Original Article

COMPARISON OF EFFECTIVENESS OF TOPICAL TACROLIMUS AND BETAMETHASONE WITH SOFT PARAFFIN IN THE TREATMENT OF PATCHY ALOPECIA AREATA

Azra Saleem[1], Moosa Khan[2], Ghulam Rasool Mashori[3], Azam Samdanl[4], S. Asif Jahanzeb Kazmi[5]

ABSTRACT

Objective: To compare the effectiveness of Topical Tacrolimus and Betamethasone with soft paraffin in the treatment of patchy alopecia areata.

Methodology: Sixty patients with mild to moderate patchy alopecia areata were evaluated in a non-randomized, open label, intention to treat clinical trial. Patients were assigned to Tacrolimus (n=20) or to Betamethasone (n=20) or to soft paraffin (n=20). All the three groups were advised to apply the treatment on the affected areas twice a day for 12 consecutive weeks. The primary study outcome was to compare the hair regrowth rate. Efficacy was evaluated at weeks 4, 8 and 12, using hair regrowth score (RGS) with a scale ranging from 0 (regrowth<10%) to 4 (regrowth>75%).

Results: Fifty six subjects (93%) completed the study. At week 12, the RGS was 3.5±0.11in Betamethasone group (p<0.001), 2.2±0.15 in Tacrolimus group (p<0.005) and 0.85±0.08 (ns) in control group respectively. RGS>3 was observed in 70% of patients in Betamethasone group as compared to 45% in Tacrolimus group and none of the patients in control group.

Conclusion: Betamethasone is more effective than Tacrolimus in promoting hair regrowth as compared with soft paraffin in patients with mild to moderate patchy alopecia areata.

KEY WORDS: Alopecia areata, Tacrolimus, Betamethasone.

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1. Dr. Azra Saleem, MBBS, M.Phil Student
2. Dr. Moosa Khan MBBS, M.Phil, Assistant Prof.
3. Dr. Ghulam Rasool Mashori, PhD
4. Prof. Dr. Azam Samdani, PhD (Dermatology), Head of Dept. of Dermatology, JPMC, Karachi.
5. Dr. S. Asif Jahanzeb Kazmi, MBBS (M.Phil)

1-3&5: Department of Pharmacology & Therapeutics, BMSI, JPMC, Karachi – Pakistan.

Correspondance:

Dr. Azra Saleem,
B-401, Decent View, Block-13,
Gulistan-e-Jauher, Karachi – Pakistan.
E mail: drazra@rediffmail.com

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INTRODUCTION

Alopecia areata is an autoimmune disease, characterized by nonscarring hair loss on the scalp or any hair bearing surface.[1]

Men and women are equally affected and the prevalence is almost the same for all ethnic groups.[1-2] It is a common disease and at any given time, about a 0.2% of people are involved with alopecia areata and 1.7% of the populations experience an episode of alopecia areata during their lifetime[3-5] The etiology and pathogenesis of alopecia areata is still uncertain but

many factors have been described in its pathogenesis e.g. genetic, family history, the atopic state, non-specific immune and organ specific autoimmune reaction, possible emotional stress, infectious agents and neurological factors.[6] A wide range of clinical presentations can occur from a single patch of hair loss to complete loss of hair on the scalp or the entire body (alopecia universalis) particularly in severe or chronic cases, alopecia areata may cause considerable psychological and emotional distress for affected individuals.[7] A range of treatments have been tried for the treatment of alopecia areata, such as topical, interlesional and systemic corticosteroids, contact sensitizers, immunomodulators and biologic response modifier.[8-11] Though different medications with various efficacies have been used for long, no definitive treatment has been introduced yet[1].

Although medically benign, alopecia areata causes tremendous emotional and psychosocial stress in affected patients and their families.[12] Researchers in the field of medicine are striving to determine improve future treatment modalities which may be immunosuppressive or immunomodulatory in nature.[5]

Effective treatment of Alopecia areata is currently the subject of several laboratory investigations focusing on biologic drugs, new selective immunosuppressive drugs and even some initial investigations into gene therapy.[13]

Betamethasone valerate is a moderately potent glucocorticoid with anti-inflammatory and immunosuppressive properties. As alopecia areata is believed to be a T-cell mediated response, restricting the T-cells plays a significant role in controlling the disease. Topical corticosteroids are easy to apply and reduce any pain or inflammation associated with the condition. The mildest form of steroids is always chosen as the first line of treatment by dermatologists.[14]

Tacrolimus is one of newer immunosuppressant that acts by inhibiting T-cell activation and cytokine release.[15] This study is aimed at determining the effectiveness of Tacrolimus in treating early alopecia areata. In the early active phases of alopecia areata, the dermal T-cell infiltrate is comparatively dense. It is a phase which is more treatment receptive.[16]

White paraffin or soft paraffin is a semi-solid mixture of hydrocarbons, used primarily promoted as a topical emollient ointment for healing skin diseases. It has been recognized by the U.S. Food and Drug Administration (FDA) as an approved over-the-counter (OTC) skin protectant which is widely used in cosmetic skin care.[17] In this study it will be used as placebo/ base line for control group patients.

