International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 13, No. 11, November 2024 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_13.11.2024.1

ORIGINAL RESEARCH

Comparison of the efficacy and safety of microneedling followed by methotrexate 1% gel versus microneedling followed by tacrolimus 0.1% solution in localised stable vitiligo

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Received Date: 27 August, 2024 Accepted Date: 30 September, 2024

ABSTRACT

Background: Vitiligo is common depigmentary disorder characterised by milky white maculae's and patches. It has a incidence of 3-4% in India with equal predisposition in both the sexes. **Aims/ objectives:** 1. To compare efficacy and safety of microneedling followed by methotrexate 1% gel versus microneedling followed by tacrolimus solution (0.1%) in localised stable vitiligo. **Method:** 40 patients of stable vitiligo of age 15 to 45 years were enrolled from the skin OPD. They were randomly divided into 2 groups of 20 each. Microneedling was done and followed by application of methotrexate 1% gel in group A and Tacrolimus ointment 0.1% in group B. Then the patients were advised to apply the agent twice daily. This procedure was repeated at 3 weekly intervals till 24 weeks. All the patients were evaluated for therapeutic outcome both objectively by Vitiligo Area Severity Index(VASI) and photographically every 3 weeks till end of 36 weeks. The result was tabulated with respect to percentage of improvement in VASI score (grading will be done from 0-4) and impact on the DLQI. **Result:** At 36 weeks follow-up, in group A very good , good, moderate , mild and no improvement was seen in 10%,15%,50%, 25% and 0 respectively whereas in group B it was 0, 15%, 45%, 25% and 15% respectively. Mean percentage of reduction in DLQI in group A and group B was 50.5% and 48.9% respectively. **Conclusion**: Significantly better outcome was observed in group A in comparison to subjects of group B. Incidence of erythema and burning sensation was significantly higher among subjects of group B.

Keywords: Methotrexate, Microneedling, Tacrolimus, Vitiligo

INTRODUCTION

Vitiligo is a frequently encounteredacquired disorder of dyspigmentation caused due to immune mediated destruction of melanocytes(1). It has a multifactorial etiology and polygenic inheritance(2).

It clinically presents as well defined, sharply demarcated achromic macules and are many times associated with leukotrichia. 1-2% of the world's population has this skin condition. The incidence in the Indian population is 3-4%(3).

Management of vitiligo requires a personalized therapeutic approach where counselling plays an important role. Various available treatment options include phototherapy (NBUVB) , steroid therapy, topical therapies like tacrolimus and pimecrolimus cream, Vitamin D analogues, methotrexate gel and other immunomodulators. Surgical modalities include punch grafting, thin thiersh's graft, epidermal grafting by suction blistering, dermabrasion and microneedling alone and with 5-fluorouracil, tacrolimus etc. (4).

Tacrolimus, an immunosuppressant derived from the fungus Streptomyces tsukubaensis, offers a new therapeutic approach for vitiligo(5).

It acts by inhibiting T- lymphocyte activation(6).

Tacrolimus attaches to an immunophilin called FK-binding protein, found within the cytoplasm of T lymphocytes. This interaction leads to the formation of a complex that blocks the activity of the phosphatase calcineurin. By inhibiting calcineurin, signal transduction pathways are disrupted, leading to the suppression of cytokine transcription, including

DOI: 10.69605/ijlbpr_13.11.2024.1

interleukin (IL) -2, IL-3, IL-4, IL-5, IL-8, tumor necrosis factor α and interferon γ(7).

Methotrexate (MTX) is a folic acid antagonist with antiproliferative and immunomodulating properties. It acts by reducing the number of TNF-α-producing T-cells while increasing the number of IL-10 producing T-cells. Moreover, it suppresses B-cells and regulates the production of IL-6 and reactive oxygen species. These combined effects contribute to the effectiveness of methotrexate in treating vitiligo (8).

