ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 03 | March - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

COMPARATIVE STUDY ON EFFICACY OF MICRONEEDLING ASSISTED TOPICAL TACROLIMUS THERAPY VERSUS TACROLIMUS ALONE FOR STABLE VITILIGO PATIENTS

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ABSTRACT

Introduction: Vitiligo is an acquired depigmentary disorder that may cause immense psychological stress and negatively affects quality of life. There are various modalities of treatment but no cure. Microneedling is used to maximize pharmaceutical absorption, boost effectiveness and reduce the therapy time. Tacrolimus has immunomodulatory activity. Combining these modalities may accelerate and improve the repigmentation in vitiligo. **Aims & Objectives:** To compare the efficacy of microneedling assisted topical tacrolimus therapy with topical tacrolimus therapy for stable vitiligo patients. **Material & Method:** 50 cases of clinically diagnosed stable vitiligo patients presenting in the OPD of Muzaffarnagar Medical College were enrolled over a period of 12 months. Detailed history, clinical examination was done for diagnostic purpose. Left sided lesion was treated with only topical tacrolimus. The right sided body lesion was treated with microneedling assisted topical tacrolimus. **Result:** Microneedling assisted topical tacrolimus showed >75% repigmentation in 32 lesions as compared to 10 lesions treated with tacrolimus alone. Earlier response was noted in patients treated with combination therapy of microneedling assisted topical tacrolimus. Most common pattern of repigmentation noted was perifollicular. No severe side effects were noted during study. **Conclusion:** The outcome points to the superiority of the combined therapy (tacrolimus and microneedling) for the treatment of vitiligo.

KEYWORDS

INTRODUCTION:
Vitiligo is an acquired chronic relapsing disease mainly characterized by depigmented patches of skin caused by secondary selective loss of melanocytes[1]. India has reported prevalence between 0.25% to 4% in various studies with highest prevalence in states of Gujarat and Rajasthan being 8.8%[2]. Diagnosis is usually clinical signified by discrete white macules surrounded by normal skin typically asymptomatic. Koebnerisation (Isomorphic response) is seen[3].

Principal purpose of therapy in vitiligo is induction of pigment and for cosmesis. There are several repigmentation-oriented medical and surgical therapies, but no cure remains. Tacrolimus (T) is a topical immunomodulator inhibiting calcineurin. In the treatment of vitiligo, it is useful as it has immunomodulatory activity without adverse effect seen with corticosteroids. By blocking the transcription of interleukin-2 (IL-2) genes (essential for the formation and multiplication of cytotoxic T lymphocytes), and also by inhibiting the transcription and formation of IL-4, IL-5, IL-10, IFN-γ and TNF-alpha, it has been successfully used in treatment of vitiligo[4].Microneedling (Mn) is a technique that is simple, productive and minimally invasive. It uses a device fitted with fine needles that generate micro holes in the skin that are invisible to the naked eye. Growth factors such platelet-derived growth factors (PDGF), transforming growth factor-alpha (TGF), and TGF-beta, are released as a result of these micro lesions. This technique is used to maximize pharmaceutical absorption, boost effectiveness and reduce the therapy time. Microneedling also leaves the epidermis partly intact, speeds up regeneration, and limits the threat of infection and scarring. The process uses 0.1 mm to 2.5 mm long, sterile needles that continuously penetrate the corneal layer. There are several brands on the market for production of microneedling instruments like derma rollers, derma pen, derma stamp, etc[5]. Dermaroller is a cylindrical roller studded with 192 medical-grade solid steel microneedles, organised in 24 circular arrays in which each array comprises of 8 microneedles. The depth of penetration by the needle is between the range of 0.5–1.5mm. It offers a relatively low cost and is a minimal invasive tool.

MATERIAL AND METHOD[*]
This study is a treatment trial study conducted on 50 patients of stable vitiligo (duration of stability considered was 6 months) recruited from the Department of Dermatology and Venereology, Muzaffarnagar Medical College and General Hospital, during the period from December 2020 to June 2022. Informed consent was obtained from patients.