The objective of this study was to compare the effectiveness of Betamethasone and Tacrolimus with soft paraffin in the treatment of patchy alopecia areata and to observe the adverse effects of these drugs.

METHODOLOGY

Study Design: This was a non-randomized, open-label, intention to treat, clinical trial carried out in the department of Pharmacology and Therapeutics, BMSI, in collaboration with Department of Dermatology, JPMC, Karachi. The ethical committee of this institution approved the study protocol.

Patients: A total of 60 patients having patchy alopecia areata met the inclusion criteria and were enrolled after taking written and informed consent. Main inclusion criteria were: patients of both sexes, patients aged>10 years, with mild to moderate patchy alopecia areata, with a duration of disease less than two months. Patients with history of previous systemic or local treatment, pregnant and lactating women, and patients with severe alopecia areata were excluded from the study.

Study Procedure: The study was extended over 12weeks period During this treatment period patients were assigned to either Betnovate (Betamethasone valerate 0.1%), Taczem (Tacrolimus 0.03%) or Soft paraffin to be applied to the affected areas twice daily for 12 weeks followed by monthly follow up visits. The baseline assessment of alopecia grading was performed using a 6-point scale score: S0 = No alopecia, S1 = hair loss <10%, S2 =hair loss 11–25%, S3 = hair loss 26–50%, S4 = hair loss 51–75%and S5 = hair loss > 75%.

Table-I: Demographic and baseline characteristics of patients

Characteristics	*Group-A Betamethasone*	*Group-B Tacrolimus*	*Group-C Soft paraffin*
Total Patients	20	20	20
Remained in	18 (90%)	19 (95%)	18 (90%)
studyLeft out	02 (10%)	01 (5%)	02 (10%)
Age	27	27	27
Mean Range	15-40	15-40	15-40
Gender			
Male	10 (50%)	12 (60%)	15 (75%)
Female	10 (50%)	8 (40%)	5 (25)
Mean affected area(in cm2)	5.3(1.4)	4.9(1.3)	5.7(1.3)
Family history of AA	3	2	2
History of Stress	15	12	14
History of Atopy	6	4	4

Efficacy was evaluated on an intention-to-treat basis, using a hair regrowth score (RGS) with a scale ranging from 0 (regrowth < 10%) to 1 (11–25%), 2 (26–50%), 3 (51–75%) and 4 (regrowth> 75%). The safety and tolerability of Betamethasone and Tacrolimus was assessed by monitoring adverse events at follow up visits throughout the study.

Statistical Analysis: All the values are taken as mean and ±SEM. The primary efficacy measurement was the mean change in the alopecia grading and to compare the hair regrowth rate by using hair regrowth score (RGS). The last observation carried forward (LOCF) approach was used and Student pair test was used to analyze the data.

RESULTS

Sixty patients were selected for treatment, 20 in each treatment group. Four patients withdrew during treatment period and therefore failed to complete the study Reason for withdrawal was noncompliance. Patients in all three groups were matched for demographic characteristics. Demographic data and clinical characteristics at baseline are shown in Table-I. At week 12, the RGS was 3.55+0.11 in Betamethasone group ($p<0.001$), 2.2+0.15 in Tacrolimus group ($p<0.005$) and 0.85+0.08(ns) in control group respectively.

At week 12, a complete or nearly complete regrowth rate in Betamethasone group (i.e. RGS>3) was observed in 70 % (14/20) of patients, as compared to 45 %(9/20) of patients in Tacrolimus group and RGS >3 was not observed in any of the patient of control group. No serious adverse effects were observed in any patient. Mild folliculitis was reported by two patients in Betamethasone group, whereas burning and tingling sensation in the first week of treatment with Tacrolimus was described by three patients in Tacrolimus group.

DISCUSSION

Patchy alopecia areata of less than one year duration is more likely to respond to treatment with a success rate estimated at 75%. Alopecia areata, which has persisted with or without treatment for more than two years, is less likely to respond to further treatment.[18]

Table-II: Evaluation of re-growth score among all groups from day 30 - 90

Groups	*Day 30*	*Day 90*	*P-value*
Group A	1.35(±0.24)	3.55(±0.11)	P<0.001
Group B	0.55(±0.18)	2.2(±0.19)	P<0.005
Group C	0.35(±0.1)	0.85(±0.08)	n.s

Values are expressed in Mean (±SEM).
Group A = Betamethasone, Group B = Tacrolimus, Group C = Soft paraffin.