Therefore, the present study was conducted to compare the efficacy and safety of microneedling followed by methotrexate 1% gel versus microneedling followed by tacrolimus 0.1% solution in localized stable vitiligo.

MATERIAL AND 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 localized stable vitiligo. The study was conducted in Department of Dermatology, Venereology and Leprology at GGSMCH, Faridkot.

***Inclusion criteria* for the present study included:**

1. Patients of age 15 to 45 years of both gender.
2. Patch should be stable for 1year without any treatment.
3. Patients who gave written consent form prior to participation in the study.

***Exclusion criteria* for the present study included:**

1. Patients with generalizedand unstable vitiligo.
2. Patients with deranged liver function tests.
3. Patients with keloidaltendency.
4. Patients with active infection.
5. Pregnant and lactating females.
6. Patients having bleeding disorders.
7. Patients who have known hypersensitivity to tacrolimus solution or methotrexateanalogue.
8. Patients with unstable Diabetes and Hypertension.

40 patients with localized stable vitiligo were enrolled after fulfilling the inclusion and exclusion criteria. They were randomly divided into 2 groups with 20 patients in each group.In Group A Methotrexate 1% gel was applied over the affected area and in Group B Tacrolimus ointment (0.1%) was applied and dressing was done and changed after 24 hours. Then the patients were advised to apply the respective topical agent twice daily. In Group A and Group B microneedling with methotrexate gel and tacrolimus solution respectively was done with subsequent dressings. The procedure was repeated every 4 weeks for maximum 6 months. All the patients were evaluated for therapeutic outcome both objectively by Vitiligo Area Severity Index (VASI) and photographically every 4 weeks till end of 36 weeks. The result was tabulated with respect to percentage of improvement in VASI score (grading will be done from 0-4) and impact on the DLQI. Analysis of all the results was done using SPSS software.

RESULTS

The mean age in Group A was 33.5 years and in Group B 36.1 years respectively. 60% of the patients of group A and 65% of the patients of group B were females while the remaining were males. Positive family history of Vitiligo was present in 15% of the patients of group A and in 10% of the patients of group B. Majority of the patches of both the study groups were located on trunk. Maximum number of patients (23) had onset of patches within last 5 years and minimum had duration of onset 16 years or more (Table 1). While analyzing the outcome statistically, it was seen that at 12 weeks, 24 weeks and 36 weeksfollow-up, significantly better outcome was observed among subjects of group A in comparison to subjects of group B (Table 2 and 3). Mean percentage of reduction in DLQI in group A and group B was 50.5% and 48.9% respectively (Table 4).

Incidence of erythema and burning sensation was significantly higher among subjects of group B (Table 5).

Table 1: Distribution of cases according to duration of onset of patches.

Duration of lesions (years)	Group A N(%)	Group B N(%)	Total
<=5	9(45)	14(70)	23
6-10	10(50)	4(20)	14
11-15	0	2(10)	2
>=16	1(5)	0	1

Table 2: Comparison of outcome at 3 weeks and 12 weeks follow-up

Grades of improvement	4 weeks		12 weeks	
	Group A N(%)	Group B N(%)	Group A N(%)	Group B N(%)
G0 :No improvement	3(15)	5(25)	2(10)	3 (15%)
G1 : Mild	9(45)	6(30)	7(35)	6(30%)
G2:Moderate	8(40)	9(45)	8(40)	10(40%)
G3:Good	0	0	3 (15)	1 (5)

