Efficacy of topical tacrolimus 0.1% in the treatment of vitiligo

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A clinical trial was carried out with thirty patients affected with vitiligo. Repigmentation was observed in 26.7% cases on the first follow up visit. At the end of 4th week with tacrolimus ointment in the next visit, it was perceptible in 15 cases 50.1% and after 12 weeks of therapy 83.3% yielded repigmentation. Among those who had repigmentation, 20% had > 75% repigmentation, 23.3% had 50-75% repigmentation. The percentage of repigmentation on head and neck (83.3%) was greater than that on extremities (55.6%). Complete (>75%) repigmentation was 33.3% cases on head and neck and 26.7% along with extremities. A total of 83.3% cases had some repigmentation and among them, 10 cases had focal presentation and 15 cases had generalised or segmental presentation. There was statistically significant ($p<0.005$) difference observed between presentation and pigmentation. By using topical steroid minimum side effects like pruritus in 6.7% cases and burning in 10% cases were evidenced. This study reflects that tacrolimus ointment 0.1% is an effective topical therapeutic option for vitiligo especially on the head and neck region with minimum side effects.

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Introduction

Vitiligo is an acquired, idiopathic disorder characterized by depigmented macules that result from destruction of melanocytes[1]. This is a chronic progressive disease in which depigmentation results intense psychological distress for the patient[2]. Vitiligo is generally benign and non-infectious in nature. The cosmetic disfigurement may lead to considerable emotional stress and the psychological trauma impairs patient's private, social and professional lives[3]. Across the globe vitiligo is relatively common. Incidence is between 1 to 2 percent of dermatological patients[4,5]. Vitiligo is a multifactorial polygenic disorder with a complex pathogenesis. Several studies also point to a significant role of genetic susceptibility to vitiligo. The association of vitiligo with autoimmune conditions is well established[5]. Abnormalities in both humoral and cell mediated immunity have been documented in vitiligo patients and they present a basis for using immunomodulating agents in the treatment of vitiligo[6]. The immunomodulators, can be used on a domiciliary basis for longer periods without aggressive monitoring[7].

Tacrolimus, a macrolide immune suppressant that comes from the fungus *Streptomyces tsukuba* is used as novel treatment for vitiligo[8,9]. Phototherapy and application of topical steroids are most commonly prescribed[10]. However, these are not always effective and corticosteroids on the face may lead to cutaneous atrophy, telengiectasias and ocular (when applied to periorbital region) complications. Successful treatment of vitiligo with topical calcineurin inhibitors has been reported. These drugs act on T cells and mast cells inhibiting T cell activation the release of pro-inflammatory mediators in mast cells by

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degranulation. Tacrolimus therapy does not cause atrophy, telengiactesia and ocular side effects of topical steroids, when applied to face and intertriginous areas[11]. There are numerous treatment options available for vitiligo but none is universally effective. Very recently topical tacrolimus 0.1% is being produced and marketed in our country but its efficacy has not been studied in our population as yet. This study is therefore designed to observe the treatment outcome of using topical tacrolimus 0.1% in patients of vitiligo.

Methods:

A clinical trial was conducted in patients with vitiligo as the study population. A total of thirty patients, who matched the inclusion criteria, was selected for the study. Sampling technique was purposive type. History and physical findings were recorded in a structured questionnaire. *Inclusion criterias were v*itiligo patients of both sex and above 2 years of age, patient who have not received any treatment for vitiligo (both systemic and topical) in the previous 2 months prior to inclusion, vitiligo of focal, segmental and generalized nature, patient willing to give informed consent and willing to comply with the study procedure. Exclusion criteria were pregnant women and lactating mother, known case of tacrolimus hypersensitivity and vitiligo universalis with widespread involvement.

Procedure of the study:

A total number of thirty patients of vitiligo was primarily selected from outdoor department of Dermatology and Venereology, BSMMU and complete history, general physical and dermatological examinations was done for all enrolled patients. For women of reproductive age reproductive history, menstrual history, lactation and pregnancy plan was carefully judged. Before inclusion in the study, all the participants and parents of children were elaborately informed about the natural history and the prognosis of their disease, proper application procedures for the therapy, possible therapeutic outcomes and adverse effects associated so that they can make independent decision about their participation. They were assured of strict privacy and secrecy of information Photographs of all lesions and clinical assessment at baseline and follow-up visit after three months were taken for subsequent assessment and further comparison. Each individual lesion was treated with tacrolimus 0.1% cream twice daily for three months. Generally, the efficacy of repigmentation therapy was recorded every 4 weekly for three months and outcome measures graded on a 4-point score (0 = none, 1 = mild or <50% repigmentation, 2 = moderate or 50–75% repigmentation, 3 = complete or >75% repigmentation). The assessment results were recorded, compiled and edited. Statistical analysis was done and level of significance was measured by using appropriate procedures like chi square test (χ^2). Level of significance (p value) was set at 0.05 and confidence interval at 95%.

