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Original Article

Efficacy of microneedling combined with calcipotriol plus betamethasone in the treatment of vitiligo

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Abstract

Objective To assess the outcome of microneedling combined with calcipotriol plus betamethasone (measured by mean change in VASI) in the treatment of vitiligo.

Methods This study involved 57 patients of both genders aged between 15-45 years presenting with vitiligo enrolled after taking informed written consents. These patients were assessed by VASI score before starting treatment. Treatment was given in the form of microneedling combined with calcipotriol plus betamethasone. VASI score was reassessed 2 weeks after 3 months of treatment. Outcome variable was mean change in VASI score which was measured by subtracting the follow-up VASI score from that at baseline and compared across various subgroups of studied patients.

Results Mean age of the patients was 26.4±8.9 years. There were 26 (45.6%) male and 31 (54.4%) female patients. Mean duration of disease was 4.56±1.71 years. Family history of vitiligo was present in 16 (28.1%) patients. The mean change in VASI score from baseline was 39.65±4.97. Mean change in VASI score across various subgroups of patients had insignificant difference (p-value>0.05).

Conclusion Microneedling combined with calcipotriol and betamethasone was associated with considerable mean change in VASI score in vitiligo patients which owing to safety and simplicity of treatment advocates its preferred use in managing such patients in future dermatological practice.

Key words
Betamethasone; Calcipotriol; Microneedling; VASI Score; Vitiligo.

Introduction

Vitiligo, a depigmentary disorder affecting the skin and infrequently the mucous membranes, arises from the progressive loss of melanocytes.[1] Clinically, it manifests as milky white sharply demarcated macules and patches.[2] Its prevalence ranges from 0.5 to 2.0 percent globally[2,3] showing no gender or racial predilection and commonly affecting individuals under 20 years of age,[4] with a reported prevalence of 4.4% in Pakistan.[5] Psychosocial repercussions, including diminished self- esteem and depression, profoundly affect patients.[6,7]

Numerous therapeutic modalities exist, aiming to induce repigmentation and halt disease progression, with treatment selection guided by patient age, vitiligo type, lesion stage, site, and

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distribution.[7,8] Studies suggest vitiligo pathogenesis involves increased anti-melanocyte antibodies and T-cell subset imbalances.[9] Betamethasone, a potent glucocorticoid steroid, exerts anti-inflammatory and immunosuppressive effects, facilitating melanocyte reactivation and repigmentation.[10,11] Calcipotriol, a synthetic vitamin D3 analogue, modulates immunity and improves calcium uptake in vitiliginous lesions, showing efficacy as monotherapy or combined with betamethasone.[11,12] Combining calcipotriol with betamethasone yields synergistic immunosuppression and melanogenesis, enhancing therapeutic outcomes with reduced adverse effects.[11,13] Microneedling, a novel dermatological intervention, augments topical therapy absorption, offering potential in pigmentation disorders like vitiligo, particularly in darker skin types.[14]

Zahoor *et al*. (2017) randomized one hundred and fifty patients into three groups and treated for three months. The combination group (Group C) demonstrated the highest improvement in pigmentation, as assessed by the Vitiligo Area Scoring Index (VASI), with a mean change of 38.77±38.19, compared to 26.23 in the betamethasone group and 18.30 in the calcipotriol group. Group C also exhibited the highest overall improvement in VASI, which was statistically significant (p=0.008). Side effects between the groups had insignificant difference.[11] In a study by Ibrahim *et al*. (2019), microneedling with calcipotriol plus betamethasone was compared to microneedling with tacrolimus in vitiligo treatment. Twenty-five patients were treated on symmetrical patches. Sixty percent of patients treated with microneedling and calcipotriol plus betamethasone showed excellent improvement, compared to 32% in the tacrolimus group. The combination therapy was particularly effective on resistant sites such as elbows, knees, extremities, and acral areas.[14]

While various medical and surgical interventions exist, research on vitiligo treatment remains limited globally, particularly in Pakistan. To address this gap, our study aims to evaluate the effectiveness of microneedling combined with calcipotriol plus betamethasone in managing vitiligo. By investigating this novel therapeutic approach, we seek to contribute valuable insights into improving treatment outcomes for vitiligo patients, potentially offering a promising solution to alleviate both the physical and psychological burden associated with this condition.

