Original Research Article

Comparison of the Efficacy of Topical Tacrolimus and Pimecrolimus in Treatment of Stable Vitiligo

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Abstract

Background: The topical calcineurin inhibitors (TCIs) are emerging treatment modalities for vitiligo patients. **Aim and objective:** The aim of this study was to assess the efficacy and tolerability of the TCIs Tacrolimus and Pimecrolimus in vitiligo patients. **Methods:** A total of 40 patients with vitiligo were enrolled in this study. They were divided into two groups: topical Tacrolimus 0.1% ointment(20) and topical Pimecrolims 1% cream(20). The efficacy of treatment was assessed 2,4,8,12 and 24 weeks. **Results:** At the end of 24th week, Tacrolimus users showed 25% repigmentation with score of repigmentation 2.62 whereas Pimecrolimus users showed 20% repigmentation with score of repigmentation 2.02. **Conclusion:** After 24 weeks, Tacrolimus 0.1% users showed more efficacy comparing Pimecrolimus 1% topical drug users.

Keywords: Tacrolimus, Pimecrolimus, & Vitiligo

Introduction

Vitiligo is an acquired, idiopathic disorder that is characterized by depigmented macules that result from damage to and destruction of melanocytes[1]. Vitiligo affects between 0.5 and 2% of the general population causing cosmetic and psychosocial problems[2]. The treatment of vitiligo is often stressful and unsatisfying and remains a challenge for dermatologists, although a wide range of therapeutic options have been proposed and are currently available.

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The mainstays of vitiligo therapy include the application of potent topical corticosteroids and the administration of phototherapy, including either psoralen-UVA (PUVA) or NB- UVB[3-5]. Topical calcineurin inhibitors are another option that has been recently introduced for the treatment of vitiligo; these compounds offer the advantage of prolonged use while avoiding the adverse events related to the long-term use of topical steroids. Topical immunomodulators include 0.1% and 0.03% tacrolimus ointment and 1% pimecrolimus cream[6,7]. The objective of the present study is to compare and contrast pimecrolimus and tacrolimus treatments and to investigate the efficacy, side effects and practicality of traditional methods and more contemporary treatments as well as the efficacy and side effects of treatment methods based on the area involved.

Materials and methods

Patients

The study included 40 patients who were diagnosed with vitiligo through clinical and Wood's light examinations and stable for past 1 year. The patients were referred to our dermatology outpatient clinic, in a tertiary care center in Jharkhand between September 2020 and June 2021.The exclusion criteria were as follows: pregnancy or lactation, infections like tuberculosis, neurological or psychiatric disorders, autoimmune disease (systemic lupus erythematosus, dermatomyositis, multiple sclerosis, or Graves' disease), immune defects, heart disease, kidney failure, previous or current history of neoplasms. For patients who were administered any local or systemic immunosuppressive therapy, a washout period of at least 6 months was required. Informed written consent was obtained from patients after the nature of the treatment was carefully explained, including details of its possible outcomes.The wash out phase for current treatment was 24 weeks.At baseline and at weeks 2, 4, 8, 12, and 24, the patients were examined with digital photography. The measurement of the efficacy of treatment was based on the percentage and score of repigmentation averaged for all of the lesions.The patients were clearly informed about their disease, possible treatment options, possible side effects and the study plan. Each patient provided signed informed consent for the treatment and the photos. No conflicts of interest concerning sponsorship of any type was noted in this study.

Treatment Protocol

The patients were scheduled on the basis of a computer-generated randomization into two groups: 20 patients were treated with 1% pimecrolimus cream b.i.d., 20 patients applied 0.1% tacrolimus ointment b.i.d. Treatment regimens were performed for 24 weeks. There was no significant difference among the groups in terms of age, sex, duration of disease, involvement percentage at the onset of the disease. Though incidence is equivalent in males and females, and females present more to OPD, males actively took part in study.

Efficacy Assessments

At baseline and at weeks 2, 4, 8, 12, and 24, the patients were examined with digital photographs. The measurement of the efficacy of treatment was based on the percentage and score of repigmentation averaged for all of the lesions. The score of repigmentation (or improvement) was graded as follows[8].

- score 0: no repigmentation or depigmentation is present at all –
- score 1: (1-25%) repigmentation
- score 2: (26-50%) repigmentation
- score 3: (51-75%) repigmentation
- score 4: more than 75% repigmentation

Side-effects, such as pruritus, burning sensation and erythema were recorded at weeks 2, 4, 8, 12, and 24 of therapy and were graded as mild, moderate or severe using a four-point scale (0, absent; 1, mild; 2, moderate; 3, severe).

Statistical Analysis

SPSS version 20.0 was used for the statistical analyses. Values obtained in the study are presented as the Mean ± SD.