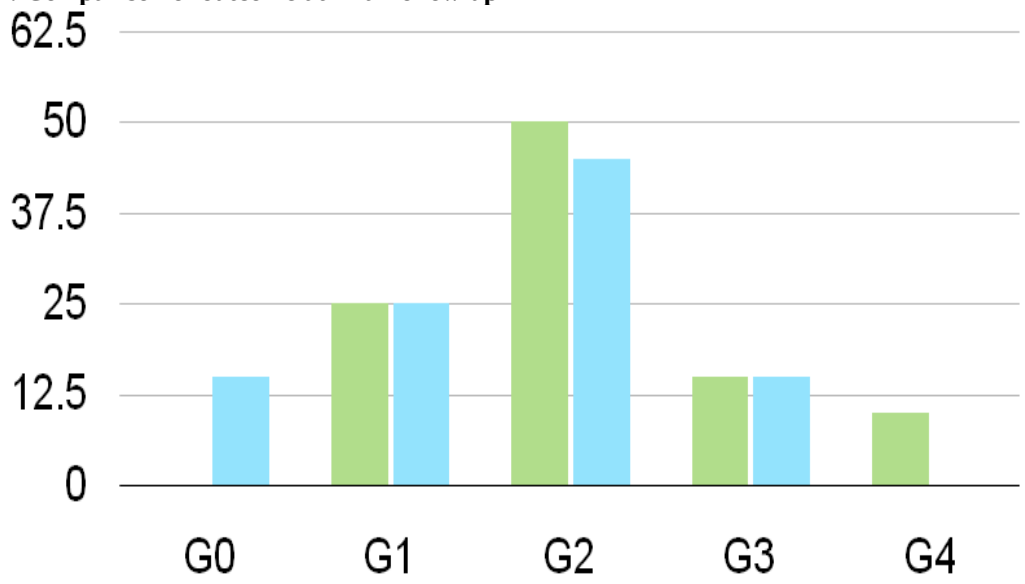
DOI: 10.69605/ijlbpr_13.11.2024.1

G4:Very good	0	0	0	0
Total	20(100)	20(100)	20 (100%)	20(100%)

Table 3: Comparison of outcome at 24 weeks and 36 weeks follow-up

Grades of improvement	24 weeks		36weeks	
	Group A N(%)	Group B N(%)	Group A N(%)	Group B N(%)
G0 :No improvement	1(5)	3(15)	0	3 (15%)
G1 : Mild	6(30)	5(25)	5 (25%)	5(25%)
G2:Moderate	9(45)	10(50)	10 (50%)	9 (45%)
G3:Good	3(15)	2(10)	3 (15%)	3 (15%)
G4:Very good	1(5)	0	2 (10%)	0
Total	20(100)	20(100)	20 (100%)	20(100%)

Graph 1: Comparison of outcome at final follow-up



* Green colour depicts group A and blue colour depicts group B.

Table 4: Comparison of change in DLQI

DLQI	Group A mean	Group B mean
Baseline	16.2	17.24
36 weeks	8.02	8.8
% reduction	50.5%	48.9%

Table 5: Adverse events

Adverse Events	Group A N(%)	Group B N(%)
Pain	1 (5)	1(5)
Erythema	2(10)	3(15)
Pruritus	1(5)	1(5)
Burning	2(10)	3(15)

DISCUSSION

Vitiligo is a chronic, autoimmune,acquired depigmentary disorder characterized by development of white macules and patches on the skin and mucous membranes. They may also effect hair follicles and could be associated with systemic conditions like thyroid abnormalities. The underlying causes of vitiligo are complex and not yet fully understood, involving a combination of genetic predisposition, autoimmune response against melanocytes, and breakdowns in immune tolerance mechanisms(9).

Methotrexate, already known for its effect in inflammatory and immune mediated conditions such as inflammatory bowel disease and psoriasis, has also been studied in treating vitiligo. Mumtaz et al in a randomised control trial demonstrated that topical tacrolimus showed similar efficacy to topical steroids

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in vitiligo but had lesser local and systemic side effects (10).

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.

In this study, the participants of Group A and Group Bhad a mean age of 33.5 years and36.1 years respectively. Females constituted the majority proportion of patients in both the study groups .

In a study conducted by Howitz et al, mean age of onset was between 40-60 years(11).

In a study conducted by Patil et al, it was observed that females were more likely to reportdepigmented lesions as compared to males but the association was insignificant(12).

