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# A Comparative Study of Combined Effect of Dermaroller and Topical Tacrolimus (50 Cases) vs Topical Tacrolimus Alone (50 Cases) in Patients of Stable Vitiligo (Total 100 Cases)

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## ABSTRACT

**Background:** Vitiligo is an autoimmune disease produced as a result of interaction of environmental, genetic, neural factors, leading to the destruction of melanocytes and appearance of depigmented macules. It is a chronic disease of great cosmetic concern. As it is often recalcitrant to medical treatment alone, many surgical techniques are used to treat stable vitiligo.

**Aims and objectives:** To evaluate the efficacy and safety of combined dermaroller and topical tacrolimus versus topical tacrolimus alone treatment in the patients of stable vitiligo.

**Materials and Methods:**

- **Material:** Dermaroller specification :192needles, 1.5 mm diameter
- **Method:** Patients were randomly assigned into two groups of 50 patients each. Group A received treatment with dermaroller followed by topical tacrolimus whereas Group B received treatment with topical tacrolimus alone. In both the groups, standard medical treatment was also given. Standard digital photographs were taken at each visit to support the data.

**Results:** The dermaroller group showed maximum patients with excellent response in 44% cases as compared to topical tacrolimus alone group which showed excellent response in 24% cases.

**Limitations:** small sample size and absence of control group were the main limitations of our study.

**Conclusion:** Dermaroller is safe and effective tool for repigmentation in vitiligo with minimum side effects for transdermal drug delivery.

***Keywords:*** Vitiligo, Dermaroller, Tacrolimus

## INTRODUCTION

Vitiligo is an acquired, progressive melanocytopenia of unknown etiology which is clinically manifested as ivory or chalky white macules of different size and shape, the disease affects both sexes equally. It can occur at any age but peak incidence is in age group of 10-30years. There is no racial bar for this condition.

The incidence is 8-20% in people with autoimmune diseases such as diabetes mellitus, thyroid diseases, pernicious anaemia, Addison's disease etc. which is less compared to general population (1-2%). [1]

Vitiligo is an asymptomatic and benign disease but sometimes it causes major psychological problems in dark skinned races. Widespread stigmas, taboos, lack of scientific appraisal and confusion around

vitiligo make it a social embarrassment for patients in the society.

As vitiligo is a disorder due to melanocyte destruction, therapy should be aimed to replenish the melanocyte population.

A lack of response to conventional medical treatment indicates that the melanocyte reservoir within the hair bulb is no longer available. Under this circumstance melanocyte repopulation of vitiliginous area is not possible unless a new source of pigment cell is placed within the depigmented lesions by surgical methods. Stable vitiligo is the term coined for the cases where the disease is inactive and no new patch developed in past 1 year.

There are various treatment modalities available for treatment of vitiligo such as:

1. Medical modalities: PUVA therapy, ACTH therapy, placental extracts, corticosteroid therapy, immuno-modulators etc.
2. Surgical modalities: miniature punch grafting, platelet rich plasma therapy, suction blister grafting, melanocyte transplant, hair follicle grafting, split skin grafting, flip top transplantation etc.

Treatment with dermaroller followed by topical application of tacrolimus, a combination of medical and surgical modalities provides promising, effective and safe modality of treatment. Dermaroller induces strong inflammatory response and local oedema, leading to increased intercellular spaces of basal layer. Active melanocytes migrate from pigmented epidermis through these spaces. The inflammatory mediators such as leukotrienes C4 and D4 and Matrix metalloproteinases from keratinocytes help in melanocyte migration and proliferation.

**Tacrolimus (FK506) [2]:** Tacrolimus is a macrolide immunosuppressant produced by bacterium streptomyces tsukubaensis. It is used intravenously and orally for prevention of organ rejection after liver or kidney transplantation. It suppresses some elements of humoral immunity and to a greater extent Cell mediated immunity. As its molecular weight is lesser than cyclosporine, it has more effective penetration into the skin.

**Topical:** Tacrolimus is available as 0.03% and 0.1% ointment and lotion.

**Mechanism of Action [2]:** It binds to cellular protein FK-506 binding protein, (a rotamase enzyme that is involved in protein folding) to form a complex which in turn binds to calcineurin enzyme thereby blocking its ability to dephosphorylate nuclear factor of activated T-cells (NFAT-1) and prevents transcription of genes encoding IL-2. Thus tacrolimus inhibits T cell activation and proliferation and cytokine production.

