5%) had the disease for less than one year, suggesting that many patients have been managing this skin disorder for a significant duration. This chronicity often correlates with treatment resistance and more entrenched psychosocial issues, necessitating comprehensive management approaches. In terms of previous treatments, many patients (57.9%) had undergone a combination of topical and phototherapy treatments. This diverse treatment history highlights the challenges of achieving satisfactory re-pigmentation with standard therapies. A small percentage of patients (5.3%) had not received any prior treatment, suggesting that some may have been unaware of available options or may have chosen to delay treatment. This could point to a gap in patient education and support that could be addressed in future healthcare initiatives.

The presence of a positive family history of vitiligo in 26.3% of participants suggests a genetic component that may predispose individuals to this condition. This aligns with existing literature indicating that familial clustering of vitiligo occurs, which could be crucial for understanding individual patient cases and informing treatment strategies. Interestingly, over half of the participants (52.6%) reported a previous history of re-pigmentation. This finding underscores the potential for treatment responsiveness in this patient population, indicating that some may benefit from further interventions, particularly those that have shown effectiveness in the past. The ability to achieve some degree of re-pigmentation may also provide hope and psychological relief to patients, emphasizing the importance of sustained therapeutic efforts. The study revealed that the acral areas (hands and feet) were the most affected sites, with 52.6% of patients exhibiting lesions in these regions. This is significant, as vitiligo lesions in acral locations can pose unique treatment challenges, often leading to stigmatization and psychosocial distress. The distribution of lesions in the upper and lower extremities, as well as on the trunk, indicates varying degrees of exposure and societal perceptions, further complicating patient experiences. The high prevalence of lesions in the acral areas suggests that a targeted approach may be warranted when considering treatment modalities, particularly given the psychological impact of visible skin changes in these regions.

The combined microneedling and 5-FU treatment showed promising results, with 52.5% of patients achieving an excellent response. This suggests it could be effective in inducing re-pigmentation in patients with stable vitiligo. However, 21% of patients had poor outcomes, highlighting the need for personalized treatment plans. Factors such as lesion location, disease duration and prior treatment responses significantly influence the efficacy of this approach. The treatment's effectiveness was highest in acral lesions, with 42.1% of patients achieving an excellent response. Lower extremity and trunk lesions showed less favourable outcomes, suggesting that treatment approaches may need to be adjusted based on lesion characteristics and locations. Future research should explore biological and environmental factors influencing treatment responses in different lesion locations, leading to more refined strategies considering the specific characteristics of the lesions being treated. The findings of this study regarding the combination of microneedling and topical 5-Fluorouracil (5-FU) for stable vitiligo treatment align with previous research highlighting the challenges in managing this persistent skin condition. Traditional therapies such as topical corticosteroids and phototherapy often show limited effectiveness, especially in longstanding cases of vitiligo[10,11]. A study by Joseph illustrated how microneedling could enhance the penetration of topical treatments, resulting in meaningful re-pigmentation for patients with vitiligo[12]. The current research reinforces these findings, demonstrating that the synergistic use of microneedling and 5-FU leads to improved treatment

outcomes, particularly in patients with acral lesions, known for their resistance to standard therapies[13]. Additionally, the observation that 52.5% of participants experienced excellent results corresponds with findings from other studies that examine the effectiveness of microneedling combined with various topical agents. For example, Chabra[7] noted comparable success rates using microneedling in conjunction with different topical immunomodulators, suggesting that this method enhances the effectiveness of topical medications[7]. However, the variability in treatment responses seen in this study, with 21% of patients experiencing poor outcomes, underscores the importance of tailoring treatment strategies. Different patient responses may arise due to factors such as the duration of the disease and prior treatment experiences. This aligns with findings by De Latorre which stress that customized treatment plans are essential for maximizing success in managing chronic conditions like vitiligo[14,15]. The demographic features of study participants, including a significant number with a family history of vitiligo and a long disease duration, reflect trends observed in broader research. According to research by Al Smadi, familial clustering is prevalent among vitiligo patients, indicating a potential genetic factor that may affect treatment responses[15]. Additionally, the study highlights that many participants had previously tried multiple treatment modalities, reiterating the complexity of managing vitiligo[16]. Such chronicity can contribute to increased psychosocial distress, as noted in the literature, which suggests that effective treatment must encompass not only medical interventions but also psychological support for those affected[17].

CONCLUSION

The results of this study highlight the multifaceted nature of vitiligo, and the complexities involved in its management. With many patients experiencing long-standing disease, a history of various treatments, and the psycho social challenges associated with visible skin changes, tailored therapeutic approaches are essential. The promising efficacy of microneedling combined with 5-FU, particularly for acral lesions, presents a hopeful avenue for improving treatment outcomes. Continued research into the factors influencing treatment efficacy will be vital for advancing our understanding and management of this condition, ultimately enhancing the quality of life for those affected by vitiligo.

