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Original Research Article

Comparing the therapeutic efficacy of topical minoxidil and finasteride with topical minoxidil and oral finasteride in androgenetic alopecia: a randomized trial

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ABSTRACT

Background: There is an increased interest in the development and use of topical finasteride for treating androgenic alopecia (AGA) due to growing evidence of side effects from oral finasteride. In this study we aimed to compare the treatment outcomes of topical 5% minoxidil with 0.1% finasteride and topical 5% minoxidil with oral 1 mg finasteride.
Methods: 50 patients of stage III and IV of Hamilton-Norwood scale were randomly assigned to either Group A receiving topical 5% minoxidil and oral finasteride 1 mg and Group B receiving topical 5% minoxidil and topical 0.1% finasteride. After taking uninterrupted treatment for 12 months, patients were assessed for hair regrowth and maintenance using global photography and trichoscopy and compared with baseline parameters. Patients in both the groups were assessed for any adverse effects as well.
Results: At baseline, patients in both the treatment groups were similar with respect to their age at the time of presentation, family history of hair loss and Hamilton Norwood scale. In group A, three discontinued treatment and of the rest 65% maintained a good hair density and reduced hairfall. In group B, five discontinued treatment, of the rest 83% patients demonstrated good improvement in hair density ($p<0.05$).
Conclusions: The results of this study strongly support the use of topical finasteride in combination with topical 5% minoxidil for AGA and this may obviate the need of taking long term oral finasteride.

Keywords: Androgenic alopecia, Finasteride, Minoxidil, Outcomes

INTRODUCTION

Androgenic alopecia, commonly referred to as male-pattern hair loss in men or as female-pattern hair loss in women, affects at least half of all men by the age of 50 years, and more later in life.[1] This androgen-dependent hair loss is heritable and occurs in a specific pattern. It has been hypothesised that the genetically predisposed hair follicles undergo miniaturization after being stimulated by androgens, which result in gradual replacement of large and pigmented hairs by thin and depigmented hairs (vellus).[2] Scalp biopsy on histological examination reveals that perifollicular lymphocytic infiltration is very common and culminates in fibrosis of the follicle. The mechanism explaining the microscopic follicular inflammation resulting in fibrosis has been poorly understood.

Minoxidil, developed as an anti-hypertensive agent, promotes hair growth through increasing the duration of anagen.[3] Finasteride is a competitive inhibitor of type 2 5-α reductase and inhibits the conversion of testosterone

to dihydrotestosterone (DHT).[4] DHT, by binding to the androgen receptors in the dermal papillae of the hair follicles, causes miniaturization of follicles, reduced duration of anagen phase and decreased anagen to telogen ratio. This presents clinically as decreased hair density.[5] Though, oral finasteride is well tolerated, numerous preclinical and clinical studies have reported significant sexual adverse effects like decreased libido, erectile dysfunction, ejaculation disorders, and orgasm disorders etc.[6,7] Given the concerning efficacy and side-effects of oral finasteride, there is an interest in the development of a better tolerated topical formulation. Since, hair follicles widely home in 5α-reductase, topical formulations of finasteride in comparison to its oral formulations are expected to potentially reduce its systemic adverse effects. In this study we aimed to compare the treatment outcomes of topical 5% minoxidil with 0.1% finasteride with topical 5% minoxidil with oral 1 mg finasteride.

METHODS

Study design

An interventional, prospective, double blinded randomized clinical trial.

Participants

Patients in the age group of 18-45 years whose primary complaint of androgenic alopecia and had stage III and IV of Hamilton-Norwood scale were included in the study. The diagnosis of androgenic alopecia was made based on the history given by the patient and the clinical examination. All patients taking treatment for androgenic alopecia from the outpatient Department of Dermatology, Venerology and Leprosy at Muzaffarnagar Medical College, Muzaffarnagar (UP) from March 2017 till March 2018 were included in the study. The patients were in good general health with no evidence of any major systemic disease. We excluded patients who were known to be hypersensitive to minoxidil or finasteride or were using other therapies for restoring hair or taking any other systemic medications (like steroids, cytotoxic drugs etc.). Informed written consent was taken from all the patients enrolled after explaining study drugs, its benefits and side effects and further approval from Institutional Ethical Committee was obtained.

Inclusion criteria

We included patients who were not taking any treatment from last 3 months; patients of age group 18-45 years; patients who will give written informed consent; patients with androgenetic alopecia stage III-IV Hamilton-Norwood classification in male.

Exclusion criteria

Exclusion criteria were below 18 years and more than 45 years; androgenic alopecia associated with other dermatological conditions; patients with alopecia other than androgenetic alopecia.

Interventions

Patients were randomized into two groups. Group A received topical 5% minoxidil and oral finasteride 1 mg. Group B received topical 5% minoxidil and topical 0.1% finasteride. Examined patients were blinded to the type of treatment being given to the patient. The patients were assigned to either of the two groups using the random number method with 1:1 allocation ratio.

