Treatment of Facial Vitiligo by 0.1% Topical Tacrolimus in the Iraqi Patients

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Abstract

Background: Although the treatment options of vitiligo have been increased during the last decades, therapy is still not satisfactory for many patients. Considering the autoimmune hypothesis of vitiligo pathogenesis, the use of topical calcineurin inhibitors seems reasonable.

Objective: To evaluate the effectiveness and safety of 0.1% Tacrolimus ointment in the treatment of vitiliginous lesions on the face

Patients and Methods: This is an open therapeutic trial. A total of 50 patients with facial vitiligo were seen and studied in the Department of Dermatology and Venereology, Ramadi Teaching Hospital, Al-Anbar, Iraq from March 2010 February 2011. Patients asked to apply topical Tacrolimus) twice daily for three months then follow up 3 months with weekly application with regular visit each month to estimate the area of reduction and record the side effect.

Results: All patients' ages were at least 15 years old with stable vitiligo, (38 females and 12 males). In 85 (70.8%) of 120 treated patches marked repigmentation (Grade III) was noted after 6 months treatment. Side effects were mild burning like sensation at the application site.

Conclusion: Facial vitiligo can be successfully treated with topical tacrolimus ointment 0.1% with fewer side effects.

Keywords: Tacrolimus**,** facial vitiligo, Iraqi patients.

Introduction:

Vitiligo is an acquired depigmenting disorder characterized by loss of functional melanocytes. It is estimated that about 1-2% of population [(1)] suffers from vitiligo.

The onset of vitiligo is usually in childhood or young adulthood. Men and woman are equally affected; all races are affected, in 50% of cases the age of onset fall within the first two decade of life. in Iraq the mean age of onset 17.9 years and in 60% of patients it develops before the age of 20years, 25% of patients had family history of vitiligo[(2)].

Current treatment of vitiligo e.g. topical corticosteroid, topical tincture iodine 5% [(3)], narrow band UVB [(4)] and PUVA are the most prescribed, corticosteroid applied to the face may lead to cutaneous atrophy, telangiectasia and ocular complication, narrow bad UVB requires expensive equipments and trained personnel and PUVA has been associated with risk of carcinogenesis, phototherapy and corticosteroid have limited effectiveness particularly on the face [(5).]

Immunomodulator such as Tacrolimus 0.1% and 0.03 %, and pimecrolimus cream 1 % are approved for treating atopic dermatitis in adult patients and pediatric patients over 2 years of age.[(5)]

Tacrolimus (FK-506) is an immunosuppressive drug membred macrolide lactone discovered in 1984[(6)] from the fermentation broth of Japanese soil sample that contained the bacteria streptomyces tsukubaensis can be used as an alternative to topical steroids in many other forms of dermatitis. This ointment does not cause atrophy, telangectasiae or adverse ocular effects of topical corticosteroids which has limited application to the face and intertregnous areas [(7)].

Tacrolimus acts on T cells and mast cells inhibiting T cell activation and the production of proinflammatory cytokines such as tumor necrosis factor (TNF) whose level are higher in vitiligo lesional skin. Moreover it prevents the release of proinflammatory mediators in mast cells by degranulation [(6)].

The aim of the study is to evaluate the effectiveness and safety profile of tacrolimus ointment 0.1% as a treatment modality in facial vitiligo patients.

Patients and Methods:

This is an open therapeutic trial. Total of 50 patients with facial vitiligo were seen and studied in the Department of Dermatology and Venereology, Ramadi Teaching Hospital, Al-Anbar, Iraq from March 2010 till February 2011, A detailed history was taken regarding the age, sex, residence, history of previous treatment, onset, duration of illness, aggravating factors like stress and sun.

The lesions on the face was examined with wood's light when needed and digital pictures of the lesions were taken to obtain an accurate measurement of the size of the lesions the contours were traced on transparent sheets at baseline and followed each visit [(7)].

