ORIGINAL RESEARCH PAPER

Dermatology

COLLATING THE THERAPEUTIC EFFECTS OF TOPICAL FINASTERIDE VERSUS ORAL FINASTERIDE IN TREATMENT OF THE ANDROGENETIC ALOPECIA IN PATIENTS ATTENDING DERMATOLOGY OPD IN KARAIKAL.

KEY WORDS: Androgenetic alopecia, finasteride, topical gel

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ABSTRACT

Background: Finasteride is a competitive and specific inhibitor of Type II 5 -reductase, an intracellular enzyme that converts the androgen testosterone into DHT thereby decreasing the dihydroxy testosterone (DHT) level, is effective in the treatment of male androgenic alopecia. **Methods:** This is a double blind, randomized clinical trial study of 45 male patients, who were referred with alopecia to dermatology out patient department in Vinayaka missions medical college and Hospital, Karaikal , Puducherry. Patients with male androgenic alopecia were selected according to the history and physical examinations. The patients were randomly divided into two: topical finasteride (A) and oral finasteride (B) groups. Topical finasteride group (A) received a topical gel of 1% finasteride and placebo tablets, while the oral finasteride group (B) received finasteride tablets (1 mg) and gel base (without drug) as placebo for 6 months. The patients were followed by clinical observation and recording of side effects prior to the treatment and at the end of first week, and then by a monthly follow-up. The size of bald area, total hair count, and terminal hair were studied. Data were analyzed by descriptive and Chi-square statistical test. **Results:** The mean duration of hair loss was 18.8±23.10 months. Each month the terminal hair, size of bald area and hair count between the two groups were compared. There were no significant differences between the two groups as a viewpoint of hair thickness, hair counts and the size of bald area. Serial measurements indicated a significant increase in hair counts and terminal hair counts between the two groups. **Conclusions:** The results of this study showed that the therapeutic effects of both finasteride gel and finasteride tablet were relatively similar to each other.

Introduction

Androgenetic alopecia (AGA) is a common chronic, cutaneous condition encountered by dermatologists globally. AGA is androgen-dependent and characterized by an hereditary inheritance pattern, beginning with the advent of puberty; in predisposed males and females scalp hair progressively thins in a defined pattern, most often at the vertex, with non-scarring, progressive miniaturization of the hair follicle and shaft. Loss of hair and alopecia are the most common problems of modern societies, which create many economical and psychological effects. Recently, a great effort has been made to treat hair loss and alopecia, in which some of them were successful. One of the most common types of alopecia is baldness or androgenetic alopecia. This kind of alopecia is recognized by progressive narrowing of hair in the vertex and fronto- temporal area of scalp, in persons with genetic potency. The alopecia is hereditary in nature and is formed due to the high testosterone receptors in scalps of involved persons. Dihydroxy testosterone is an active form of testosterone that is produced by enzyme type II, 5-a reductase from testosterone[1]. Testosterone affects hair follicle, resulting in hair shaft thinning, shortening of anagen phase and prolongation of telogen phase[2]. The most recommended treatment for androgenic alopecia is composed of local minoxidil, hormonal therapy such as local and oral anti-androgen or local progesterone containing products[3,4,5,6,7,8].

Finasteride is an effective drug for treatment of male alopecia that can be used orally or locally. The drug decreases loss of hair by inhibiting 5- reductase enzyme activity, which converts testosterone to its active form, namely di-hydrotestosterone which is the main cause of male pattern hair loss[9,10,11,12]. Topical finasteride 0.005% is used to treat male alopecia[10]. Since, long-term drug therapy by finasteride is needed for treatment of male alopecia; its oral route is associated by complications such as decreased libido, erectile dysfunction, and decrease volume of ejaculation, depression and gynecomastia[8,13] . In this research, during a controlled study, we attempted to compare the effect of local finasteride gel on scalp, its target and to measure fewer complications with the oral type of finasteride, in treatment of androgenic alopecia in men. If topical form is effective, it will prevent the undesirable side effects of systemic form of drug. In addition, it will be a suitable treatment for this social problem, especially in adolescence and young age groups in which hair protection, as a cosmetic, is important for them.