METHOD:
A detailed history of every patient along with the complaints, duration of illness, family history was taken. General physical examination and systemic examination was conducted.

Lesion over left side of the body were treated with tacrolimus 0.1% ointment as monotherapy on a. Right side lesion selected, received tacrolimus ointment combined with microneedling. On the right sided lesions, topical anesthetic was applied for 40-60 min pre-procedure, dermaroller was used to cause pin-point bleeding. A combination of horizontal, vertical, and oblique device passes over the treated zone were used in the technique. Then, a thin layer of tacrolimus 0.1% ointment was applied. All patients were prescribed topical antibiotic post procedure along with oral antihistamine if required. The sessions were repeated every 2 weeks until repigmentation occured or for a maximum of 12 sessions (6 months). The patients were followed up monthly for 3 months in order to observe any additional repigmentation or complications. The patients were also instructed to apply topical tacrolimus ointment over the vitiliginous patches once daily until the next session. Any side effects during or after the procedure were inquired before every session. All patients were advised not to use any drug for the treatment of vitiligo other than tacrolimus ointment during the study and in the follow-up period.

Evaluation Of Response:
Evaluation of response was done every 2 months and 1 month after the final session and the follow-up period.

Response was assessed on the percentage of repigmentation achieved based on subjective assessment scale of 0-4:

0: no improvement;
1: 1–25% mild improvement;
2: 26–50% moderate improvement;
3: 51-75% good improvement;
4: 76-100% excellent improvement.

RESULTS:
A total of 50 patients with vitiligo were enrolled in this study, their ages ranged from 6-70 years with mean years 23. Maximum participants (34%) belong to 21-30 years of age group. Least were 3 (6%) who were of the age >50 years. Regarding gender, the results showed the ratio of female (66%) more than male (34%).

In the group treated with only tacrolimus, 15 patients (30%) had associated leukotrichia, while 35 (70%) patches showed no leukotrichia. Out of 15 (30%) patients with leukotrichia 2 (13%)

showed >50% response (1 each giving good and excellent response), 6 showed moderate while 7 gave mild (1-25%) repigmentation.

In the group treated with microneedling + tacrolimus, 17 patients (34%) had associated leukotrichia while 33 (66%) patches were not associated leukotrichia. Out of 17 (34%) patients with leukotrichia 5 (29%) showed >75% response, 10 (59%) showed good to moderate while 2 (12%) gave mild (1-25%) repigmentation.

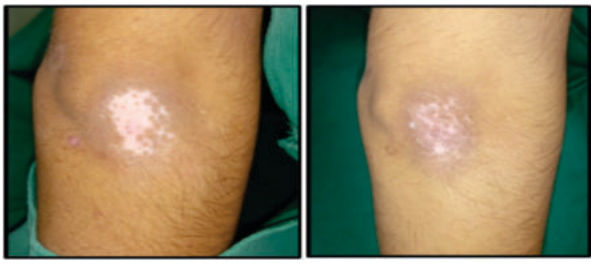
Only 8 (16%) of patients had burning as side effect post treatment with tacrolimus alone. Out of 50 patients, 13 had sideffects post tacrolimus and dermaroller treatment with pain in 11 patients, burning in 5 patients and itching in 3 patients. All side effects reported were mild and lasted for maximum 2-3 days post-procedure.

Most common type of repigmentation seen in both groups is perifollicular followed by diffuse and least common was marginal.

Therapeutic response: Out of 50 patients received treatment as tacrolimus alone, 09 (18%) of the patients had mild (<25% response) response to the treatment. Maximum (40%) of them responded moderately (26-50% repigmentation), 11(22%) of patients had good response and 20% (10) patients showed excellent (>75% repigmentation) around. As seen in table 1.3.