This was a comparative study, in which efficacy of tacrolimus in promoting hair growth was first time compared with Betamethasone as well as efficacy of both Betamethasone and Tacrolimus were compared with soft paraffin, used as placebo in control group. Tacrolimus is a steroid free topical immunomodulator developed for the treatment of atopic dermatitis.[15] It is indicated in a range of dermatological disorders, including alopecia areata.[16]

Intralesional glucocorticods are considered as first line therapy for alopecia areata.[19] However pain during injections and dermal atrophy are common, as transient, side effects. In addition, intralesional steroids are time and cost consuming. Some authors have reported promising clinical results from alopecia areata treatment with topical corticosteroids.[14] However most authors consider monotherapy with topical corticosteroids to be of little benefit in alopecia areata treatment.[13] Our results suggest that topical corticosteroid, Betamethasone valerate could be used as first line therapy in mild to moderate patchy alopecia areata of less than 6 months duration. Our results further suggest that Betamethasone is still a better choice than Tacrolmus ointment in promoting hair re-growth in patchy alopecia areata.

Though different modalities of treatment, local and systemic,have been used to induce hair regrowth,all of them have their own complications and efficacies. The high spontaneous remission rate of alopecia areata sometimes makes it difficult to clearly assess the true efficacy of a given therapy.[3] In conclusion this study demonstrates that topical corticosteroids are still the safe and well tolerated treatment option as compared to the new steroid free immunomodulator, Tacrolimus in the treatment of mild to moderate patchy alopecia areata.

REFRENCES

1. Epstein E.Evidence based treatment of alopecia areata. JamAcad Dermatol 2001;45:640-2.
2. Sharma VK.Dawn G.Kumar B.Profile of alopecia areata in northern India. Int J Dermatol 1996;35:22-7.
3. Firoz A, Firozabadi MR, Ghazisaidi B, Dowlati Y. Concepts of patients withalopecia areata about their disease. BMC Dermatol 2005;5:1-5.
4. Safavi KH, Muller SA, Suman VJ, Moshell AN, Melton LJ, Incidrnce of alopecia areata in Olmsted Country, Minnesota, 1975 through 1989. Mayo Clin Proc 1995;70;628-33.
5. Strober BE, Siu K. Alexis AF, Kim G, Washenik K. Sinha A, et al. Etanercept does not effectively treat moderate to severe alopecia areata; An open-lable study. J Am Acad Dermatol 2005;52:1082-4.
6. Mc-Donagh AJ, Tazi-Ahnini R. Epidemiology and genetics of alopecia areata. Clin Exp Dermotal 2002;27:405-9.
7. Tang L, Lui H, Sundberg JP, Bissonnette R, McLean DI, Shapiro J. Restoration of hair growth with topical diphencyprone in mouse and rat models of alopecia areata. J Am Acad Dermatol 2003;49:1013-9.
8. Gilhar A, Ullmann Y, Berkutzki T, Assy B, Kalish RS. Autoimmune hair loss (alopecia areata) transferred by T lymphocytes to human scalp explants on SCID mice. J Clin Invest 1998;101:62-7.
9. Shaprio J. Price VH, Hair regrowth. Therapeutic agents. Dermatol Clin 1998;16:341-56.
10. Hoffmann R. Happle R. Topical immunotherapy in alopecia areata; what, how and why? Dermatol Clin 1996;14:739-44.
11. Fiedler VC. Alaiti S. Treatment of alopecia areata. Dermatol Clin 1996;14:733-7.
12. Schmidt S, Fischer TW, Chren MM. Strategies of coping and quality of life in women with alopecia. Br J Dermatol 2001;144:1038-43.
13. Shapiro J. Price V. Hair regrowth: Therapeutic agents. Dermatol Clin 1998;16:341-356.
14. Charuwhicitratanas. Randomized double-blind placebo-controlled trial in the treatment of alopecia areata with 0.25% desoximetasone cream. Arch Dermatol 2000;10:241-243.
15. Price VH, Willey A, Chen BK. Topical tacrolimus in alopecia areata. J Am Acad Dermatol 2005;52(1):138-9.
16. Ruzicka T, Assman T, Lebwohl M. Indications of topical tacrolimus. Eur J Dermatol 2003; 13(4):331-42.
17. Desouza. Vaseline and burns. Vaseline should not be used as first aid for burns. BMJ 2008;21(6):1078.
18. Taylor CR, Hawk JL. PUVA treatment of alopecia areata partialis, totalis and universalis. Br J Dermatol 2006;133(6):914.
19. Sharma Feldmann KA, Kunte C, Wollenberg A, Wolfe H. Is topical tacrolimus effective in alopecia areata universalis? Br J Dermatol 2002;147(5):1031-2.