MATERIALS AND METHODS

This is a double blind clinical trial study. The number of samples (according to previous studies) was 45 young adult men[3,9]. They were selected among patients referred to Dermatology department at Vinayaka missions medical college and hospital in the City of karaikal, during July 2019 to August of 2020. All of the subjects were having androgenetic alopecia, according to their history and clinical examination. They were placed in the study after they wrote the letter of agreement and satisfaction. Inclusion criteria were as follows: males under 30 years of age, hair loss duration less than 5 years; maximum hair density 20 hairs/cm^2; maximum diameter of the bald area less than 10 cm; and having complete physical and psychological health. Exclusion criteria were patients with male alopecia that were under treated, and patients with baseline disease that causes hair loss.

Method of finasteride gel preparation

Since the water solubility of Finesteride gel is very low, thus, at the beginning of work, solubility had to be increased. For this reason, solvent-aid was used. The solvents-aid is water mixable organic solvents, in which by decreasing solubility, and with surface tension of water, will cause increase water solubility of non-polar materials. An adequate amount of ethanol to increase solubility was determined by several examinations and by setting the drug solubility in different percentages of water-ethanol. After setting and preparing the suitable solvent to solve finasteride, several examinations to select the best polymer were done by different materials. For this reason, first the selected polymer was poured on a glass

surface, containing an adequate drug solving system, and was maintained in lab temperature for 24 hours. Then, the receiving system was mixed by an electric mixer by velocity of 600 cycles per minute, until it was completely pure. The results showed that 40% water and 60% ethanol are the best solvent system, and hydroxyl propyl methyl cellulose (HPMC) is the best polymer. Preparation of this drug did not need a preservative. Physical stability of the drug as a viewpoint of deposition or opacity in 4°C in refrigerator was evaluated. Since the time frame between drug production and consumption was about one week, there was no need for chemical assessment. In addition, the placebo gel without drug was prepared by the same system. Because, finasteride 1% has the most dermal absorption, therefore, in this study finasteride gel 1% was prepared and used.

Method

A two-part questionnaire was prepared. The first part was related to the demographic characteristics, and the second part was related to record the information about hair loss (size of bald area, number of terminal hair, and vellus hair).The patients entered the study based on inclusion criteria, and divided in two groups randomly; Group A (Finasteride gel and placebo tablet), and group B (Finasteride tablet and placebo gel). Finasteride tablet and gel, as well as placebo tablet and gel in the same size, shape and color were made by pharmaceutics faculty of Vinayka missions medical college and hospital , and were given to the researchers by a code, which was kept secretive until the end of this study.

Therapeutic method

Patients in two groups received one tablet daily (Finasteride or placebo), associated with local gel (placebo or finasteride). The patients were advised to use the gel twice daily by gently massaging their scalps. Duration of treatment was six months. To evaluate the drug effectiveness, prognosis and side effect, patients visited before the study and the end of first week of treatment, and then followed-up monthly. To assess therapeutic response, the shoblons already made by size of 10 cm^2 was used . Then the shoblons were placed on the defect and at least 3 squares, selected randomly, and the size of bald area, the number of total hair counts and the number of terminal hair were counted by naked eye. The mean was calculated, and finally, the result number was recorded in the form. Using variables for therapeutic response were categorized as size of bald area; the total hair count; and the terminal hair count. To evaluate the total response to treatment, the following descriptions was defined: the size of bald area per cm (8.1-9.5 cm : point 1, 6.6-8 cm : point 2, 5.1-6.5 cm : point 3, 3.5-5 cm : point 4); the total hair count(100-124 : point 1, 125-149: point 2, 150-174 : point 3, 175-200 : point 4), and the number of terminal hair (65-89 : point 1, 90-114 : point 2 , 115-139 : point 3, 140-165 : point 4). The resulting scores were summarized: the score 3-6 was considered as bad response, the score 7-9 moderate response, and the score 10-12 good response to the treatment[14]. Finally, the analysis was done by descriptive and Chi-square statistical approach.

RESULTS

Of the 45 androgenetic alopecia patients who were enrolled, 7 were excluded from the study due to incomplete or discontinuation of the entire study period. The patient's age range was 22.8±3.3 years. The average time of hair loss in patients, were 23.10 ±18.8 months. Seven (18.4%) were married and 31(81.6%) were single. Among referred patients, 31(81.6%) had a positive family history of male alopecia and in 7(18.4%), it was negative. Nineteen patients entered in group A, while 19 in group B randomly. The average total hair count, terminal hair count and the size of bald area in both groups in the beginning and end of treatment respectively are shown in (table 1) .There were no significant statistical differences in the terminal hairs, size of alopecia area and hair count between two groups. In A group (Finasteride gel and placebo tablet), increased terminal hair count were observed at the third month of treatment (P =0.001), but increased in terminal hair count was shown in the second months in the B group (Finasteride tablet and placebo gel) (P =0.015). During therapeutic period, the size of alopecia area was not significantly altered in group A, but in group B, the change in size of alopecia area was significant in the fourth month of treatment (P =0.027). Increased hair count in two groups were significant in 4 months of treatment (P =0.001, in group A and P =0.000 in group B). Therapeutic response during therapeutic period in both A and B groups was evaluated by scoring system which shown in (table 2) .Only one of the patients complained the erythema in affected site as a complication of using local finasteride gel that was subsided immediately after discontinuation of the gel. One of the finasteride tablet user described the decreasing libido.