Table 1.3: Response in Patches Treated with Tacrolimus Alone

Grade	Response	No. of Patients	Percentage
0	0% (None)	0	0
1	1-25% (Mild)	09	18
2	26-50% (Moderate)	20	40
3	51-75% (Good)	11	22
4	>75% (Excellent)	10	20

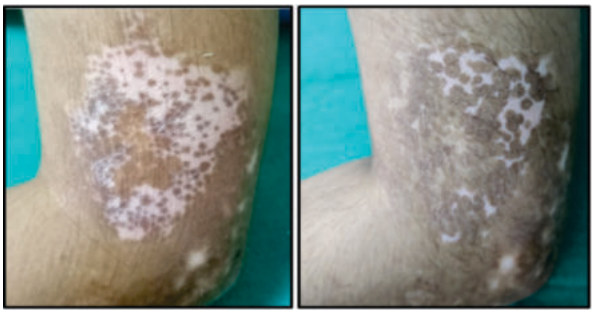


Picture 1: Excellent repigmentation seen after 6 months of topical tacrolimus therapy alone

Out of 50 patients receiving treatment with microneedling assisted topical tacrolimus, majority 32 patients i.e., 64% of them showed excellent (>75%) repigmentation. 10% (5) patients had good (51-75%) response. Moderate (26-50%) response was shown by 11 (22%) patients and 4% (2) patients mild (1-25%) response to the treatment. Given in table 1.4.

Table 1.4: Response in Patches Treated with Tacrolimus Assisted Microneedling

Grade	Response	No. of Patients	Percentage
0	0% (None)	0	0
1	1-25% (Mild)	2	4
2	26-50% (Moderate)	11	22
3	51-75% (Good)	5	10
4	>75%	32	64



Picture 3: Excellent Repigmentation seen after 12 sessions using dermaroller assisted topical tacrolimus

DISCUSSION:

Vitiligo is a skin disease of spontaneous depigmentation characterized by white patches on different areas of the body. Underlying pathology being melanocyte destruction or dysfunction, the pathogenesis yet largely remains unclear. This disease is easy to diagnose, but even with various modalities of treatment being available, patient quality of life is negatively affected. Many medical modalities have been tried, but current attention has been placed on surgical methods. The benefit of microneedling therapy is that it is an office-based procedure, which guarantees patient compliance to therapy. Additionally, it has no systemic adverse effects when compared to oral drugs.

In the present study, principal findings are microneedling with tacrolimus showed excellent repigmentation in 32 (64%) out of 50 patients. While other 18 (36%) patients showed mild to good repigmentation. Patches treated only with tacrolimus revealed excellent repigmentation in 10 (20%) patients among 50 patients. Rest of all showed mild to good pigmentation result. Majority of the patients showed perifollicular type of repigmentation in both the groups. Difference in success rate via chi square test was found statistically significant (p= 0.0039).

This result of the present study was similar to the study conducted by Howyda M Ebrahim, Reham Elkot, et al.[6] Reviewing the efficacy of combining microneedling with tacrolimus versus tacrolimus 0.1% ointment for the treatment of vitiligo. 48 patients were divided into the two groups mentioned. Fifty percent patients in the group combining modalities showed more than 75% repigmentation compared to 29.2% in the group treated with only tacrolimus.

Similar study comparing microneedling with tacrolimus efficacy with either modality alone by Ebrahim et al.[7] The study found that the overall improvement (76.6%) was significantly higher in the combined group compared with other groups comparable to our study. While repigmentation was 66.6% in the group using only microneedling vs 33.3% in the group using tacrolimus alone.

In 2020 Andrade Lima et al.[8] presented the clinically effective findings of cutaneous microneedling procedure in 12 patients with stable localised vitiligo. Each patient underwent four sessions with dermaroller at an interval of 15 days. Topical tacrolimus 0.1% was the only medication used to treat everyone during the sessions. 10 (83%) patients showed good pigmentation. This is in concordance with our study.

CONCLUSION

At the end of the study, we reached the conclusion that dermaroller assisted tacrolimus therapy is more effective than tacrolimus therapy alone for treatment of stable vitiligo patients. Also, tacrolimus as a lone therapy may be used in localized vitiligo with few patches as it has shown good results and has an advantage of lesser side effects as compared to steroids that are often used a topical agent. Micro-needling assisted topical tacrolimus therapy as a modality for treatment of stable vitiligo patients shows significant results as a re-pigmentation modality, is easy to carry out, and is less time consuming in comparison to other surgical techniques.

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