Outcomes

Patients in both the groups received treatment for 12 months. Primary endpoint was photographic score at the end of 12 months from baseline. Standardized digital photographs of the frontal and parietal region were taken every three months with the patient's head in a similar position to ensure consistency of photography. Secondary endpoint was trichoscopy examination done by two doctors blinded to the treatment. Quality of life assessment was done according to the male androgenetic alopecia quality-of-life (QoL) Questionnaire.[8] Safety evaluations were done on every visit by asking patients about any adverse event related to medication. Routine investigations were ordered as and when required.

Assessment criteria

- Photographic assessment at every visit.
- Trichoscan (measurement of hair density and diameter).
- Patients overall satisfaction at the end of treatment.

Statistical analysis

Using SPSS version 23 treatment outcomes were compared using the chi square or Fisher's exact test. P value less than 0.05 was considered statistically significant.

RESULTS

During the study period, 50 men with androgenic alopecia were enrolled and were allocated to the treatment arms. The age of the patients ranged from 18 to 45 years, with an average of 29.4±3.62 years. At baseline, patients in both the treatment groups were similar with respect to their age at the time of presentation, age when hair loss began, family history of hair loss and Hamilton Norwood scale (Table 1). In Group A three patients discontinued treatment and the remaining 22 patients who received an uninterrupted treatment, 14 patients' hair density was moderately maintained, as shown in Figure 1. 5 patients in Group B discontinued treatment, and of the remaining patients 20 demonstrated good hair growth and maintenance. The rate of favourable treatment outcome was slightly higher in receiving topical finasteride (Group B) (p value less than 0.05). The findings of digital

photography and trichoscopy are as shown in Figure 2. Adverse events encountered in both the groups are shown in Table 2**,** most interesting side effects of oral finasteride in our patients facial edema (3 patients) and dryness of mouth (5 patients). Mean quality of life was comparable in both groups at baseline (Table 3) (p=0.72), but it was significantly higher in patients of Group A as compared to patients of Group B at final follow up (46.27 vs. 40.53; p<0.05). At the end of study period, six cases in Group A and only one patient in Group B were labelled as non-responders to the treatment (Table 4).

Table 1: Baseline characteristics of the patients included in the study.

	Group A	Group B
Number of patients	25	25
Age at the time of presentation to hospital	28.5±4.4	29.2±4.9
Age when hair loss began	23.2±5.1	24.6±5.3
Family history of hair loss	18	17
Hamilton Norwood scale		
Stage 3	14	12
Stage 4	11	13

Table 2: Side effect of finasteride in patients.

Side effect	Group A (%)	Group B (%)
Erectile dysfunction	2 (8)	0 (0)
Ejaculatory dysfunction	2 (8)	0 (0)
Anxiety/depression	4 (16)	0 (0)
Loss of libido	3 (12)	0 (0)
Facial edema	3 (12)	0 (0)
Dryness of mouth	5 (20)	0 (0)
Itching	0 (0)	5 (20)
Erythema (over scalp)	0 (0)	4 (16)
Heaviness	0 (0)	3 (12)
Mood changes	2 (8)	0 (0)

Table 3: Comparison of improvement in quality of life of patients.

Quality of Life	Group	Mean	SD	P value
Baseline	A	38.60	11.17	0.72
	B	34.67	10.02	
6 months	A	46.27	13.10	<0.05
	B	40.53	12.53	

Table 4: Distribution of patients as per response of treatment.

Response	Group		Total
	A (n=22)	B (n=20)	
Responders	16	19	35
	72.72%	95%	79.54%
Non responders	6	1	7
	27.27%	5%	0.7%
Total	22	20	42

P value less than 0.05.

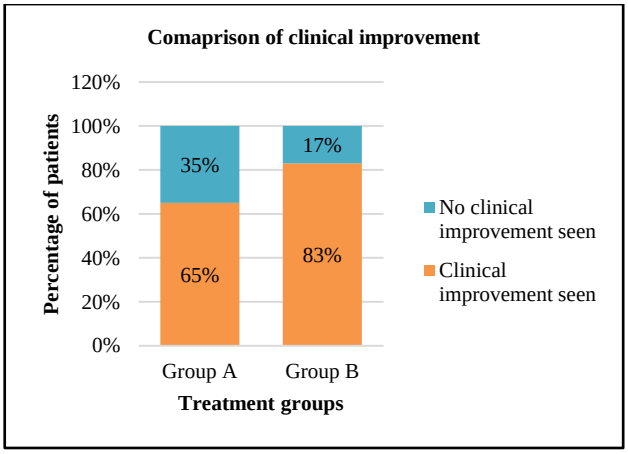

Figure 1: Bar graph comparing the treatment outcomes in the two groups.

Group A: Topical 5% minoxidil + Oral finasteride 1 mg; Group B: Topical 5% minoxidil + Topical finasteride 0.1%; P value using chi square less than 0.05.

