

## Original Research

### **Evaluation of efficacy of microneedling followed by methotrexate 1% gel versus microneedling followed by tacrolimus solution (0.1%) in localised stable vitiligo: A comparative study**

<sup>1</sup>Gunjan Aggarwal, <sup>2</sup>Yash Paul Jindal

<sup>1</sup>Assistant Professor, Department of Dermatology, KM Medical College and Hospital, Sonkh Road, Mathura, Uttar Pradesh, India

<sup>2</sup>Assistant Professor, Department of Surgery, ICARE Institute of Medical Sciences and Research, Haldia, West Bengal, India

#### **ABSTRACT:**

**Background:** The present study was conducted for comparing the efficacy and safety of microneedling followed by methotrexate 1% gel versus microneedling followed by tacrolimus solution (0.1%) in localised stable vitiligo. **Materials & methods:** 20 patients with localised stable vitiligo were enrolled after meeting the inclusion and exclusion criteria. They were randomly divided into 2 groups of 20 patients each. A 1% gel of methotrexate was administered to Group 1; a 0.1% ointment of tacrolimus was applied to Group 2. Both groups had their dressings changed after 24 hours. Then, it was suggested to the patients to apply the drug twice daily. Up to 24 weeks, this operation was done every three weeks. In Groups 1 and 2, Microneedling was carried out using tacrolimus solution and methotrexate gel, respectively, and was followed with dressings. For a maximum of six months, the operation was repeated every three weeks. Patients were subsequently instructed to apply the medication twice each day. Each patient's therapy success was assessed objectively by the Vitiligo Area Severity Index (VASI). **Results:** The mean age in Group 1 was 35.5 years and in Group 2 34.2 years respectively. 60 percent of the patients of group 1 and 70 percent of the patients of group 2 were females while the remaining were males. As assessed by VASI Score, significant better results were obtained among patients of group A. **Conclusion:** Microneedling followed by methotrexate 1% gel in comparison to microneedling followed by tacrolimus solution (0.1%) in localised stable vitiligo showed significantly better improvement.

**Key words:** Microneedling, Methotrexate, Vitiligo

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**Corresponding author:** Yash Paul Jindal, Assistant Professor, Department of Surgery, ICARE Institute of Medical Sciences and Research, Haldia, West Bengal, India

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#### **INTRODUCTION**

Vitiligo is an acquired disease with a variable course. It is characterized clinically by well-defined depigmented macules or patches thought to occur secondary to melanocyte dysfunction and loss. It is the most common depigmentation disorder, affecting approximately 0.5 to 2.0 percent of the population and has no predilection for gender or race.<sup>1</sup> Vitiligo is categorized into nonsegmental (NSV) and segmental (SV) subtypes, the latter occurring in a minority (5–16%) of patients. Onset and disease course may vary by subtype. In addition, individuals with vitiligo may

experience significant psychosocial manifestations, including low self-esteem and depression.<sup>1-3</sup>

MTX as an antimetabolite and antifolate drug is a time-tested effective treatment extensively used in various autoimmune disorders like psoriasis, psoriatic arthritis, alopecia areata, lupus erythematosus, and rheumatoid arthritis in low to moderate doses with good efficacy, safety, and tolerability on a long-term basis. An increase in the production of proinflammatory cytokines such as IL-6 and IL-2 in vitiligo patients may play an important role in melanocytic cytotoxicity, as observed by Singh, Singh, and Pandey (2012).<sup>4-6</sup> The mechanism of action

of TAC-O differs from those of TCS. Topical tacrolimus inhibits the activation of pro-inflammatory cells such as T lymphocytes and mast cells and prevents the progression of cytokine-driven inflammation.<sup>7</sup> Hence; the present study was conducted for comparing the efficacy and safety of microneedling followed by methotrexate 1% gel versus microneedling followed by tacrolimus solution (0.1%) in localised stable vitiligo.

**MATERIALS & METHODS**

The present study was conducted for comparing the efficacy and safety of microneedling followed by methotrexate 1% gel versus microneedling followed by tacrolimus solution (0.1%) in localised stable vitiligo. 20 patients with localized stable vitiligo were enrolled after meeting the inclusion and exclusion criteria. They were randomly divided into 2 groups of 20 patients each. A 1% gel of methotrexate was administered to Group 1; a 0.1% ointment of tacrolimus was applied to Group 2. Both groups had

their dressings changed after 24 hours. Then, it was suggested to the patients to apply the drug twice daily. Up to 24 weeks, this operation was done every three weeks. In Groups 1 and 2, Microneedling was carried out using tacrolimus solution and methotrexate gel, respectively, and was followed with dressings. For a maximum of six months, the operation was repeated every three weeks. Patients were subsequently instructed to apply the medication twice each day. Each patient's therapy success was assessed objectively by the Vitiligo Area Severity Index (VASI). SPSS software was used to analyse every outcome.

**RESULTS**

The mean age in Group 1 was 35.5 years and in Group 2 34.2 years respectively. 60 percent of the patients of group 1 and 70 percent of the patients of group 2 were females while the remaining were males. As assessed by VASI Score, significant better results were obtained among patients of group A.