Results

The efficacy of both drugs was interpreted in terms of percentage of repigmentation and the corresponding score given for that. At the end of 2 weeks, percentage of repigmentation was negligible. At the end of 4 weeks, Tacrolimus users showed 1.67 % and Pimecrolimus users showed 1.23% repigmentation. At the end of 8th and 12th week, Tacrolimus users showed better efficacy comparing Pimecrolimus users. At the end of 24th week, Tacrolimus users showed 25% repigmentation with score of repigmentation 2.62 whereas Pimecrolimus users showed 20% repigmentation with score of repigmentation 2.02.

Table 1:Demographic and clinical data of patients with vitiligo

	Tacrolimus 0.1%	Pimecrolimus 1%
Men	12	14
Women	8	6
Age range (years)	12-45	12-45
Age*	20±4.7	18±5.2
Duration*	6±3.5	5±2.9

Table 2: Weekly treatment responses of patients with vitiligo lesions in Mean ± SD

		Tacrolimus 0.1%	Pimecrolimus 1%
Baseline	**Percentage of involvement**	35±20.7	20±10.6
2nd week	**Percentage of involvement**	0.22±0.1	0.18±0.1
	Percentage of repigmentation	0.45±0.3	0.34±0.2
4th week	**Score of repigmentation**	1.67±0.2	1.23±0.2
	Percentage of repigmentation	0.54±0.3	0.43±0.2
8th week	**Score of repigmentation**	6.78±0.2	5.56±0.2
	Percentage of repigmentation	1.58±0.3	1.05±0.3
12th week	**Score of repigmentation**	18.03±0.3	14.09±0.6
	Percentage of repigmentation	1.78±0.5	1.23±0.3
24th week	**Score of repigmentation**	25.08±4.6	20.07±3.2
	Percentage of repigmentation	2.62±0.6	2.02±0.6

Table 3:Development of side effects in groups in Mean ± SD

		Tacrolimus 0.1%	Pimecrolimus 1%
2nd week	**Erythema**	0.76±0.83	0.55±0.33
	Burning	0.56±0.32	0.43±0.22
	Pruritis	0.45±0.23	0.35±0.13
12th week	**Erythema**	0.34±0.12	0.45±0.13
	Burning	0.36±0.14	0.23±0.14
	Pruritis	0.39±0.13	0.23±0.16
24th week	**Erythema**	0.27±0.16	0.24±0.12
	Burning	0.24±0.13	0.13±0.13
	Pruritis	0.23±0.12	0.16±0.12

Discussion

Several treatment alternatives including topical corticosteroids, topical calcipotriol, topical calcineurin inhibitors and phototherapy (PUVA, UVB and NB-UVB) are employed either individually or in combination in the treatment of vitiligo. Despite this variety of treatment alternatives, the responses to treatment vary widely[9,10]. It is well known that face and neck lesions may respond better whereas acral lesions show resistance to treatment even when both lesion types occur in the same patient[11,12]. In the present study, we compared and contrasted the efficacy and side effects of two topical calcineurin inhibitors tacrolimus 0.1% and pimecrolimus.

Topical calcineurin inhibitors possess a dual mechanism of action for the treatment of vitiligo: immunosuppression and melanocyte induction. First, TCIs inhibit cytotoxic $CD8^+$ T cells, an effector arm of autoimmunity in vitiligo, by inhibiting calcineurin-mediated phosphorylation of the nuclear factor of activated T cells. In in vivo studies, TCI treatment led to a decrease in tumor necrosis factor and an increase in IL-10 in vitiligo lesions.Second, TCIs induce the repigmentation of vitiligo by stimulating melanocyte proliferation and migration and melanin synthesis[13,14]. This process involves increasing MMP-2 and MMP-9 activity, increasing endothelin B receptor expression in melanoblasts, and promoting the secretion of stem cell factor from keratinocytes following TCI treatment. In addition, reduced oxidative stress and increased antioxidant capacity have also been observed in the serum samples of patients treated with topical tacrolimus.

We identified a positive treatment response of TCI monotherapy for vitiligo. We found that TCI monotherapy achieved a favorable

treatment response rate, with 55.0% of patients achieving an at least mild response (≥25% repigmentation) after a median treatment duration of 3 months. Topical calcineurin inhibitor monotherapy was particularly effective in pediatric patients: 66.4% of children achieved an at least mild response and 31.7% achieved a marked response (≥75% repigmentation). Among the body parts, face and neck showed the best response, and an at least mild response was achieved in 73.1% of patients, whereas such a response was not found for other body parts. Some hypotheses can help to explain these results. Since hair follicles, which serve as reservoirs of melanocytes, are built in the early fetal period and move apart according to the growth of the skin after birth, children have a higher hair follicle density than adults and so do the face and neck. In addition, daily exposure to sunlight for the head and neck is likely to be associated with better outcomes.

