

Original Article**Topical Finasteride in Hirsutism: A Double Blind Randomized Clinical Trial on Adult Women**F. Iraj^{*}, S. Karbasioun^{**}, A. Aminorroaya^{***}**ABSTRACT**

Background: Finasteride partially blocks the conversion of testosterone to dihydrotestosterone through inhibition of 5α -reductase in hair follicles. Finasteride cream can penetrate to dermis to arrive at hair follicle due to its solubility. Therefore, it is expected to be used in treatment of hirsutism with less systemic adverse effects. This study was designed to determine the efficacy of finasteride cream 0.5% in management of idiopathic hirsutism.

Methods: Finasteride (0.5%) and placebo creams were administered to 35 women with hirsutism on the face. Medication and placebo creams, each one was used on one side of the face in an area of excessive hair growth, which were not necessarily symmetrical. The side for the finasteride and placebo creams were chosen randomly and blindly in 1cm² areas on each side of the face. Hair numbers were counted and the thickness of all hairs was also measured by micrometer and their mean was calculated, at the start of therapy and after 6 months. Statistical analysis was done in SPSS software using Paired and Student t-tests. P-values less than 0.05 were considered significant.

Results: The mean of hair numbers decreased at placebo-applied side from 12.20 ± 6.15 to 10.50 ± 4.90 ($P < 0.0001$) and at finasteride-treated side from 11.37 ± 6.15 to 8.47 ± 4.62 ($p < 0.0001$). Mean of hair thickness at placebo side decreased from $2.92 \pm 0.84 \mu\text{m}$ to $2.72 \pm 0.79 \mu\text{m}$ ($p < 0.0001$) and at finasteride side from $3.17 \pm 0.90 \mu\text{m}$ to $2.37 \pm 0.79 \mu\text{m}$ ($p < 0.0001$). Comparison of hair number and thickness showed no statistically significant changes in finasteride versus placebo treated sides. But, according to patients' view points, hair growth rate was diminished and hair was looser on finasteride treated side.

Conclusion: Six months of topically applied finasteride (0.5%) does not affect on number and thickness of facial hirsutism significantly. Despite lack of objective changes, on questioning, most patients in finasteride group perceived a decrease in hair growth with time.

Keywords: finasteride, cream, hirsutism

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Finasteride, a 5α -reductase inhibitor, has been extensively studied and clinically used for treatment of prostatic hyperplasia^{1, 2, 3}. Because both the prostate and the hair follicle contain the same enzyme to convert testosterone to its more potent metabolite, DHT, oral form of finasteride has also been used to treat male pattern baldness^{4, 5, 6}. Stimulation of 5α -reductase in hair follicles causes male pattern hair growth in androgen sensitive areas on the face and body (hirsutism) and loss

of scalp hair because of different mechanism for hair growth on the scalp and face. In tissue culture, the hair follicle isoenzyme (type1) was less affected by finasteride than the prostatic tissue isoenzyme (type2)⁷.

The degree of 5α -reductase activity may account for the various severity of hirsutism found in women with the same levels of circulating androgens⁸. Even though the isoenzymes

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of 5- α reductase in the prostate and the hair follicle have different structures, some cross-reactivity of finasteride on the hair follicle isoenzyme may occur^{9, 10}. In women whose androgen levels are lower than men, one might expect finasteride to have much more effect on body areas containing 5 α - reductase¹¹. In men with inherited 5 α - reductase deficiency, facial hair is sparse, and baldness does not develop^{12, 13}. Women with idiopathic hirsutism may have an increased sensitivity to male hormones in the hair follicle.

These women have also increased 5 α - reductase activity in their genital skin¹⁴. Gonadotropins in women have been shown to be unaffected by finasteride¹⁵.

