ORIGINAL ARTICLE

To Assess the Efficacy of Topical 0.03% Tacrolimus Ointment in the Treatment of Vitiligo

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ABSTRACT

Aim: To assess the efficacy of topical 0.03% tacrolimus ointment in the treatment of vitiligo.
Study Design: A randomized controlled trial
Place and duration of study: Outpatient Department of Dermatology, Sargodha Medical College/District Teaching hospital, Sargodha from July to December 2015.
Methodology: A total of 66 patients of vitiligo were selected for this study and randomly divided into study and control groups, using random numbers table, comprising 33 patients each. All patients in the study group were counselled to apply 0.03% tacrolimus ointment, two time a day for a duration of three months, while the patients which were included in control group were asked to apply 0.1% betamethasone valeratetwo time a day for three months. Every month the patients were followed up for the total duration of 3 month.The treatment was considered efficacious when 50% or more involved vitiliginous area of the body showed re-pigmentation of skin after three months of treatment.
Results.In the study group, patients' mean age was 26.1±7.2 years and in control group was 26.4±8.7 years. In the distribution of patient by efficacy of treatment after completion of therapy, in study group, there were 25(75.8%) patients who had efficacy of treatment and 8 (24.2%) patients who had no efficacy of treatment. In control group, there were 28 (84.8%) patients who had efficacy of treatment and 5 (15.2%) patients who had no efficacy of treatment.
Conclusion: It is concluded that tacrolimus ointment is innocuous and effective for the treatment of vitiligo, sparing the adverse effects seen with topical corticosteroids.
Keywords: Vitiligo, efficacy, tacrolimus ointment, re-pigmentation.

INTRODUCTION

Vitiligo is a common, acquired disorder of pigmentation, characterized by well circumscribed milky white macules and patches due to progressive loss of melanocytes from the epidermis.[1]Its incidence in world is about 1% with equal sex ratio.[1] In Pakistan, the reported prevalence is 4.4%[2].Pathogenesis of vitiligo is complex and governed by multiple factors and genes[3].Although, in vitiligo, many theoriessuggests to explain the loss of epidermalmelanocytes, the exact cause is still unknown[3]. Theories include autoimmune, cytotoxic, biochemical, oxidant-antioxidant, neural and viral mechanisms of destruction of epidermal melanocytes[3]. Genetic susceptibility also plays important role[3]. Between 30 to 40% of patients have a positive family history.Many environmental factors likedrugs, sunburn, infections, trauma, systemic illness and emotional stress are thought to trigger the diseases.[4]In the affected individual and their families, there is a rise of frequency of other autoimmune and/or endocrine diseases, like atopy, autoimmune thyroiditis, Addison's disease, alopecia areata, pernicious anemia, hyperparathyroidism, myasthenia gravis, lupus erythematosus, type-I diabetes mellitus and malignant melanoma[5]. Vitiligo can affect any area of the body, but most commonly in sun exposed areas like face, neck and hands[6] sometimes the scalp[7]. The hair may turn white or grey due to lack of melanin in those areas.[7] Vitiligo is classified as segmental, acrofacial, generalized and universal, or by pattern of involvement as focal, mixed and mucosal types[3]. In generalized vitiligo, de-pigmented patches are widely and symmetrically distributed while in focal vitiligo single or few white macules are localized to one area of the body[3]. Mucosal vitiligo is limited to only mucous membranes and acrofacialvitiligo involves only distal fingers and peri-orificial area.[3] Stable vitiligo is when no new de-pigmented lesion is formed in last twelve months[8]. The standard therapies for vitiligo include topical corticosteroids and phototherapy[9,10]. Other treatment options include topical calcipotriol, tacrolimus, pseudocatalase, PUVA therapy, systemic steroids, narrowband UVB radiation, excimer (308nm) laser, grafting techniques

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like mini-punch grafts and transplantation of autologous cultured melanocytes.[9,10] But there are lots of hazards and limitations associated with mostly available therapies[9,10]. Topical corticosteroids can cause irreversible cutaneous atrophy, telangiectasia and striae.[9,10] Phototherapy can lead to dermatitis, blistering, intense pruritus, severe photo-toxicity reactions and cutaneous malignancies[9,10]. The use of grafting and transplantation techniques may be limited bykoebner phenomenon[9,10].Although vitiligo is a medically benign condition, but cosmetic disfigurement associated with this disease can cause a lot of emotional and psychological stress in such patients and their loved ones. It has been suggested that patients with vitiligo, especially young adults, unmarried females, suffer from low self-esteem, poor body image, social stigmatization and poor quality of life especially inorthodox society like ours. The side-effect profile and ineffectiveness of standard therapies have led many clinicians to offer no therapy of vitiligo. However, the potentially devastating psychosocial effectsof vitiligo cannot be ignored. So there is a dire need for an innovative approach with maximum efficacy and minimum or no side effects. The present study is being planned to evaluate the effectiveness of topical 0.03% tacrolimus ointment in patients of vitiligo.

METHODOLOGY

A total of 66 patients of vitiligo were selected for this study and randomly divided into study and control groups, using random numbers table, comprising 33 patients each.All patients in the study group were counselled to apply 0.03% tacrolimus ointment, two time a day for a duration of three months, while the patients which were included in control group were asked to apply 0.1% betamethasone valerate two time a day for three months. Apart from advising non-medicated hypoallergenic soaps, patients were advised not to apply anything over the affected part of their skin during 3 months of the treatment. All the patients were followedup monthly. The efficacy of the drug was assessed after three months of treatment by measuring the percentage area of vitiliginous region which shows re-pigmentation. The treatment was considered efficacious, when 50% or more involved vitiliginous area of the body shows re-pigmentation of skin. The two groups were compared for efficacy by applying Chi-square test. A p-value of ≤ 0.05 was considered as significant.