**Other Mechanisms of Action:**

- Tacrolimus has direct effect on neurons through an effect on calcineurin, by desensitization of TRPV1 and calcium currents through the PIP2 regulation pathways
- Tacrolimus also increases activity of tyrosinase and promote melanogenesis.
- Tacrolimus also stimulates expression of MITF and melanocyte migration. (Melanocyte migration by tacrolimus is more significant than by endothelin 1)

This study was undertaken to compare the efficacy of combined dermaroller and topical tacrolimus versus topical tacrolimus alone in the patients of stable vitiligo.

## MATERIAL AND METHODS:

### STUDY DESIGN:

The study was carried out in accordance with the good clinical practices and in compliance with the institutional regulations. This prospective, single center, parallel, interventional comparative study of combined effect of dermaroller and topical tacrolimus versus topical tacrolimus alone in treatment of stable vitiligo was undertaken in outpatient department of Skin, V.D. and leprosy in a tertiary care hospital over a period of two years. The permission for the study was taken from the Institutional Ethics Committee. A total of

hundred patients having stable vitiligo were included and were divided into two groups of fifty patients each. Fifty patients were allotted to each group, one group was treated with dermaroller followed by topical application of tacrolimus while the other group was treated with topical tacrolimus alone . Standard medical treatment was also given to all patients irrespective of group . Clinical and photographic record was made at baseline visit and subsequent follow up visits.

**INCLUSION CRITERIA:**

1. Patients willing to participate in the study.
2. Age more than 2 years
3. Stability of lesions for a duration of at least 1 year (stable vitiligo )

**EXCLUSION CRITERIA:**

1. Patients with vitiligo patches on mucosa
2. Patients with koebner phenomenon , keloidal or hypertrophic scar tendency of skin.
3. Pregnant and lactating females.
4. Any prior history of hypersensitivity to tacrolimus or lignocaine.
5. Any evidence of immunosuppression including HIV
6. Age less than 2 years
7. Any uncontrolled systemic diseases.
8. Patients with unrealistic expectations.
9. Patients not giving consent.
10. Patients with history of bleeding tendencies.
11. Patients with infection at the site to be treated.

Patients satisfying the inclusion criteria were explained the treatment protocol and study procedure in detail and were asked to sign an informed consent form document.

**INITIAL ASSESSMENT:**

Patients with stable vitiligo satisfying the inclusion criteria were enrolled to attend a baseline assessment in which a medical history was recorded and physical examination was done.

After clinical history, examination and basic investigations , patients were divided into two groups:

- 1st group : Combined Dermaroller and topical tacrolimus treatment
- 2nd group: Topical tacrolimus alone treatment

**1ST GROUP:**

In these patients, topical lignocaine cream is applied on the patch 20 -30 min before procedure. The affected area is cleaned and sterilized using Betadine solution. Area is treated using dermaroller until pinpoint bleeding is seen. Blood is wiped using Betadine gauze and then a thick layer of topical tacrolimus is applied on treated area. Patients are advised to apply the mixture of tacrolimus and antibiotic cream twice daily for next 2 days followed by tacrolimus only until next session. Maximum of 6 sessions of therapy done at two weeks interval.

**2ND GROUP:**

In these patients , twice daily application of tacrolimus is advised and followed up at two weeks interval.

In both the groups, standard medical treatment is also given. Digital photographs are recorded at each visit for comparison.

**FOLLOW UP:**

Patients were asked for a regular follow up visit at two weeks interval. Treated site was examined and photographic record was made. Any side effect and complication was noted down and managed accordingly . Assessment of repigmentation of lesion was done using subjective assessment score of repigmentation using following table. [3]

| Repigmentation | Grade | Response |
|---|---|---|
| Absent | G0 | No response |
| <25% | G1 | Poor |
| 25%-50% | G2 | Good |
| 50%-75% | G3 | Very good |
| >75% | G4 | Excellent |

## RESULTS AND STATISTICAL METHODS

### DERMAROLLER AND TOPICAL TACROLIMUS COMBINED TREATMENT:

Out of 50 patients, 22 patients (44%) showed excellent response, 20 patients (40%) showed very good response, 4 patients (8%) showed good response, 3 patients (6%) showed poor response, 1 patient (2%) showed no response at all.