Patients asked to apply topical Tacrolimus twice daily for three months then up to 3 months with weekly application with regular visit each month to estimate the area of reduction and record the side effect. During spring and summer time the patients were advised to avoid sun exposure and put sun block, Thyroid function test done for patients suspected to have thyroid problem. Clinical examination was done for other autoimmune diseases. Patients on other treatment and pregnant females were excluded.

Each monthly visit clinical and wood light assessment of repigmentation of the lesions was made; the outline of the lesion was drawn on transparent paper and measures the surface area of the lesions each month. Side effects were also checked up. Subsequently the percentage of the area

reduction or repigmentation in the lesions was calculated. This percentage of repigmentation was the main parameter to measure treatment effectiveness.

The responses to therapy were evaluated according to the following scale [8].

Grade 0: no response.

Grade I: slight response, when there is quarter of size of patch or less showed marginal or follicular repigmentation.

Grade II: moderate response, when there is half of size of path showed marginal or follicular repigmentation.

Grade III: marked response, when there is more than half of size of patch showed marginal or follicular repigmentation.

Results:

A total of 50 patients 38 females and 12 males were recruited for 6 months therapeutic trial , ,their ages ranged from15-22 years with mean±SD years 19.1±3.4,all patients had multiple patches on the face with duration ranged from 9-24 months with mean ±SD 17.22±12 months, the size of patches ranged from 1-5 cm2 in diameter.

The number of patches in 45 patients was 120 with a mean of 3-6 patches in each patient.

All patients were at least 15 years old with stable vitiligo (not expanding during the last 1 year) on the face, 5 patients were defaulted for unknown reason

Before treatment the mean± SD of sizes of patches were 3.4cm2 ± 1.94, after 1 month the mean ±SD of the sizes of patches were 2.9cm2 ±1.69, after 2 months the mean ±SD of the sizes of patches were 2.1cm2 ±1.145, after 3 months of treatment the mean SD of the sizes of patches were 0.7cm2 ±0.43, after 3 months of follow up the mean±SD of sizes of patches were 0.4cm2 ±0.32 (Table 1).

Table 1: Shows the treatment response regarding the size of patches

	No. of patches	Mean size cm2	SD
Before treatment	120	3.4cm2	1.94116
After 1 month	120	2.9cm2	1.69312
After 2 months	120	2.1cm2	1.14641
After 3 months	120	0.7cm2	0.89521
Follow up 3 months	120	0.4cm2	0.49651

Regarding the grades of response, after 1 month of treatment Grade: 65 patches (54.1%), Grade II: 40 patches (33.33%), Grade III: 15 patch (12.5%).

After **2** months of treatment:

Grade I: 50 patches (41.6%).

Grade II: 45 patches (37.5%).

Grade III: 25 patch (20.8%).

After **3** months of treatment:

Grade I: 33 patches (27.5%).

Grade II: 62 patches (51.6%).

Grade III: 25 patches (20.8%).

After **6** months:

Grade I: 8 patches (6.66%),

Grade II: 27 patches (22.5%),

Grade III: 85 patches (70.8month %) (Table 2).

Side effects of the drug were limited to mild erythema with slight tingling sensation.

Table 2: Shows Grades of response to treatment after six months

Grades	**no. and% of patches response after 1 month**	**no. and% of patches response after 2 months**	**no. and% of patches response after 3 months**	**no. and% of patches response after 3months**
Grade I	65(54.1%)	50(41.6%)	33(27.5%)	8(6.66%)
Grade II	40(33.33%)	45(37.5%)	62(51.66%)	27(22.5%)
Grade III	15(12.5%)	25(20.8%)	25(20.8%)	85(70.8%)

Discussion:

Vitiligo is a common skin disease seen every day. High number of patients has limited areas of vitiligo especially on the face that not need systemic treatment, in this area topical treatment like corticosteroid, tincture iodine and other modalities of treatments are considered. the use of topical steroids on the face for a long time lead to many side effects like atrophy, telangiectasia while this study showed that tacrolimus is safe even if used for a long period with mild reversible side effects[5].

The present work was arranged to evaluate the effectiveness of topical tacrolimus ointment.1% in treatment of facial vitiligo.