RESULTS

In study group, there were 14(42.4%) males and 19(7.6%) females. In control group, there were 14(42.4%) males and 19 (7.6%) females (Table I).

The mean age of the patients in study group was 26.1± 7.2 years and in control group was 26.4 ± 8.7 years (Table II).

In the distribution of patient by follow up of first visit (i.e.,) ≥50% of vitiliginous area of the body shows re-pigmentation of skin), in both the groups, there were no patients who showed efficacy of treatment. (Table III).

In the distribution of patient by follow up of 2nd visit (i.e.,) ≥ 50% of vitiliginous area of the body shows re-pigmentation of skin), in study group, there were 4(12.1%) patients who had efficacy of treatment and 29(87.9%) patients who had no efficacy of treatment. In control group, there were 10(30.3%) patients who had efficacy of treatment and 23 (69.7%) patients who had no efficacy of treatment (Table IV).

In the distribution of patient by follow up of 3rd visit (i.e.,) ≥50% of vitiliginous area of the body shows re-pigmentation of skin), in study group, there were 25(75.8%) patients who had efficacy of treatment and 8 (24.2%) patients who had no efficacy of treatment. In control group, there were 28(84.8%) patients who had efficacy of treatment and 5(15.2%) patients who had no efficacy of treatment (Table V).

Table I: Distribution of patients according to sex

Gender	Study group	Control group
Male	14(42.4%)	14(42.4%)
Female	19(57.6%)	19(57.6%)
Total	33(100%)	33(100%)

Table II: Distribution of patients according to age

Age (yrs)	Study group	Control group
11-20	9(27.3%)	9(27.3%)
21-30	16(48.5%)	18(54.5%)
31-40	7(21.2%)	3(9.1%)
41-50	1(3%)	3(9.1%)
Mean±SD	26.1±7.2	26.4±8.7

Table III: Re-pigmentation of vitiliginous skin at 1st follow-up visit

≥50% repigmentation of skin	Study group	Control group
Yes	0	0
No	33(100%)	33(100%)
Total	33(100%)	33(100%)

Table IV: Re-pigmentation of vitiliginous skin at 2nd follow-up visit

≥50% repigmentation of skin	Study group	Control group
Yes	4(12.1%)	10(30.3%)
No	29(87.9%)	23(69.7%)

Total	33(100%)	33(100%)

Table V: Re-pigmentation of vitiliginous skin at 3rd follow-up visit

≥50% re-pigmentation of skin	Study group (n=33)	Control group (n=33)
Yes	25(75.8%)	28(84.8%)
No	8(24.2%)	5(15.2%)
Total	33(100%)	33(100%)

Table VI: Distribution of patients according to efficacy of treatment at completion of study

Efficacy	Study group (n=33)	Control group (n=33)
Yes	25(75.8%)	28(84.8%)
No	8(24.2%)	5(15.2%)
Total	33(100%)	33(100%

X^2 =25.6, df =1, p = 0.08

DISCUSSION

Vitiligo is an acquired pigmentary skin disorder and about 1% of the world's population has been affected. It is characterized by de-pigmented macules that correspond histologically with reduced or absent cutaneous melanocytes[11]. There are two major theories regarding pathogenesis: autoimmune and auto-toxicity theory[12].In adults and children over two years of age, who suffers from atopic dermatitis, immuno-modulators like pimecrolimus cream 0.1%, tacrolimus ointment 0.1% and 0.03% have been approved for the treatment[12].For the treatment of many forms of dermatitis like vitiligo, tacrolimus can be prescribed rather than steroid as it does not cause skin atrophy, telangiectasia or other adverse effects as seen with the use of topical steroids, which is prescribed infrequently and very cautiously to apply over face and intertriginous areas.[13]As the levels of pro-inflammatory mediators and cytokines such as Tumor Necrosis Factor(TNF) are elevatedin the skin lesion of vitiligo, tacrolimus acts by inhibiting the activation of T-cells and degranulation of mast cells thereby decreasing these pro-inflammatory chemicals.[14]

We enrolled 66 patients. They were divided into study and control groups using random numbers table each having 33 patients. All patients in study group were advised to apply 0.03% tacrolimus ointment twice daily for three months and patients in control group were asked to apply 0.1% betamethasone valerate ointment twice daily for three months. The mean age of patients in study group was 26.1±7.2 years and in control group was 26.1±8.7 years. 42.4% males and 57.6% females. After completion of treatment in study group, 75.8% patients had efficacy of treatment and in control group 84.8% patients had efficacy of treatment. It is suggested in many studies that the rate of re-pigmentations improves when tacrolimus is introduced along with other treatment modalities[15,16,17]. A study conducted by Fai et al[19], for a period of 30 months, on 110 patients suffering from chronic and refractory vitiligo on face, trunk and limbs, suggested that the use of topical tacrolimuscould be highly effective when it is used along with NBUVB phototherapy. Helium neon laser and topical tacrolimus, in combination, has also been reported as effective modality[20].Similarly a study conducted by Silverberg et al[21]showed that the effectiveness of tacrolimus ointment as an alternative treatment for vitiligo in children,particularly on head and neck areas.It is concluded that tacrolimus ointment is effective and safe for treating vitiligo sparing the adverse effects seen with topical corticosteroids.For better understanding the safety and efficacy of topical tacrolimus ointment in treating vitiligo, further studies with long term follow up are required to evaluate the stability of re-pigmentation.

CONCLUSION

It is concluded that, for the treatment of vitiligo, tacrolimus ointment is both effective and safe while sparing the adverse effects seen with topical corticosteroids.

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