

Comparison of the Efficacy and Safety of Topical 5% Minoxidil Solution Alone and in Combination with 0.05% Betamethasone Dipropionate Cream in the Treatment of Alopecia Areata

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Background: Alopecia Areata (AA) is a fairly common skin problem, accounting for approximately 2% of new dermatological outpatients worldwide. There is a dire need for an innovative approach in the treatment of this disorder.

Objective: Our objective was to assess the efficacy and safety of topical 5% minoxidil solution alone and in combination with 0.05% betamethasone dipropionate cream in the treatment of alopecia areata.

Method: Fifty patients with alopecia areata, ages ranging from 18 to 55 years, were enrolled in the study. They were randomly divided into two groups, each having 25 patients. The patients in group A, were advised to apply 5% minoxidil solution, twice daily for a period of three months. Whereas the patients of group B, were advised to apply 5% minoxidil solution followed by, 30-60 minutes later, the application of 0.05% betamethasone dipropionate cream. Patients of both groups applied the medicines for a period of three months after which they were followed up for the next three months. The efficacy of the drugs was assessed on the basis of percentage re-growth of hair as: Excellent (> 90%), Good (70 – 90%), Satisfactory (50-69%) and Poor (< 50%). The safety of treatment administered was assessed on the basis of local or systemic side effects of the drugs.

Results: Out of 50 evaluable patients, there were 39 males and 11 females. Minoxidil 5% alone showed an excellent result in 3 (12%) patients, a good response in 10 (40%) and poor in 12 (48%) patients. Minoxidil 5% plus Betamethasone dipropionate cream revealed an excellent response in 11 (44%) patients, good in 9 (36%) and poor in 5 (20%) cases. Comparison of hair re-growth count in the bald patches over a 24 weeks period, showed both treatments to be effective. The combination therapy, however, seemed to be more effective in the re-growth of hair at week 12 and 24. Both treatments were well tolerated.

Conclusions: Both treatments are effective and safe over a 12 weeks period. However, the combination therapy is more effective than minoxidil solution alone in the treatment of alopecia areata.

Key Words: Alopecia areata, minoxidil solution, betamethasone dipropionate.

Introduction

Alopecia areata (AA) is a recurrent non-scarring type of hair loss, patchy or confluent, that can affect any hair bearing area of the body especially scalp.^{1,2} Approximately, 0.2% of the population at any given time has AA, but there are wide geographic and ethnic variations in the incidence and prevalence of AA.^{1,2} Both genders are equally affected. It can occur at any age with a peak incidence in early childhood and young adulthood (15-29 years).³

AA is a chronic organ-specific autoimmune disease, probably mediated by auto-reactive T-cells, which affect hair follicles and, sometimes, the nails, in genetically predisposed individuals.⁴⁻⁶ There is an increased frequency of other autoimmune diseases in affected individuals and their families like atopy, allergic disorders, autoimmune thyroiditis, vitiligo, pernicious anemia, rheumatoid arthritis, lupus erythematosus and type-I diabetes mellitus.^{7,8} A variety of environmental factors including infections, drugs, trauma and emotional stress are thought to trigger the disease.⁹ Clinically, AA may present with patchy (single or multiple)

or confluent hair loss on the scalp or body.² About 5% patients of AA may lose all scalp hair which is called Alopecia Totalis.¹⁰ In 1-2% cases of AA, there is a total hair loss of the whole body including pubic and scalp area that is termed Alopecia Universalis.¹⁰ Ophiasis refers to a band-like pattern of hair loss over the periphery of the scalp.¹¹

There are a lot of treatment options for AA including topical and systemic steroids, topical minoxidil, dithranol, tacrolimus, tretinoin, PUVA therapy, contact immunotherapy and oral immunosuppressive drugs.^{11,12} The minoxidil was originally invented to treat high blood pressure.¹³ Hair growth was seen as a side effect of the medication, and now it is widely used as a topical 2% and 5% solution to treat alopecia.^{13,14} Topical minoxidil solution especially its 5% preparation, is found highly efficacious in treating alopecia areata.¹²⁻¹⁴ When it is used topically in therapeutic doses, its side effects are very rare due to minimum systemic absorption.¹⁴

The present study was planned to see the efficacy and safety of topical 5% minoxidil solution alone and in combi-

nation with topical steroids in patients of AA, because no study of this kind has been done previously in our community.

Patients and Methods

The present study was an open randomized comparative study, carried out in the Department of Dermatology Unit-I, King Edward Medical University/ Mayo Hospital, Lahore from 1st September, 2009 till 28th February, 2010. Fifty patients of either sex, aged 18 years or above, clinically diagnosed of alopecia areata, localized to scalp and beard area with a recent onset (duration less than 3 months), were enrolled. Those patients were included who had ≤ 3 patches of AA with size of the patch less than three centimeters in diameter. Patients who had co-morbidity like diabetes mellitus, renal failure, liver disease, hypertension, atopy, vitiligo, lupus erythematosus, autoimmune thyroiditis, etc were excluded. Patients who had a history of any treatment for AA during the last two months were also excluded. Females with child-bearing potential, without adequate contraception (i.e. Intrauterine device or oral contraceptives), pregnancy or breast-feeding women were omitted from the study. Patients of ophiasis or with underlying immunosuppression, either due to disease or treatment-induced, were also excluded.