REFERENCES

1. Gauthier, Y., T. Anbar, S. Lepreux, M. Cario-André and L. Benzekri, 2013. Possible Mechanisms by Which Topical 5-Fluorouracil and Dermabrasion Could Induce Pigment Spread in Vitiligo Skin: An Experimental Study. ISRN Dermatol., 2013: 1-10.0.
2. Bertolani, M., E. Rodighiero, M.B.D.F. del Giudice, T. Lotti, C. Feliciani and F. Satolli, 2021. Vitiligo: What's old, what's new. Dermatol. Rep., Vol. 13 .10.4081/dr.2021.9142 1-10.0.
3. Pazyar, N., M. Hatami, R. Yaghoobi, S.Y. Parvar, M. Radmanesh and M. Hadibarhaghtalab, 2023. The efficacy of adding topical 5-fluorouracil to micro-needling in the treatment of vitiligo: A randomized controlled trial. J. Cosmet. Dermatol., 22: 1-10.0.
4. Sagar, A. Sachin and K.S. Akhil 2021. Role of Topical 5-Flurouracil Combined with Microneedling in Stable Vitiligo. IJPHRD [Internet] 12: 1-10.0.
5. Galal, S., M. Ali and F. Elzeiny, 2021. Evaluation of Efficacy and Safety Topical 5-Fluorouracil 0.5% in Treatment of Resistant Vitiligo [Alone or After Microneedling]., A pilot Study. Int. J. Med. Arts, 3: 1-10.0.
6. Giorgio, C.M., S. Caccavale, E. Fulgione, E. Moscarella, G. Babino and G. Argenziano, 2019. Efficacy of Microneedling and Photodynamic Therapy in Vitiligo. Dermatologic Surg., 45: 1-10.0.
7. Chhabra, S., Y.S. Chahar and A. Singh, 2021. A Comparative Study of Microneedling Combined with Topical 5-Fluorouracil versus Microneedling Alone in Treatment of Localized Stable Vitiligo. Indian J. Dermatol., Vol. 66 .10.4103/ijd.ijd_130_21 1-10.0.
8. Adil, M., F. Zahra, S. Amin, M. Mohtashim, R. Bansal and H. Khan, 2020. Efficacy of topical 5% 5-fluorouracil with needling versus 5% 5-fluorouracil alone in stable vitiligo: A randomized controlled study. J. Cutaneous Aesthetic Surg., 13: 1-10.0.
9. Tsuji, T. and T. Hamada., 1983. Topically Administered Fluorouracil in Vitiligo. Arch. Dermatol., 119: 1-10.0.
10. Matharoo, P., S. Sharma, J. Kaur and R. Bassi, 2022. Comparison of the efficacy of microneedling combined with 5-fluorouracil 5% cream versus microneedling combined with tacrolimus 0.1% ointment in the treatment of vitiligo. TURKDERM, 56: 1-10.0.
11. Kubelis López, D., N. Zapata Salazar, S. Said Fernández, C. Sánchez Domínguez and M. Salinas Santander *et al.,* 2021. Updates and new medical treatments for vitiligo (Review). Exp. Ther. Med., Vol. 22 .10.3892/etm.2021.10229 1-10.0.
12. Bailey, A.J.M., H.O.Y. Li, D. Zheng, S.J. Glassman and M.G. Tan, 2021. Microneedling as an Adjuvant to Local Therapies for Vitiligo: A Systematic Review and Meta-Analysis. Dermatologic Surg., 47: 1-10.0.
13. Dillon, A.B., A. Sideris, A. Hadi and N. Elbuluk., 2017. Advances in Vitiligo: An Update on Medical and Surgical Treatments. J. Clin. Aes. Der., 10: 1-10.0.

14. Dellatorre, G., V.M. Fava and C.C.S. de Castro, 2023. Vitiligo., 10.1007/978-3-031-13505-7_26, http://dx.doi.org/10.1007/978-3-031-13505-7_260 1-10.0.
15. AL-smadi, K., M. Imran, V.R. Leite-Silva and Y. Mohammed, 2023. Vitiligo: A Review of Aetiology, Pathogenesis, Treatment and Psychosocial Impact. Cosmetics, Vol. 10 .10.3390/cosmetics10030084 1-10.0.
16. Abdel-Malek, Z.A., C. Jordan, T. Ho, P.R. Upadhyay, A. Fleischer and I. Hamzavi, 2020. The enigma and challenges of vitiligo pathophysiology and treatment. Pigment Cell and Melanoma Res., 33: 1-10.0.
17. Salama, A.H., L. Alnemr, A.R. Khan, H. Alfakeer, Z. Aleem and M. Ali-Alkhateeb, 2023. Unveiling the Unseen Struggles: A Comprehensive Review of Vitiligo's Psychological, Social and Quality of Life Impacts. Cureus, Vol. 15 .10.7759/cureus.45030 1-10.0.