**Table 1: Comparison of outcome at 3 weeks and 12 weeks follow-up according VASI score**

Grades of improvement	3 weeks follow-up		12 weeks follow-up	
	Group 1 N (%)	Group 2 N (%)	Group 1 N (%)	Group 2 N (%)
No response	2 (20%)	3 (30%)	1 (10%)	2 (20%)
Mild	3 (30%)	3 (30%)	3 (30%)	5 (50%)
Moderate	5 (50%)	4 (40%)	5 (50%)	2 (20%)
Good	0	0	1 (10%)	1 (10%)
Very good	0	0	0	0
Total	10 (100%)	20 (100%)	10 (100%)	10 (100%)
p- value	0.72		0.001 (Significant)	

**Table 2: Adverse events**

Adverse events	Group A N (%)	Group B N (%)
Pain	1 (10%)	1 (10%)
Erythema	1 (10%)	2 (20%)
Pruritus	1 (10%)	1 (10%)
Burning	2 (20%)	2 (20%)

**DISCUSSION**

Vitiligo persists to evade the researchers and patients in spite of the considerable advancement in basic understanding of the disease process and the treatment protocol over the years. Conservative medical therapy continues to be besieged with capricious and derisory outcome. When the disease becomes refractory to conventional therapy, transplantation techniques are the only options left to replenish the lost melanocytes. Various surgical modalities and transplantation techniques have evolved during last few decades. But, till date none of the medical or surgical therapeutic choices could assure guaranteed success in all the cases. This is primarily because of the obscure etiopathogenesis and elusive activity profile of the disease itself. Not only with medical therapy but also with any of the surgical modus operandi deployed to achieve accomplishment, proper

selection of cases is of paramount importance. The specific criteria for selection have been well defined. Any endeavor of defining norms or principles for selection is based on one single criterion, i.e. stability of the disease. It is taken as the most important parameter before opting for any transplantation technique to treat vitiligo. Stability is the decisive factor, the cornerstone of vitiligo therapy.<sup>7- 10</sup> Hence; the present study was conducted for comparing the efficacy and safety of microneedling followed by methotrexate 1% gel versus microneedling followed by tacrolimus solution (0.1%) in localised stable vitiligo.

The mean age in Group 1 was 35.5 years and in Group 2 34.2 years respectively. 60 percent of the patients of group 1 and 70 percent of the patients of group 2 were females while the remaining were males. As assessed by VASI Score, significant better

results were obtained among patients of group A. Methotrexate (MTX), is an antimetabolite and antifolate drug. Methotrexate (MTX), is an antimetabolite and antifolate drug. It is used in the treatment of cancer, autoimmune diseases, ectopic pregnancy, and for the induction of medical abortions. It acts by inhibiting the metabolism of folic acid. It is used as a treatment for some autoimmune diseases including: psoriasis and psoriatic arthritis, Crohn's disease, and rheumatoid arthritis. It has also been used for multiple sclerosis. It was shown in one study that methotrexate treatment results in a decreased number of T cells capable of TNF $\alpha$  production, whereas the number of T cells producing IL-10 after polyclonal activation increased. Methotrexate possibly suppresses TNF $\alpha$ -induced NF- $\kappa$ B activation. There is only one case report in the literature about the effect of MTX on vitiligo. In that report, a 54-year-old female patient with a 10-year history of rheumatoid arthritis presented with a 6 month history of rapidly progressing vitiligo lesions over trunk and limbs. She was started on a once weekly dose of 7.5 mg methotrexate. At three months follow up after starting methotrexate her arthritis had improved and it was noticed that she had stopped developing new depigmented lesions, The rapid spread of depigmentation had ceased and there was considerable repigmentation of the existing vitiligo lesions (Sandra et al., 1998).<sup>11-13</sup> Sisti A et al undertook a comprehensive literature review, searching for studies evaluating clinical response to tacrolimus topical therapy for vitiligo. A search was performed on PubMed/Medline using the term "vitiligo", combined with "topical" and "ointment". Their inclusion criteria were: use of tacrolimus ointment as monotherapy to treat vitiligo. They found 29 studies from 2002 to 2014. Overall, 709 patients were treated in 29 studies. Pooling the lesions, 50% repigmentation of vitiligo patches was never achieved before 2 months of treatment, with a peak after 6 months of therapy. The best results were obtained on lesions of the cephalic region, especially the face, with tacrolimus 0.1% ointment two times daily. The percentage of non-responsive patients ranged from 0% to 14%. Treatment was generally well-tolerated; only localized adverse effects were reported. Their objective was to verify the effectiveness and safety of tacrolimus ointment monotherapy. It has good efficacy and tolerability. At present, only small trials and case series are available in the literature.<sup>14</sup>

## CONCLUSION

Under the light of above obtained results, the authors conclude that microneedling followed by methotrexate 1% gel in comparison to microneedling followed by tacrolimus solution (0.1%) in localised stable vitiligo showed significantly better improvement.

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