Recent studies have demonstrated the effectiveness of oral finasteride on idiopathic hirsutism^{16, 17, 18, 19, 20, 21}. Finasteride has also been compared with spironolactone to treat hirsutism and they had similar effect^{22, 23}. Because finasteride is readily soluble through the skin, a cream containing this medication might be a beneficial therapy for mild facial hirsutism²⁴. The potential percutaneous absorption of finasteride exists on the basis of its steroid structure, resulting in a Food and Drug Administration warning that pregnant women should not even handle broken tablets²⁵. There are limited studies about the effectiveness of finasteride cream on hirsutism with controversial outcomes in the USA^{24, 26}. We designed this study to investigate the efficacy of finasteride cream in Iranian women just to know if it has any effect on hirsutism treatment. Would it be a practical approach for mild to moderate hirsutism? Can it really reduce the number and thickness of hair in hirsute women?

Subjects and Methods

Study volunteers

Thirty-five adult women with idiopathic hirsutism were enrolled in the study by convenience method. Endocrinologists referred these patients and none of them had endocrinological problems. The patients were informed about the previous uses of finasteride in the treatment of male pattern baldness. All the

women were told that finasteride could affect a male fetus and that pregnancy was contraindicated during the use of this medication. This study was approved by Institutional Review Committee of the Isfahan University of Medical Sciences.

Protocol

For preparing finasteride cream 0.5%, 30 tablets of finasteride (5 mg each) were triturated (ground into a fine power) and then wetted with 2ml of propylene glycol. The mixture was incorporated into Dermabase by levigation (that is mixing evenly by high speed mixer and gradually incorporation). The final cream contained 0.5% finasteride. 30g of mixture was put into a tube. The placebo cream consisted of the Dermabase alone in the same size and type of tube. No difference in color or texture was evident between the placebo and medication containing creams.

The patient's hair density was determined by counting the terminal hairs in a 1cm² area on each side of the patient's chin or in another area of maximal hair growth on the face by a flexible scaled ruler that had a 1cm² square within. The distance between middle of inferior line of the chin and chosen 1cm² square of the face with regard to its angle with that line was recorded to know the exact location of area after 6 months. Four hairs from area inside the square were plucked and saved for later measurement of thickness. The thickness of the midshaft of the previously plucked hairs was blindly determined by the use of a direct measurement by ocular micrometer on the light microscope.

Patients applied a thin layer of cream to the areas of the excessive hair growth twice daily. The patients were instructed to use the cream labeled "Red" on the right side of their face and the cream labeled "Light blue" on the left side of the face. The women and the researcher were both blind to the identity of the cream in each of the tubes.

Each patient's hair growth had stabilized before the study. Stabilization was confirmed by the frequency of hair- removal techniques used by the study subjects. The study partici-

pants received no other medication for hirsutism during the study and for at least 2 months before the beginning of the study.

The finasteride cream and placebo cream were continued for the entire study. After the 6-monthes study period, the patients were given the option of continuing the finasteride treatment indefinitely or changing back to their previous medication. The patients were given consultations at 2-monthes intervals and questions were asked about mediations side effects, menstrual abnormalities, missed menstrual periods, and changes in libido.

The subjective view of the effect of the medication on the rate of hair growth was ascertained by questioning about the number of times the patient had shaved or clipped hairs per week. Patients' perceptions about changes of hair quality on both sides of the face were also asked at each visit. They were asked whether they noted any differences between the two sides.

The women had consented to just clip or shave their hairs and not to use electrolysis, waxing and plucking during the period of the study.

Statistical analysis

We enrolled 35 women in the study. Five of them did not continue the study, therefore we evaluated 30 women, aged 19-40 years old. Data are presented as mean \pm SD. Means of hair numbers and hair thickness for two groups were compared within groups with paired student's t-test and with t-student test between groups in SPSS software. A P-value less than 0.05 was considered statistically significant.

Results

Tolerability and safety

None of the women reported any problems with irregularity of menstrual periods, changes in libido, and changes in energy level, nausea, vomiting, diarrhea, abdominal pain, or headache. Allergic reaction to the medication or skin eruption in the areas in which the creams were applied was not observed.

Clinical effects

From 35 patients by subjective evaluation, 25 patients noted a considerable diminished rate of hair growth on both sides of the face, especially on the one side that they had guessed that side is medication. Five patients noted mild diminished rate of hair growth and the other five patients didn't note any difference and discontinued the usage of creams after 2 months. They were excluded from the study.