Result

The demographic study revealed that the majority of patients suffering from vitiligo (66.6%) were under the age of 30 years. The highest percentage (43.3%) was in the age of 10-20 years. Sex incidence revealed higher incidence in case of female 60%, with a male-female ratio 1:1.5. The information obtained and recorded in the questionnaire demonstrated that 16.67% patients had vitiligo among their relatives. It is evidenced from the table 1 that repigmentation was observed 26.7% cases on the first follow up visit at the end of 4th week, at the next visit, it was observed in 50.1% and after 12 weeks of therapy with tacrolimus ointment 25 cases 83.3%. Among those who had repigmentation, 20% had >75% repigmentation, 23.3% had 50-75% repigmentation. Table 2 showed that the percentage of repigmentation on head and neck (83.3%) was greater than that on extremities (55.6%). Complete (>75%) repigmentation was 33.3% cases on head and neck and 26.7% on extremities.

Table 3 represented that 83.3% had some repigmentation and among them, 10 cases had focal presentation, 1 case had segmental presentation and 14 cases had generalised involvement. There was statistically significant

(p<0.005) different observed between presentation and pigmentation. Table 4 showed minimum side effects by using topical steroid. Pruritus was observed in 6.7% cases and burning in 10% cases.

Table 1:Distribution of patients by repigmentation score

Repigmentation score	4th week	8th week	12th week
None	22 (73.3)	15 (50.0)	5 (16.7)
<50%, Mild	5 (16.7)	8 (26.7)	12 (40.0)
50-70%, Moderate	2 (6.7)	5 (16.7)	7 (23.3)
>75%, Complete	1 (3.3)	2 (6.7)	6 (20.0)
Total	**30 (100.0)**	**30 (100.0)**	**30 (100.0)**

#Figure within parentheses indicates in percentage

Table 2:Distribution of repigmentation status by site of body involvement.

	Affected sites			Total
	Face, Head & Neck	Trunk & Extremities	Combined	
None	1 (16.7)	4 (44.4)	0 (.0)	5 (16.7)
<50%, Mild	1 (16.7)	2 (22.2)	9 (60.0)	12 (40.0)
50-70%, Moderate	2 (33.3)	3 (33.3)	2 (13.3)	7 (23.3)
>75%, Complete	2 (33.3)	0 (.0)	4 (26.7)	6 (20.0)
Total	**6 (100.0)**	**9 (100.0)**	**15 (100.0)**	**30 (100.0)**

Table 3:Distribution of repigmentation status by types of vitiligo.

Pigmentation	Presentation			Total
	Focal	Segmental	Generalised	
Some pigmentation	10 (90.9)	1 (33.3)	14 (87.5)	25 (83.3)
No pigmentation	1 (9.1)	2 (66.7)	2 (12.5)	5 (16.7)
Total	**11 (100.0)**	**3 (100.0)**	**16 (100.0)**	**30 (100.0)**

Chi square test was done. Chi-square value = 6.055, df = 2, p value = 0.048

Table 4:Distribution of patients by adverse effects.

Adverse effects	Base line	4th week	8th week
Pruritus	2 (6.7)	2 (6.7)	0 (.0)
Irritation/burning	3 (10.0)	2 (6.7)	1 (3.3)

Discussion

The result of the study demonstrated that a total of 43.3% vitiligo cases was within the age group of 11-20 years and 20% were in the age group of 21-30 years which mostly correlates with the findings of many researchers[12,13]. Sex prevalence indicated that higher occurrence was found in females (60%) with a male –female ratio 1:1.5. According to different earlier studies adults and children of both sexes were found equally affected, although the greater number of reports among females is probably due to the greater social consequences to women and girls affected by this condition[14, 15, and 16]. The incidence of a positive family history has variously been reported with a range between 6.25% to 38%[17]. However, in our study the positive family history was attributed to vitiligo cases found in 13.33 % cases which corroborates with another study as 12% [18].

The efficacy of treatment is judged by studying the overall response to topical tacrolimus in the treatment of vitiligo has been observed, which shows that 83.3% cases had at least some repigmentation at the end of study, which concurs with other similar studies as 83.3%[11], 100%[19], 86.4%[20], 84%[21], 87%[22], and 90% [23]. Among those who exhibited repigmentation, complete repigmentation (>75%) were in 20% cases, which is almost similar to other studies as 20%[22], 25% [1], 57.9% [20]. The percentage of repigmentation at the end of 12thweek on head and neck region was greater (83.3%) than that of extremities (55.6%) which correlates with the findings of other studies[11, 21]. In this study only two patients reported to be affected with pruritus (6.7%), and three mild irritation and burning (10%). These are among the clinical side effects of topical tacrolimus described in the literatures which include pruritus, irritation, burning and erythema. No serious adverse events or death occurred during the 12 week study. The symptoms are of mild intensity that concurs with the references; as burning sensation found in 10%[23], 13.3%[11], 3.5%[21] of cases and pruritus and burning in 12% [20] of cases. Nobody had to discontinue the therapy for side effects. In this study dermatological side effects were infrequent and mild one that disappeared with the continuation of therapy and the disorder completely cured after the completion of treatment. The present study found tacrolimus 0.1% ointment to be effective in the treatment of vitiligo, with reduction in the number of vitiligenous spots by increased repigmentation significantly.

Conclusion

This study reflects that tacrolimus ointment 0.1% could be an effective topical therapeutic option for vitiligo especially on head and neck region with minimum side effects that subside with the continuation of therapy. Proper selection of patient as well as appropriate topical use of drug for adequate duration will often result in significant clinical improvement.

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