In the present study, 15% of the patients of group A and 10% of the patients of group B had given positive family history of vitiligo. In the study conducted by Sehgal and Srivastava, the reported incidence of family history ranges between 6.25% to 18% in the Indian population(13).

In the present study, while analyzing the outcome, it was seen that group A had better outcome as compared to group B at 12 weeks, 24 weeks and 36 weeks follow-up whereas group B had shown more complications.

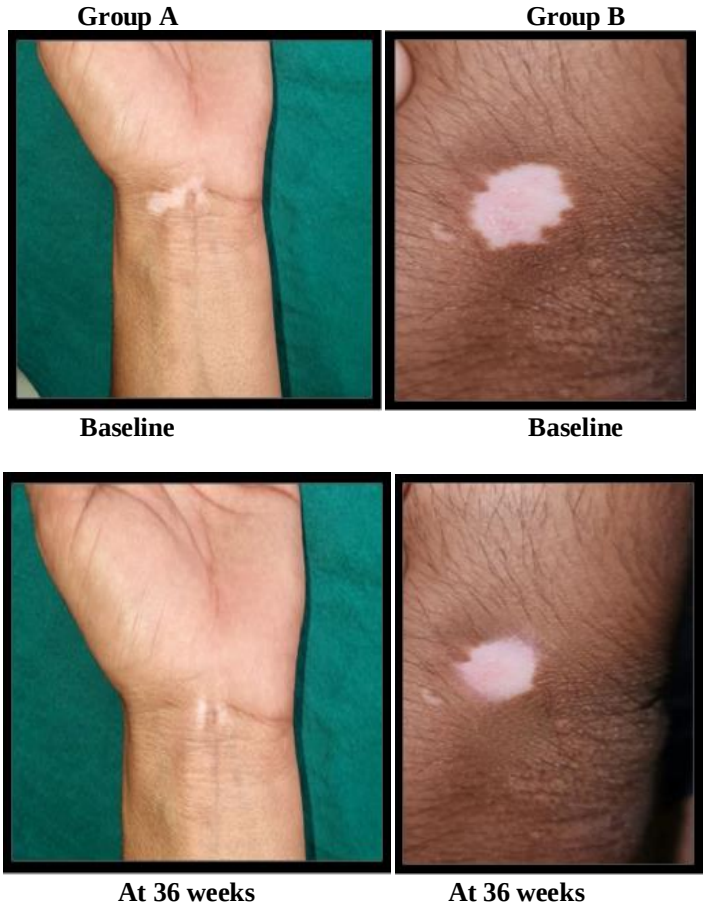
In a previous study conducted by Bhuvana K et al, the effectiveness of 0.1% tacrolimus ointment in localised vitiligo was assessed. Patients with vitiligo on facial areas like the eyelids, around the ears, and the post auricular region often show better outcomes, potentially due to a higher concentration of hair follicles providing a larger reserve of melanocytes.

Topical steroids are commonly used for vitiligo covering less than 10% of the body surface area.Topical steroids and topical tacrolimus have shown equal efficacy in terms of skin repigmentation in vitiligo. However, steroids can lead to side effects such as skin atrophy, telangiectasia, hypertrichosis, and acne, which are not associated with tacrolimus. Hence tacrolimus can be a safer and a preferred treatment option for small localized areas of vitiligo, especially on the face (14).

A case of stable vitiligo was reported to show significant improvement upon topical application of 1% methotrexate gel twice daily for 12 weeks with no local or systemic side effects(15).

3 patients of vitiligo were prescribed low-dose methotrexate (12.5-25 mg per week) with folic acid supplementation for 11-16 months. These patients showed clinically significant skin repigmentation without any severe adverse effects(16).

Therefore, methotrexate can be considered a safe and effective treatment option for stable vitiligo.



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CONCLUSION

Microneedling followed by methotrexate 1% gel, when compared to microneedling followed by 0.1% tacrolimus solution, in localised stable vitiligo showed significantly better improvement.

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