Methods

This quasi experimental study was conducted at Dermatology Outpatient Department, Sir Ganga Ram Hospital Lahore for a period of six months 20/10/2020 to 19/04/2021. Sample size of 57 patients with stable vitiligo was calculated with 95% confidence level and d=10 while taking expected mean change in VASI score to be 38.77±38.19.[11] Inclusion criterion were patients of both genders with age between 15-45 years showing vitiligo i.e. no progression of lesions for at least 2 years, having upto 5 patches and patch size <10 cm in diameter. The patients had no local infection and not received any local and systemic therapy for at least previous 6 months. However, patients with keloidal tendency, active infection, bleeding disorders or immunocompromised patients were excluded. Likewise, patients with baseline mean VASI less than 50% and Pregnant and lactating females were also excluded. The procedure was performed with 1.5 mm dermapen from one border to another by multiple, parallel strokes (in side to side and top down fashion). It resulted in appearance of multiple tiny, punctate, bleeding points. It was immediately followed by application of calcipotriol plus betamethasone

topically and rubbing over the affected area for about 2 minutes. Occlusive dressing was then done and kept for 1 day. The procedure was repeated every 15 days till repigmentation was achieved or up to 3 months with total sittings not exceeding more than 6. After completion of treatment, patients were observed after 2 weeks for the outcome of treatment. Outcome assessment in vitiligo treatment employed the VASI score. Body areas were divided into hands, upper extremities, trunk, lower extremities, and feet. One hand unit, covering the palm plus digits, estimated 1% of total body surface, aiding baseline vitiligo involvement assessment. Follow-ups tracked repigmentation and residual depigmentation within patches, gauged to the nearest percentage increment (0%, 10%, 25%, 50%, 75%, 90%, or 100%). VASI scores were derived for each region based on standardized criteria: 100% depigmentation signified absence of pigment, 90% showed specks, 75% indicated depigmented area surpassing pigmented, 50% depicted equal areas, 25% showed pigmented area exceeding depigmented, and 10% represented specks of depigmentation. Clinical response was measured by taking mean change in VASI score after the treatment from baseline. Age, gender, family history and duration of vitiligo and educational status were all the variables that were considered during data collection.

The entirety of the collected data underwent entry and analysis utilizing SPSS version 22.0. Numerical variables, including age, duration of disease, VASI score at baseline and follow-up, as well as the change in VASI score, were summarized using mean±standard deviation (SD). Meanwhile, categorical variables such as gender, educational status, and family history of vitiligo were presented in terms of frequency and percentage. To account for potential effect modifiers, the data was stratified based on age, gender, duration of disease, educational status, and family history of vitiligo. Following this stratification, t-tests were employed, with a significance level set at p-value ≤0.05, to ascertain statistically significant differences post-stratification.

Results

Patient's age was in the rage of 15 years to 45 years with a mean of 26.4±8.9 years. There were 26 (45.6%) male and 31 (54.4%) female patients. The duration of disease ranged from 2 to 8 years with a mean of 4.56±1.71 years. 18 (31.6%) patients were illiterate. Family history of vitiligo was present in 16 (28.1%) patients (**Table 1)**. The VASI score ranged from 55 to 83 at baseline with a mean of 70.40±8.17. It ranged

Table 1 Baseline characteristics of study sample.

Characteristics	*Study Sample (n=57)*
Age (years)	26.4±8.9
<30 years	38 (66.7%)
≥30 years	19 (33.3%)
Gender	
Male	26 (45.6%)
Female	31 (54.4%)
Duration of Disease (years)	4.56±1.71
<5 years	34 (59.6%)
≥5 years	23 (40.4%)
Family history of Vitiligo	
Yes	16 (28.1%)
No	41 (71.9%)
Educational Status	
Illiterate	18 (31.5%)
Middle Pass	16 (28.1%)
Matric	11 (19.3%)
Intermediate and above	12 (21.1%)

Table 2 Mean VASI Score at baseline and follow-up and change in VASI score with treatment.

Time	*VASI Score (Mean±SD)*	*P-value*
Baseline	70.40±8.17	
Follow-up (2 weeks after last session)	30.75±9.05	<0.001*
Mean Change	39.65±4.97	

Paired sample t-test comparing baseline and follow-up VASI scores,
* the observed difference was statistically significant.

Table 3 Comparison of mean change in VASI score from baseline across various subgroups of patients with vitiligo.

Subgroups	*n*	*Change in VASI (mean±SD)*	*P-value*
Age			
<30 years	38	39.66±5.13	0.985
≥30 years	19	39.63±4.78	
Gender			
Male	26	39.58±5.88	0.921
Female	31	39.71±4.16	
Duration of Disease			
<5 years	34	39.76±5.19	0.833
≥5 years	23	39.48±4.74	
Family history of Vitiligo			
Yes	16	39.25±6.39	0.708
No	41	39.80±4.38	
Educational Status			
Under Matric	34	39.74±5.28	0.875
Above Matric	23	39.52±4.58	

from 11 to 54 with a mean of 30.75±9.05 at the end of study. This change in mean VASI score was statistically significant on paired sample t-test (p-value<0.001) **(Table 2)**. The mean change in VASI score from baseline was 39.65±4.97 **(Table 2)**. Mean change in VASI score had insignificant difference across various subgroups **(Table 3)**.