These results were comparable to study conducted by Ebrahim H M et al where excellent response was observed in 50% patients. [4]

Visible repigmentation started 4-6 weeks after initiation of treatment. This finding is comparable to study by Mina M et al who observed initiation of repigmentation within 6 weeks. [5]

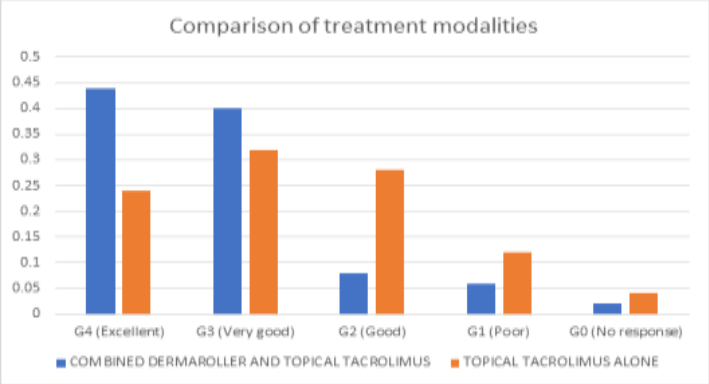
### TOPICAL TACROLIMUS TREATMENT ONLY:

Out of 50 patients, 12 patients (24%) showed excellent response, 16 patients (32%) showed very good response, 14 patients (28%) showed good response, 6 patients (12%) showed poor response, 2 patients (4%) showed no response at all.

These results were comparable to study conducted by Ebrahim H M et al where excellent response was observed in 29.2% patients. [4]

**TABLE 1 COMPARISON OF TREATMENTS**

| TREATMENT | G4 (Excellent) | G3 (Very good) | G2 (Good) | G1 (Poor) | G0 (No response) | TOTAL |
|---|---|---|---|---|---|---|
| COMBINED DERMAROLLER AND TOPICAL TACROLIMUS | 22(44%) | 20(40%) | 4(8%) | 3(6%) | 1(2%) | 50 |
| TOPICAL TACROLIMUS ALONE | 12(24%) | 16(32%) | 14(28%) | 6(12%) | 2(4%) | 50 |
| TOTAL | 34 | 36 | 18 | 9 | 3 | 100 |




### STATISTICAL COMPARISON:

We applied chi square test for the above data as it was categorical. The chi square value come out to be 10.2745 and p value come out to be 0.036 ($p < 0.05$) suggesting the study to be statistically significant.

**TABLE 2 COMPLICATIONS**

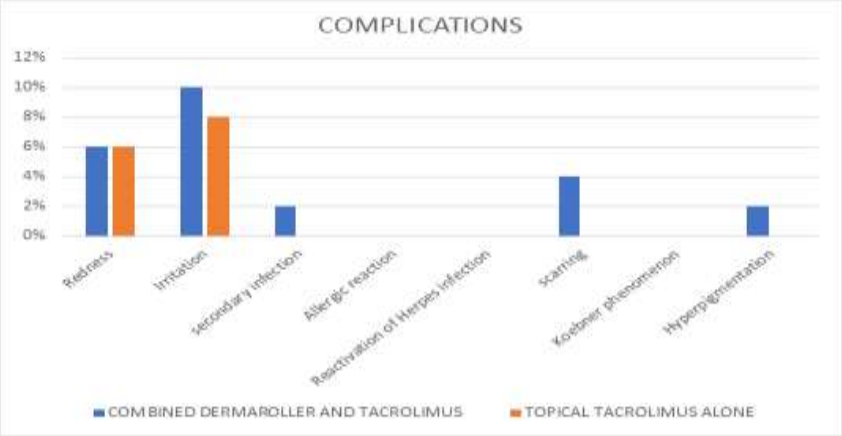
| COMPLICATIONS | COMBINED DERMAROLLER AND TOPICAL TACROLIMUS | TOPICAL TACROLIMUS ALONE |
|---|---|---|
| Redness | 3(6%) | 3(6%) |
| Irritation | 5(10%) | 4(8%) |
| Secondary infection | 1(2%) | - |
| Allergic reaction | - | - |
| Reactivation of Herpes Infection | - | - |
| Scarring | 2(4%) | - |
| Koebner phenomenon | - | - |
| Hyperpigmentation | 1(2%) | - |
| Total | 12(24%) | 7(14%) |

Table 2 shows complications observed in both the groups.