The efficacy of pimecrolimus in the treatment of vitiligo is still controversial. Choi, et al.compared the treatment efficacy in 52 vitiligo patients who was administered an immunomodulator treatment (51 tacrolimus and 1 pimecrolimus) for 6 months and 27 vitiligo patients who received topical steroid treatment. They reported that repigmentation started in a statistically shorter period of time in the topical immunomodulator group, but the outcomes of both treatments were similar, and topical immunomodulators were only as effective and reliable as topical steroids. There are other studies that report similar results.Kose, et al[15]. used mometasone cream and pimecrolimus cream for 3 months in 40 pediatric patients with vitiligo. Although the mean rate of repigmentation was found to be higher in the patients using mometasone cream (65%) relative to those using pimecrolimus cream (42%), the difference was not statistically significant. However, that study concluded that mometasone cream was more effective on the body lesions whereas pimecrolimus was more effective on the facial lesions but not on others. In contrast to this study, Ho, et al[16]. established that pimecrolimus was as effective as clobetasol propionate in facial and non-facial lesions. The concerned study registered 100 pediatric patients with vitiligo between the ages of 2 and 16 and compared three different treatments (0.1% tacrolimus, 0.05% clobetasol propionate and placebo). Moreover, the patients were divided into two groups (those with facial lesions and those with non-facial lesions) and were followed for a period of 6 months. The use of tacrolimus and clobetasol propionate were found to have similar efficacy in both the facial and non-facial groups, and a statistically significant improvement was observed in both groups compared with the placebo group.

The current study shows the efficacy of both drugs were interpreted in terms of percentage of repigmentation and the corresponding score given for that. At the end of 2 weeks, percentage of repigmentation was negligible. At the end of 4 weeks, Tacrolimus users showed 1.67 % and Pimecrolimus users showed 1.23% repigmentation. At the end of 8th and 12thweek, Tacrolimus users showed better efficacy comparing Pimecrolimus users. At the end of 24th week, Tacrolimus users showed 25% repigmentation with score of repigmentation 2.62 whereas Pimecrolimus users showed 20% repigmentation with score of repigmentation 2.02.

The common side effects like erythema, burning sensation and pruritis was noted in the study population. At the end of 2ndweek, Tacrolimus users showed more side effects comparing Pimecrolimus users. At the end of 12th and 24thweek, both topical users got negligible side effects.

Conclusion

After 24 weeks, Tacrolimus 0.1% users showed more efficacy comparing Pimecrolimus 1% topical drug users.

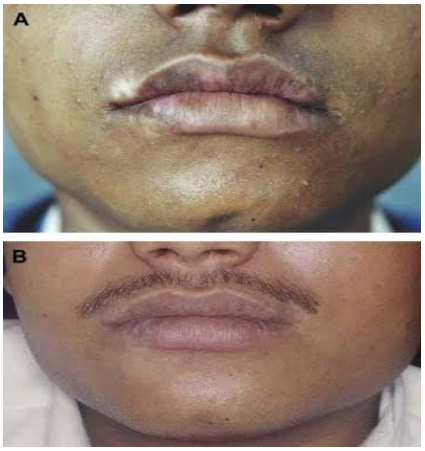

Fig 1: 36 male showing repigmentation after 24 weeks of Tacrolimus 0.1%

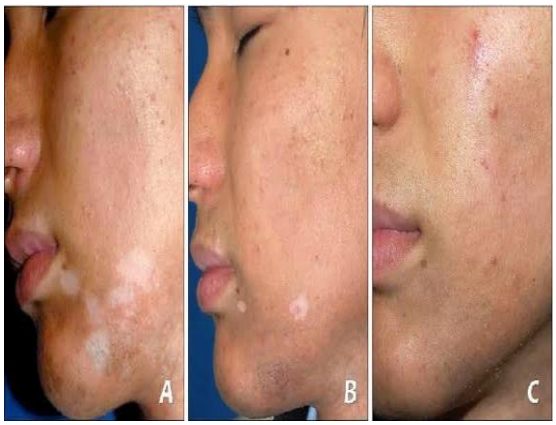

Fig 2: Patient showing improvement after 24 weeks of Tacrolimus 0.1% usage

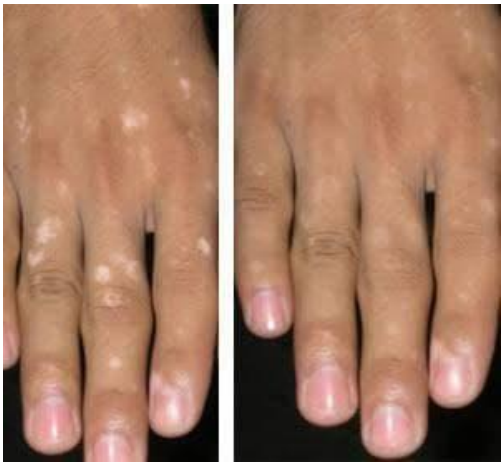

Fig 3: Patient showing repigmentation after 24 weeks of Tacrolimus 0.1% usage

Fig 4: Patient showing improvement after 24 weeks of Tacrolimus 0.1% usage

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