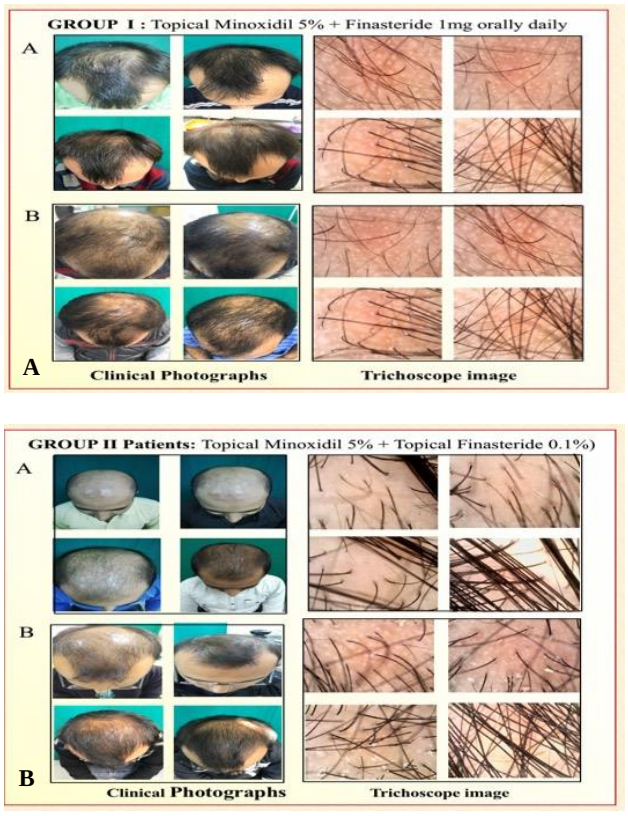

Figure 2: Digital photography and trichoscopy comparing the treatment outcomes in the two groups: (A) Group A patients, (B) Group B patients.

DISCUSSION

Oral 1 mg finasteride was FDA approved in year 1997 for androgenetic alopecia of males. Since then no new drug was introduced except dutasteride this drug has been approved for the treatment of scalp hair loss in South

Korea since 2009 and in Japan since 2015.[9,10] It has not been approved for this indication in the United States.

Androgenetic alopecia is more of cosmetic concern rather than a disease. It has tremendous psychological effect on young adult males. To maintain better density of hair over scalp almost lifelong treatment with oral finasteride is required, though side effects are thought to be very less with oral medication but still present. Till now various studies have been done on oral finsteride for its efficiency and side effects, but few on topical finasteride. Sintov et al studied the effects of the topical base formulation for finasteride and flutamide on the growth of human hair in a murine transplantation model.[11] According to them the effective topical delivery of flutamide and finasteride for alopecia is feasible, giving similar results to those obtained with oral finasteride that is with no systemic side effects as demonstrated by Testosterone/ Dihydrotestosterone monitoring.

Another double blind randomized study done by Hajheydari et al demonstrated similar effectiveness of 1% finasteride in increasing total hair content, after 6 months of treatment, topical finasteride response was better in 2nd, 3rd and 4th months of treatment, but equated that of oral formulation of finasteride in the 5th and 6th month of treatment, we have also demonstrated similar results in our study.[12]

Study done by Chandrashekar in cases previously treated with oral finasteride, followed by topical finasteride their study shows that topical medication alone is beneficial in maintaining hair growth density as well as improving hair growth.[13] There are two school of thought about sexual side effects of oral finasteride.

Some studies say that these are as minimal as with placebo, and according to FDA, there is no clear cause and effect relationship between finasteride and sexual adverse events that continued after stopping the drug. While other state that, for some patients the adverse effects were manifested in loss of libido, diminished libido, erectile dysfunction and in some cases contemplating suicide.[14-18]

In our study, patient with oral finasteride presented with erectile dysfunction (2 patients 8%), ejaculatory dysfunction (2 patients 8%) and loss of libido (3 patients 12%). These side-effects were not present in patients with topical drug and hair growth was comparable in both the groups at 6 months. Other interesting side effects observed in our study were facial edema (in 3 patients) and dryness of mouth (in 5 patients). Our study also show that sexual side effects do exist with oral finasteride.

For this IADVL therapeutic guidelines committee also recommend that in apprehensive patients, lower doses of finasteride 0.2 mg/day can be started as this dose gives adequate suppression of DHT in the scalp skin and serum.[19]

CONCLUSION

Among different studies there are controversies about sexual dysfunction associated with oral finasteride. Sexual side effects either significant or not, they do exist and vary with patient's psychological state because of easy availability of information about everything on internet and media, patients are more conscious about side effects of drugs. They should be properly counselled and informed about the drug, especially younger ones who are going to marry in near future. Higher therapeutic efficacy of topical minoxidil and finasteride was demonstrated as compared to topical monixidil and oral finasteride for androgenic alopecia.

The results of this study strongly support the use of topical finasteride in combination with topical minoxidil especially in younger ones and this may obviate the need of taking lifelong oral finasteride. Further long term studies on larger samples at multiple centers are required to support the results of this study.

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Ethical approval: The study was approved by the institutional ethics committee

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