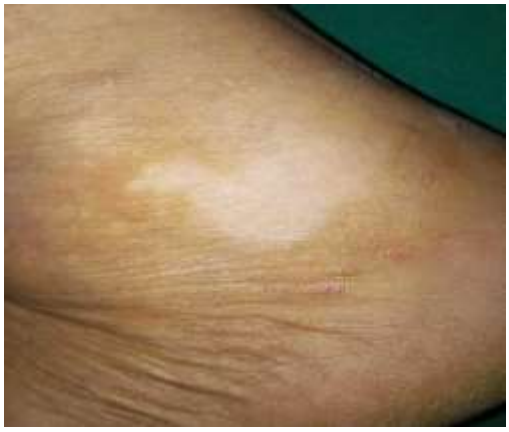
In dermaroller and topical tacrolimus treatment group, most commonly observed complication was Irritation (10% patients) followed by Redness (6% patients) , Scarring (4% patients),Secondary infection (2% patients) , hyperpigmentation (2% patients) .

In topical tacrolimus treatment group, complications were less and transient. Irritation at local application site (8% patients) and Redness (6% patients) were observed.

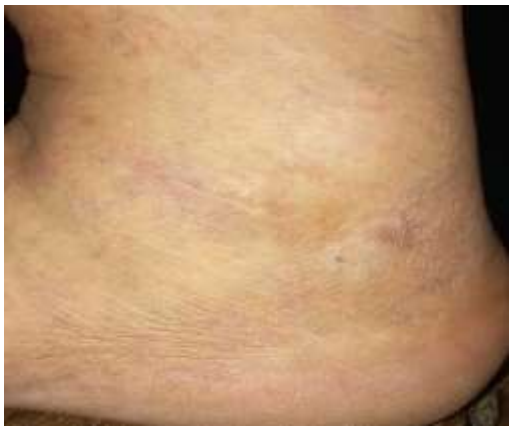
None of the patients developed koebner phenomenon, reactivation of Herpes Infection, allergic reactions.




## DERMAROLLER AND TOPICAL TACROLIMUS COMBINED TREATMENT

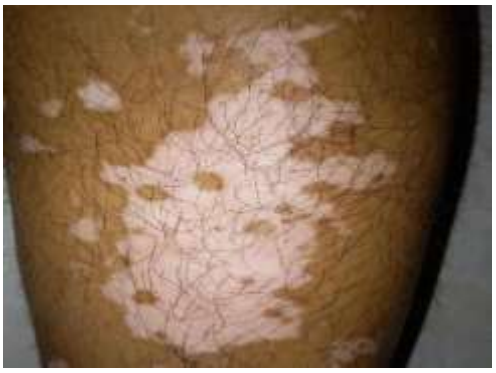


**Pre-treatment photograph.**

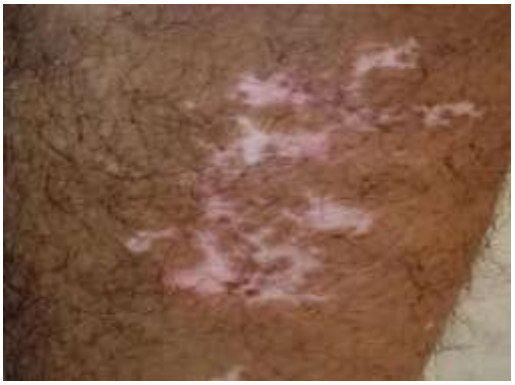


**Post treatment photograph**

## TOPICAL TACROLIMUS TREATMENT ONLY



**Pre-treatment photograph.**



**Post treatment photograph**

## DISCUSSION & CONCLUSION

This study suggested that dermaroller with topical tacrolimus was more effective than topical tacrolimus alone in treatment of stable vitiligo but the incidence of complications was much higher in dermaroller group.

Although topical tacrolimus is a safe, well tolerated medication for repigmentation in vitiligo it may be associated with a prolonged course of treatment , especially for acral lesions. Microneedling with dermaroller followed by topical application of tacrolimus enhances penetration of drug, having better repigmentation rates, shorter treatment course to achieve same degree of repigmentation with minimal and easily manageable side effects.

The patient should be briefed in detail about the efficacy as well as associated complications to clarify his expectations and accordingly treatment should be advised.

### *Declaration by Authors*

**Ethical Approval:** Approved

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**Source of Funding:** None

**Conflict of Interest:** The authors declare no conflict of interest.

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