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Original Research Article

Comparative Study of 0.1% Tacrolimus Gel Vs 1% Methotrexate Gel in Focal Vitiligo

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Abstract

Aim: The aim of the present study was to compare the efficacy and safety of 0.1% tacrolimus ointment with 1% methotrexate gel in focal vitiligo.

Methods: This study was done in the Department of Pharmacology and department of Dermatology, Venereology & Leprosy, Patna Medical College and Hospital, Patna, Bihar, India for one year. The study was conducted after approval from Institutional Ethical Committee, Patna Medical College, Patna.

Results: The mean age in Group A was 36.7 years and in Group B 35.4 years respectively. 60 percent of the patients of group A and 70 percent of the patients of group B were females while the remaining were males. As assessed by VASI Score, significant better results were obtained among patients of group A. In group A, adverse effects were burning and in group B, adverse events were burning and erythema.

Conclusion: The present study concluded that microneedling followed by methotrexate 1% gel in comparison to microneedling followed by tacrolimus solution (0.1%) in localized stable vitiligo showed significantly better improvement.

Keywords: 0.1% tacrolimus ointment, 1% methotrexate gel in focal vitiligo.

Introduction

Vitiligo is a dermatological disorder of uncertain etiology, characterized by the appearance of white macules due to the selective loss or dysfunction of melanocytes, making it the most prevalent skin depigmentation condition. [1,2] Globally, it affects approximately 0.4%–2% of the population. [2] The condition is frequently linked with stigmatization and a significant decrease in quality of life (QoL), which is exacerbated in patients with more extensive or rapidly progressing disease later in life. [3] Moreover, vitiligo is associated with various psychological conditions, including depression, which appears to have a linear relationship with the condition's duration, and stress, which is prevalent among patients and may exacerbate the disease. [4]

While autoimmunity is widely accepted as the primary mechanism underlying vitiligo development, several other factors have been proposed, including genetic predisposition, oxidative stress, production of inflammatory mediators, and melanocyte detachment processes.[1] Clinically, vitiligo manifests as achromic macules and patches that increase in number and size over time. [5] Treatment strategies aim to arrest the disease, achieve depigmentation and prevent relapse. [6] The present review discusses the pharmacological, physical and depigmentation treatment options for vitiligo, used either as monotherapy or in combination. In general, combining therapies results in superior outcomes. [7]

Treatment of vitiligo aims to halt disease spread and facilitate depigmentation. Choice of treatment depends on several factors including: the subtype of the disease, the extent, distribution and activity of disease as well as the patient's age, phototype, effect on quality of life and motivation for treatment. The face, neck, trunk and mid-extremities respond best to therapy, while the lips and distal extremities are more resistant. [8] The 2021 BAD Guidelines recommend that first-line treatment consist of high potency or very high potency TCS or topical tacrolimus.8 Commonly prescribed TCS include betamethasone dipropionate, betamethasone valerate, clobetasol dipropionate and fluticasone propionate. Use of the TCS or tacrolimus ointment, to treat vitiligo is off-label.9 Topical tacrolimus, as monotherapy or in combination with phototherapy, is just as effective as TCS therapy but has a safer side-effect profile. Second-line treatments consist of phototherapy NB-UVB or psoralen PUVA and systemic steroid treatment. Third-line treatment consists of surgical grafting techniques. Despite the autoimmune nature of vitiligo, there is insufficient evidence to support the use of immunosuppressive therapies in managing vitiligo.8 Phototherapy has been a mainstay of treatment for vitiligo for several years. Phototherapy is typically administered three times per week and is more effective if commenced early on in the disease. It is used as first-line therapy in extensive disease. It can be used in combination with TCS or topical tacrolimus. [9]

The aim of the present study was to compare the efficacy and safety of 0.1% tacrolimus ointment with 1% methotrexate gel in focal vitiligo.

Materials and Methods

This study was done in the Department of Pharmacology and Department of Dermatology, Venereology & Leprosy, Patna Medical College and Hospital, Patna Bihar, India for one year. The study was conducted after approval from Institutional Ethical Committee, Patna Medical College, Patna.