In comparison with baseline, hair counts in both finasteride- applied and placebo-treated areas decreased significantly ($P < 0.0001$) from 11.37 ± 6.15 to 8.47 ± 4.62 and from 12.20 ± 6.15 to 10.50 ± 4.90 , respectively.

The hair thickness decreased significantly at both sides, in finasteride treated side from $3.17 \pm 0.90 \mu\text{m}$ to $2.37 \pm 0.79 \mu\text{m}$ and in placebo side from $2.92 \pm 0.84 \mu\text{m}$ to $2.72 \pm 0.79 \mu\text{m}$ ($P < 0.0001$).

We compared finastride and placebo treated groups with together. There was no significant difference in thickness ($P = 0.09$) and number of hairs ($P = 0.104$) between finastride and placebo-treated subjects.

Discussion

Hirsutism, a devastating problem for many women, may lead to psychological abnormalities, including low self-esteem, withdrawal from social interaction, isolation, and depression^{9, 27}. Affected women may be ridiculed or pitied by others throughout their lives. They become extremely self-conscious about their appearance. Because the most conspicuous unwanted hairs are that grow on the face, women may resort to plucking, waxing, bleaching, or shaving in attempts to eliminate this embarrassing trait. With the rapidity of hair growth seen in some women, these hair-removing procedures achieved the desired result for only a brief period of time and this methods can produce roughness of area, and post inflammatory hyper pigmentation (PIP) at the site of hairs because androgenic hairs are very thick and hard to plucking. No topical drug had been approved by the Food and Drug Administration (FDA) for this condition

until recently, when eflornithine hydrochloride cream was approved for inhibiting the growth of unwanted facial hair ¹¹. Systemic drugs that use for treatment of hirsutism have major side effects ^{9, 22, 27, 28, 29, 30, 31}.

The use of finasteride for treatment of hirsutism is logical because of its specific effect on 5α -reductase, the enzyme responsible for sensitizing the hair to testosterone. In previous studies, orally administered finasteride has been successfully used in the treatment of hirsutism ^{11, 21, 32, 33}. Its contraindications in women include the effect on the developing male fetus. It inhibits development of normal male genitalia ¹¹.

The current investigation was a study designed to observe the clinical effects of topically applied finasteride cream on facial hirsutism.

Although the effect of finasteride and placebo was equal in our study, part of the response to the placebo cream may be attributable to a crossover effect of the finasteride cream used on a small area of the chin onto the other side of the chin or because of its systemic absorption ²⁵. The other reason of placebo effect may be the role of psychological factors on the hirsutism. At least some reasons such as complicated mechanisms or genetic difference and testosterone effect cause lack of objective changes. In a study done by Price et al in the USA, blinded application of topical 0.25% finasteride solution (n=2), 0.5% finasteride solution (n=3), or placebo solution (n=4) for 6 months to treat hirsutism showed no difference on hair count and thickness ²⁶. Despite lack of objective changes, on questioning, all patients in the finasteride group perceived a decrease with time in hair growth, whereas in the placebo group 50% perceived a decrease, 25% an increase, and 25% no change. All subjects

reported that they would use a product like this if available. The outcome of this study is similar to ours, especially in objective and subjective findings. In another study, which has been done by Lucas KJ in 2001, in America, on eight women treated with finasteride cream (0.25%) and placebo cream for 6 months, both hair count and thickness decreased significantly ²⁴. It had totally different findings, although the preparation was cream (similar to present study), not a solution, and the concentration of the cream was half of ours (0.25%). Maybe genetic differences or other mechanisms caused that we had less effectiveness than Lucas study. It seems that sort of preparation (cream or solution) does not have any impact on the efficacy of the medication.

In all three studies, hair follicles became looser and easier to pluck^{24, 26}. These effects helped the patients to have fewer problems with their hirsutism, as they managed to pluck hairs in longer intervals.

We concluded that six months of topically applied finasteride (0.5%) does not affect on number and thickness of facial hirsutism significantly in Iranian women. Despite lack of objective changes, on questioning, most patients in finasteride group perceived a decrease with time in hair growth. We did not measure the bioavailability of finasteride in the tubes after two months and it can be a problem in our study.

It seems that topical finasteride would not have a major role in management of patients with hirsutism.

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