Discussion

Skin color is influenced by factors like skin thickness, light absorption properties, and melanin pigment levels. Melanocytes, responsible for melanin production, are most concentrated on the central face and least in distal nails.[1] Disorders disrupting melanocyte function cause hypopigmentation.[3] Vitiligo, an acquired pigmentation disorder, results from melanocyte destruction, leading to hypo- or achromic patches.[1,2] Treatment aims to halt progression and induce repigmentation, often utilizing corticosteroids, calcineurin inhibitors, and UV therapy.[1,3] Despite options, treatment resistance is common. Ongoing research explores new therapies and assesses the outcome of microneedling combined with calcipotriol plus betamethasone (measured by mean change in VASI) in treatment of vitiligo.

In this study, patients had a mean age of 26.4±8.9 years. This aligns with findings by Zahoor *et al*. (2017)[11] who noted a mean age of 26.3±13.0 years in vitiligo patients at Mayo Hospital Lahore. Similarly, Habib *et al*. (2012)[14] reported a mean age of 27.0±18.3 years among patients at Combined Military Hospital, Abbottabad. Zandi *et al*. (2016)[16] observed a mean age of 27.8±10.9 years in Iranian patients, while Kumaran *et al*. (2006)[17] reported a mean age of 25.2±17.6 years among Indian patients.

We noted a slight female predominance among vitiligo patients showing a male to female ratio of 1:1.2. This aligns with findings by Habib *et al*. (2012),[14] who reported a similar female predominance at Combined Military Hospital, Abbottabad, with a ratio of 1:1.2. Dogan *et al*. (2015)[18] observed a comparable female predominance in a Turkish study, with a ratio of 1:1.5, while AL Fahaad *et al*. reported a ratio of 1:1.2 in KSA. Kumaran *et al*. (2006)[17] also reported a similar female predominance among Indian vitiligo patients, with a ratio of 1:1.5.

In our study, 28.1% of vitiligo patients had a family history of the condition. This aligns with findings by Habib *et al*., who reported a similar frequency of 27.8% at Combined Military Hospital, Abbottabad. Zandi *et al*. (2016)[16] observed a comparable frequency of positive family history (28.8%) in Iranian vitiligo patients, while Kumaran *et al*. reported a frequency of 30.0% in India. In contrast, AL Fahaad *et al*. (2015)[19] reported a much lower frequency of 5.9% in KSA.

We observed that microneedling combined with calcipotriol and betamethasone was associated with significant change in VASI score from baseline with a mean of 39.65±4.97. Our observation is in line with a similar study

conducted at Mayo Hospital, Lahore where Zahoor *et al*. (2017)[11] also observed similar significant reduction in mean VASI score after microneedling combined with calcipotriol and betamethasone and reported a mean change of 38.77±38.19 in patients with vitiligo.

Mean change in VASI score had insignificant difference across various subgroups of patients (p-value>0.05) Thus, the response to treatment was not affected by age, gender, duration of disease and family history of vitiligo and this novel combination was suitable for all patients with vitiligo.

The present study adds to the already published limited research evidence on the topic. In the present study, we found that microneedling combined with calcipotriol and betamethasone was associated with considerable change in mean VASI score in vitiligo patients which owing to safety and simplicity of treatment advocates its preferred use in the management of such patients in future dermatological practice.

Conclusion

In the present study, microneedling combined with calcipotriol and betamethasone was associated with considerable mean change in VASI score in vitiligo patients which, owing to safety and simplicity of treatment, advocates its preferred use in the management of such patients in future dermatological practice.

Limitations & recommendations The strengths of the present study were its strict exclusion criteria. We also stratified the results to address various effect modifiers. A very strong limitation to the present study was lack of a control group. We also didn't consider recurrence of disease which would have required a longer follow-up. A study addressing these limitations is very important and is highly recommended in future dermatological research.

Declaration of patient consent The authors certify that they have obtained all appropriate patient consent.

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Conflict of interest Authors declared no conflict of interest.

Authors' contribution

SM,AS,RH: Substantial contribution to conception and study design, manuscript writing, has given final approval of the version of the manuscript to be published.

AS,AM: Substantial contribution to analysis and interpretation of data, critical review of the manuscript, has given final approval of the version of the manuscript to be published.

NAA: Substantial contribution to analysis and interpretation of data, manuscript writing, has given final approval of the version of the manuscript to be published.

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