Table 1 : mean of hair count , number of terminal hair and size of alopecia area before and after therapy in both A and B groups of patients by androgenic alopecia.

	Kind of treatment	Before therapy	After therapy	P-value in each group	P- value between 2 group
Hair counts	Gel	139.7 34.21	147.833.91	0.0000	0.642
	Tablet	137.8935.33	153.5636.28	0.0000	
Number of terminal hair	Gel	108.42 37.6	113.2739.74	0.001	0.661
	Tablet	105.5839.33	118.6137.49	0.0000	
Size of alopecia (cm)	Gel	7.21 2.08	6.722.41	0.08	0.453
	Tablet	7.552.28	7.182.17	0.07	

Table 2 : therapeutic response during therapeutic period in A and B groups, in patients with androgenic alopecia.

Response to treatment Time (month)		Mild		Moderate		P Value
		Count	%	Count	%	
1	Gel	12	34.2	6	17.1	1
	Tablet	11	31.4	6	17.1	
2	Gel	13	37.1	5	14.2	0.4
	Tablet	10	28.5	7	20	
3	Gel	12	34.2	6	17.1	0.7
	Tablet	10	28.5	7	20	
4	Gel	12	34.2	6	17.1	0.7
	Tablet	10	28.5	7	20	
5	Gel	12	36.3	6	18.1	1
	Tablet	10	30.3	5	15.1	
6	Gel	12	36.3	6	18.1	1
	Tablet	10	30.3	5	15.1	

DISCUSSION

The results of this study revealed the moderate therapeutic response, but not a good response, in both groups. Comparing finasteride gel 1%, with finasteride tablet (54.5% versus 56%) showed the relatively similar therapeutic response, that was not statistically significant (P =0.643). 5a-reductase enzyme causes testosterone conversion to di-hydrotestosterone. The therapeutic effect of the enzyme inhibitors on androgenetic alopecia such as finasteride by dose of 1mg orally, has been proven in different studies[1,2,15,16,17].

In addition, in this study, serial measurements of hair count and terminal hair increase showed that increasing in total hair count and terminal hair in both therapeutic groups between the beginning and end of study was significant. Like other studies, the total hair in both groups, finasteride gel and tablet, demonstrated significant differences between first referral and 6 months after therapy (P =0.000), this indicates the therapeutic efficacy of both drugs[1,10]. The

terminal hairs in finasteride gel group were always more than the finasteride tablet group, until third month of therapy. However, they were similar in both groups during the fourth month of treatment. At 5 th and 6 th months, the terminal hair counts were more in the group who were receiving tablets, thus explaining the efficacy of the tablet during therapeutic period[1]. The size of bald area in tablet and gel groups had significant decrease at fourth month, noting there was no change in gel group, which indicates the greater therapeutic effect of tablet than gel. Although, the total hair growth in both groups was significant during the fourth month, in the gel group, we did not find any decrease in the size of alopecia area and consequently the better appearance of person. Over all, in this recent study, by comparing finasteride tablet and gel groups with each other, it was found that in second, third and fourth months of patients being referred, the therapeutic response to the tablet group was better than gel group, but in fifth and sixth months of treatment, the therapeutic response in both groups was the same.

In previous studies, the finasteride tablet efficacy began after third to sixth months of therapy and if the patient had no response after 12 to 24 months, continuation of usage probably did not appear to be effective[2]. In our study, there was no significant positive therapeutic response in both groups; one reason could be the duration of treatment that was only for 6 months, thus, if the duration of treatment was longer, the results could have indicated a better therapeutic effect. Like other studies, these results show local finasteride gel[5,11,12], has a considerable efficacy and if used for male alopecia patients, who experienced hair loss in recent years, it will be a good replacement of oral therapy, especially in those who worry about oral drug complications. Finally, we suggest replication study of more samples, with longer period and assessment of patients' satisfaction after treatment.

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