Those who fulfilled the inclusion criteria were subjected to therapy. They were randomly divided into two groups, each having 25 patients. A detailed history and clinical examination (general, systemic and cutaneous) of each patient was carried out. All the personal data of the patient, severity of AA (its site, size and number of lesions) and results of routine investigations (complete blood and urine examination, random blood sugar, renal and hepatic profiles) were recorded in a predesigned proforma. The scraping for fungus and skin biopsy was performed, if and when needed.

All the patients in group A were advised to apply 5% minoxidil solution, twice daily for a period of three months. Whereas the patients of group B were advised to apply 5% minoxidil solution followed by, 30-60 minutes later, the application of 0.05% betamethasone dipropionate cream. Patients of both groups were provided medicines for a period of three months and after the completion of therapy, they were followed up for another 3 months. The patients were also asked not to use anything on the affected area other than the prescribed treatment and non-medicated, hypoallergenic shampoos during the study period were advised. Throughout the study, all patients were followed up monthly in order to assess the efficacy and safety of drugs. The efficacy was assessed by measuring the percentage area of the AA patch which showed re-growth of hair. It was graded as Excellent (>90% re-growth of hair), Good (70-90% re-growth of hair), Satisfactory (50-69% re-growth of hair) and Poor (<50% re-growth of hair). The safety, of treatment administered, was judged according to the clinical parameters which included any local or systemic side effects of the drugs.

All the data was entered into SPSS 11 version and was analyzed. The quantitative variables like age, number of patches, size of patches etc. were presented in the form of mean and standard deviation along with frequency tables. The qualitative variables like gender, socioeconomic status, density of hair and side effects of drug were presented in the form of percentage along with frequency tables. The statistical analysis was done by using Chi-square test and a *p*-value of < 0.05 was considered significant.

Results

A total of 53 patients were enrolled in the study. The total number of patients studied, was 50 including 39 males and 11 females. There was one delayed exclusion while two patients lost to follow-up. Of 50 evaluable patients of alopecia areata, two groups were devised i.e., A and B, with 25 patients in each, by random allocation. The age range noted in both groups was 18-55 years with a mean of 30.6+5.4 years in group A and 31.4+6.2 years in group B. The majority of patients belonged to 25-35 years of age in both groups. Male to female ratio in group A was 3.2:1 while it was 4:1 in group B and the difference was statistically insignificant (*p* value > 0.05). Twenty-one patients in group A suffered from alopecia areata on scalp while four patients had AA on the beard area whereas nineteen patients in group B had scalp involvement and six cases presented with involvement of beard area. Twelve patients had a total of two patches of alopecia areata, five had three patches and eight patients had a single patch in group A while ten patients suffered from two patches, six had three patches and nine with one patch in group B. Majority of patients had their disease for the last 2 to 3 months in 92% and 85%, 1 to 2 months in 6% and 12% and 2 to 4 weeks in 2% and 3% in group A and B respectively. Most of the patients were office workers 24%, followed by teachers 22%, housewives 22%, policemen 12%, students 8%, businessmen 8%, shopkeepers 2% and doctors (2%). Tiny pits in fingernails were seen in 2 cases while 9 patients gave a positive family history of diabetes mellitus.

Minoxidil 5% alone (Group A) showed an excellent result in 3 (12%) patients, with a good response in 10 (40%) and poor in 12 (48%) patients. Minoxidil 5% plus Betamethasone dipropionate cream (Group B) revealed an excellent response in 11 (44%) patients, good in 9 (36%) and a poor response in 5 (20%) cases. Comparison of efficacy of the two drug groups showed a significant difference (*p* value < 0.05) Table 1. The combination therapy seemed to be more effective in the re-growth of hair in the lesions at week 12 and 24. The recovery seen in terms of number of patches in both groups is also shown in Table 2.

There were no abnormal changes found in the laboratory investigations done during the study. Both treatments were well tolerated and the adverse events were few, of mild intensity and reversible in nature in each group. Four patients complained of mild pruritus and erythema which settled spontaneously after few days, with minoxidil therapy alone.

Two patients developed folliculitis with the combination therapy which settled after regular washing of hair in a few days.