Inclusion Criteria:

1. Patients of either sex, and

2. Age between 15 to 40 years having focal or locular vitiligo for at least the last three months duration.

Exclusion Criteria:

1. Pregnant or lactating females

2. Women with childbearing potential not using an adequate contraception method

3. Patients with a known sensitivity to the study drug or class of study drug

4. Patients suffering from co-morbid conditions like neurological or psychiatric disorders, an autoimmune disease (especially thyroid disease), immune defects, heart diseases, kidney failure, or previous or current history of neoplasms.

This was a prospective open label study conducted in the department of Pharmacology, Patna Medical College, Patna in 60 patients visiting OPD of department of Dermatology, Venereology & Leprosy, Patna Medical College and Hospital, Patna over a period of 6 months fulfilling the inclusion criteria. Written informed consent was taken from all the patients.

The disease was diagnosed on the basis of clinical features and the Assessment scale proposed by Hossain was used to monitor and grade the response. Patients were randomly allocated into two groups. Group A, having 30 patients was given topical 0.1% tacrolimus ointment whereas Group B, having 30 patients was given topical 1% methotrexate ointment.

Patients were followed up every four weeks. On the 12th week of treatment, effectiveness was assessed by measuring the Assessment scale proposed by Hossain. Data analysis was done using Statistical Package for Social Sciences (SPSS) version 21 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to calculate mean and standard deviation (SD) for age and weight. Frequencies and percentages were presented for gender and effectiveness of drugs in both groups. A Chi-square test was applied to compare the effectiveness between the two groups. P-value of < 0.05 was taken as significant. Stratification of age, weight, and gender was done to control the effect modifiers and the Chi-square test was applied to see the effect of these on outcome variables.

Results

Table 1: Demographic data

Gender	Group A	Group B	Total
Male	12	9	21
Female	18	21	39
Total	30	30	60
Mean age	36.7 years	35.4 years	

The mean age in Group A was 36.7 years and in Group B 35.4 years respectively. 60 percent of the patients of group A and 70 percent of the patients of group B were females while the remaining were males.

Table 2: 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 AN (%)	Group BN (%)	Group AN (%)	Group BN (%)
No response	6 (20%)	9 (30%)	3 (10%)	6 (20%)
Mild	9 (30%)	9 (30%)	9 (30%)	15 (50%)
Moderate	15 (50%)	12 (40%)	15 (50%)	6 (20%)
Good	0	0	3 (10%)	2 (10%)
Very good	0	0	0	0
Total	30 (100%)	30 (100%)	30 (100%)	30 (100%)
p- value	0.60		0.001	

As assessed by VASI Score, significant better results were obtained among patients of group A.

Table 3: Adverse events

Adverse events	Group AN (%)	Group BN (%)
Pain	3 (10%)	3 (10%)
Erythema	3 (10%)	6 (20%)
Pruritus	3 (10%)	3 (10%)
Burning	6 (20%)	6 (20%)

In group A, adverse effects were burning and in group B, adverse events were burning and erythema.

Discussion

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.1 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. [10-12]

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. [13-16] The mean age in Group A was 36.7 years and in Group B 35.4 years respectively. 60 percent of the patients of group A and 70 percent of the patients of group B were females while the remaining were males. As assessed by VASI Score, significant better results were obtained among patients of group A. In group A, adverse effects were burning and in group B, adverse events were burning and erythema.

Sisti A et al [17] 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% depigmentation 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. Shah et al [18] performed an open-label, randomized, prospective study using bFGF related decapeptide solution in combination with tacrolimus 0.1% ointment compared with monotherapy with tacrolimus 0.1% in patients with stable vitiligo. Both treatments were applied daily. The interim analysis at 6 months was >50% depigmentation in 22.5% of patients in the combination group compared with 6.8% of patients in the monotherapy group.

Conclusion

The present study concluded that microneedling followed by methotrexate 1% gel in comparison to microneedling followed by tacrolimus solution (0.1%) in localized stable vitiligo showed significantly better improvement.

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