Topical FK 506 (Protopic, Astella) is approved for the treatment of atopic dermatitis [9] growing number of case reports and small series demonstrate that it can also induce repigmentation in

vitiligo especially on the face and neck [10].

The full role of autoimmune T-cells in vitiligo remains unclear. Thus, it is uncertain if the anti T-cell activity of FK 506 underlies its mechanism in treating vitiligo recent studies have investigated how topical FK 506 alters the inflammatory environment on the skin [11].

Topical tacrolimus may also act on keratinocytes to create signals that cause proliferation of melanocytes [12], in addition tacrolimus may act on suppression of autoantibody recognition of cell surface melanocyte antigen and inhibition of subsequent cytotoxic T lymphocytes reactions.[13]

The result of topical tacrolimus ointment in treatment of facial vitiligo is promising since 85 patches (70.8%) showed marked response after 6 months when there is more than half of the size of patch showed marginal repigmentation. [14]

Also we found that more than half of patients showed clinical repigmentation at the end of first month of treatment this will encourage the patient to continue the treatment course and this explain the small number of patient defaulted.

Conclusion:

In conclusion patients with facial vitiligo can be successfully treated with topical tacrolimus ointment0.1% with fewer side effects.

References:

1. David B. Mosher, Thomas B. Fitzpatrick, Jean-Paul Ortonne &Yoshiaki Hori. Hypomelanosis and Hypermelanosis. Fitzpatrick's Dermatology in General Medicine;5th edition, volume 2;USA; library of Congress Cataloging-in-publication Data;1999;945-61.
2. Sharquie KE. Vitiligo in Iraq, ***Iraqi medical J*** 1987; 35:2; 31-2.
3. Sharquie KE and Majeed MH. Treatment of vitiligo by Topical Application of Iodine Tincture 5% in Comparison with 8-methoxypsoralen Lotion 0.3%. ***J Pan-Arab league of Dermatologists*** 2001; 12; 27-33.
4. Njoo-MD, Bos JD &Westerhof W. Treatment of Generalized Vitiligo in Children with narrow band (TL-01) UVB radiation therapy ***Am Acad Dermatol*** 2000; 42:245-53.
5. Zabawski EJ, Costner M, Cohen JB, et al. Tacrolimus: pharmacology and therapeutic uses in dermatology**.** ***Int J Dermatol***.2000; 39:721-727.
6. Kino T, Hatanaka H, Hashimoto M, Nishiyama M, Goto T, Okuhara M, Kohsaka M, Aoki H, Imanaka H. Fk-506, a novel immunosuppressant isolated from a Streptomyces. I. fermentation, isolation, and physio-chemical and biological characteristics; J ***Antibiotic (Tokyo)*** 40(9):1249-55.
7. Njoo, Bosssyt PM, Westerhof W. Management of vitiligo: result of questionnaire among dermatologists in the Netherlands. ***Int J Dermatol***.1999:38:866-872**.**
8. Sharquie KE and Abdulla MS. Treatment of Vitiligo with Topical 15% Lactic Acid Solution in Combination with UVA. ***Saudi Med. J*** 2005; 26:1013-14.
9. Silverberg NB. Tacrolimus ointment promotes repigmentation of vitiligo in children review of 57 cases ***Am Acad Dermatol***.2004; 51:760-766.
10. Lan CC. FK506 independently up regulates transforming growth factor beta and down regulates inducible nitric oxide synthesis in cultured human keratinocytes: possible mechanisms of how tacrolimus ointment interacts with atopic skin. ***J Dermatol***.2004:151:679-648.
11. Grimes PE. Topical tacrolimus therapy for vitiligo: therapeutic responses and skin messenger RNA expression of proinflammatory cytokines ***Am Acad Dermatol***.2004; 51:52-61.
12. Kovacs S. Vitiligo. ***J Am Acad Dermatol***.1998; 38:647-666.
13. Myers SA. Update on new immunomodulatory agents. ***Adv Dermatol***.2007; 16:213-251.
14. Kostovic K. New modalities for vitiligo: focus on topical immunomodulators Drugs 2005:65:447-459.

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