Discussion

Alopecia Areata (AA) is a common disorder seen in our society that causes loss of hair from the scalp and elsewhere.^{12,15} Topical steroids are a common form of treatment for alopecia areata.^{15,16} Moderate to high-potency topical steroids can be applied twice daily to the affected area and have an advantage in localized alopecia areata, since they're easy to use, inexpensive, painless and have no serious hazards.^{16,17} Treatment must be continued for at least three months, as hair re-growth may not occur before that time.¹⁶ Various international studies have shown the efficacy of topical minoxidil solution in the treatment of alopecia areata.^{13,14,17-19} The exact mechanism of action remains unclear. Minoxidil, most likely, has a direct mitogenic effect on epidermal cells, both in vitro and in vivo.¹⁷ Minoxidil has also been shown to prolong the survival time of keratinocytes in vitro.^{17,19} It is further noted that minoxidil may oppose intracellular calcium entry.^{17,19} Calcium influx normally enhances epidermal growth factors to inhibit hair growth.^{17,19} Minoxidil is converted to minoxidil sulfate, which is a potassium channel agonist and enhances potassium ion permeability, thus opposing the entry of calcium into cells.^{17,19}

Most of the patients were in the 25-35 years age group, similar to the trend seen worldwide.^{11,15,18} This is probably due to the fact that emotional stress and anxiety are at their peak in this age group. The present study revealed a greater preponderance of males as compared to females. This is in contrast to various international studies^{15,18} and can be attributed to the fact that, in our community, males are more conscious and worried about their hair. Moreover, the male patients are usually informed by their hair-dressers about the bald patch to seek advice from a dermatologist for treatment. The duration of disease, size and number of patches is also important to note because the longer the person has the disease, the greater is its severity and the lesser are the chances of successful treatment.^{15,18-20} Nail pitting was noted in only two patients reflecting the fact that it is associated with more severe and chronic disease^{15,18} while we selected cases of mild to moderate disease of short duration. The family history of diabetes mellitus in our patients reveals that alopecia areata occurs in people who have relatives with autoimmune disease.^{15,20,21}

The results of our study confirm the efficacy of twice-daily applications of 5% topical minoxidil alone and 5% topical minoxidil followed, 30-60 minutes later, by the application of 0.05% betamethasone dipropionate cream in patients of mild to moderate alopecia areata.

Topical 5% minoxidil solution showed an excellent efficacy regarding re-growth of hair in 12% of the patients, a good response in 40% and poor in 48% of the patients. A

Table 1: Effect of treatment on recovery in both groups.

Treatment Group	Recovery in Terms of			Patients (n)
	Excellent	Good	Poor	
Group A	3 (12%)	10 (40%)	12 (48%)	25
Group B	11 (44%)	9 (36%)	5 (20%)	25
Total	14	19	17	50

Group A= Minoxidil, **Group B=** Minoxidil and Betamethasone dipropionate

Chi-Square=7.506, p-value=0.023

Table 2: Comparison of recovery in terms of number of patches.

Treatment Group	Number of Patches			Patients (n)
	Single Patch	Two Patches	Three Patches	
Group A	8 (70%)	12 (40%)	5 (20%)	25
Group B	9 (90%)	10 (70%)	6 (40%)	25
Total	17	22	11	50

Group A= Minoxidil, **Group B=** Minoxidil and Betamethasone dipropionate

similar trend is observed in other studies.^{13,14,19} Minoxidil 5% plus betamethasone dipropionate cream revealed an excellent response in re-growth of hair in 44% of the patients, good in 36% and a poor response in 20%. The previous studies mention that the simultaneous use of topical steroids increases the local tissue concentration of minoxidil, probably through vasoconstriction and secondary reduced clearance and so the results are better with combination therapy rather than minoxidil solution alone.¹⁸⁻²⁰ Comparing the efficacy profile of two treatments, both were effective causing re-growth of hair in the bald patches at week 24 with a significant difference (*p value* ≤ 0.05). These results correlate well with other international studies.^{12,19,20}

The patients, who did not respond to topical minoxidil treatment alone is probably due to the short duration of treatment (3 months). The previous studies show that long term treatment is essential to get good results.^{13,14,18,19} However, the success of short term treatment lies in the fact that it should be combined with another therapeutic modality like topical steroids to enhance the efficacy of this new drug.^{18,19} Other factors that may cause failure include a hereditary component, family history of autoimmunity and patients with continuous stress and anxiety in our set up.¹⁵ The poor response seen in group B with combined therapy may be due to the fact that topical steroids frequently fail to penetrate the skin deep enough to affect the hair bulbs, which are the main target.¹⁵

Safety profile of topical minoxidil revealed that pruritus was the side effect seen in few patients followed by burning and mild erythema, in accordance with other studies.^{15,18-20}

These adverse events subsequently reduced, after continued use of the drug. The side effect noted with minoxidil and topical steroid application was local folliculitis which can be attributed to the topical steroid, similar to that mentioned in other studies.^{17,22} However, all these adverse effects were of mild intensity and reversible in nature, otherwise both the drugs were well tolerated.

Conclusion

In conclusion, the present study showed both treatment modalities to be effective, well-tolerated and safe for mild to moderate alopecia areata. However, the combination therapy is more effective in the treatment of alopecia areata and continued application of topical minoxidil solution alone for a long period is required to achieve good results.

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