A systematic review of clinical trials using single or combination therapy of oral or topical finasteride for women in reproductive age and postmenopausal women with hormonal and nonhormonal androgenetic alopecia

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Abstract

Female pattern hair loss (FPHL) is a hereditary form of hair loss in women and the most common patterned progressive hair loss in female patients with androgenetic alopecia (AGA). One of the best methods for treating hair loss in women is the finasteride treatment. This systematic review includes a summary of the pharmacology of finasteride and the effect of the drug on women, especially those in the menopausal age group, and is aimed at elucidating methods of preventing systematic side effects. A search of all published literature from 1999 to 2020 has been conducted with the use of PubMed/MEDLINE, Embase, PsycINFO, TRIP Cochrane, as well as Cochrane Skin databases. A total of 380 articles were found, of which 260 articles were removed and 87 review studies were excluded. Lastly, full texts of 33 original articles were reviewed and 14 articles that met the inclusion criteria were selected. Ten out of the 14 articles reported a high rate of alopecia recovery in women taking finasteride. Based on the results, it can be stated that 5 mg of oral finasteride per day could be an effective and safe treatment in normoandrogenic women with FPHL, especially when used in combination with other drugs, such as topical estradiol and minoxidil. We also found that topical finasteride is more effective than other topical formulas for treating hair loss.

Key words: oral, FPHL, finasteride, topical, female pattern hair loss

Introduction

Hair loss is a part of the natural hair growth cycle. When the balance between new hair growth and old hair loss is disturbed, excessive hair loss occurs. A medical term for excessive hair loss is alopecia.[1] Female pattern hair loss (FPHL) or androgenetic alopecia (AGA). is the most common cause of hair loss in women, which could be genetic or inherited.[2–6] Androgenetic alopecia becomes more severe during menopause due to decreased estrogen levels. In less than 50% of women who reach the age of 65, their normal volume of hair remains unchanged, and the rest of women experience this form of hair loss.[7,8] Androgenetic alopecia causes regional baldness in men and a decrease in the overall density and thickness of the hair in women.

In women, AGA usually has 3 stages: 1) reduction of hair density on both sides of the vertex; 2) expansion of low-density areas; 3) specific baldness in the vertex and a decrease in hair density in lateral parts. At different stages, pattern hair loss could be graded using the Savin scale.[9,10] Pattern hair loss begins with widening of the central part of the hair and thinning of the hairs at the top and crown of the head.[11] Female pattern hair loss is characterized by the miniaturization of hair follicles, resulting in shorter, thinner and more brittle hairs, and eventually in halted hair production, reducing the total number of hair follicles on the head. In female, unlike male pattern baldness, the hairline is preserved and does not regress, and hair loss rarely leads to complete baldness.[12] Underlying diseases and tumors could cause female pattern baldness. Moreover, smoking can increase incidence or severity of the disease. Most people with AGA experience significant hair loss between the ages of 40 and 50.[13]

Regarding the mechanism of hair loss in women, molecular changes cause follicular damage, in which the role of androgen hormones is very prominent.[14] The role of genetic and other influencing factors (described below) has not yet been fully elucidated; however, they play an important role in the pathogenesis of FPHL.[15] In women who do not have high androgen levels, genetic predisposition is more likely to cause hair loss. Genetic susceptibility affects the increase in circulating androgen levels and hormones involved in developing FPHL through binding to follicular target cells, particularly intracellular androgen receptors.[16] Studies on genome have shown that genetic defects play a role in the severity of hair loss.[17–20]

One of the most important medicines used in the treatment of hair loss is finasteride. The drug was approved by the Food and Drug Administration (FDA) in 1997.[21] Finasteride with the chemical formula of $C_{23}H_{36}N_2O_2$ is insoluble in water but soluble in dilute solutions.[22,23] It is well absorbed in the gastrointestinal tract and food does not affect its absorption. The drug is metabolized in the liver and converted to inactive compounds that are excreted in the bile.[24]

Finasteride prevents the body from converting testosterone to dihydrotestosterone (DHT); moreover, it crosses the blood–brain barrier, albeit in small amounts.[25] Finasteride is used to treat male and female PHL as well as the symptoms of benign prostatic hyperplasia in male patients with an enlarged prostate. However, later studies showed that finasteride could be used to treat hair loss.[26] The drug suppresses scalp DHT levels by up to 43% in 28 days and up to 65% in 42 days,[27] and selectively inhibits the activity of 5α-reductase type II. This enzyme is required for the activity of some androgen hormones, hair follicles and sebaceous glands in the skin; also, it is sensitive to androgen hormones.[28] Along with finasteride, minoxidil is the mainstay of treatment for FPHL, which is often used as a treatment for different types of hair loss.[26–28]

Objectives

Regarding its effective form and efficacy on different age groups of women, as well as considering its effect on hereditary hormonal diseases, finasteride has its supporters and opponents. To the best of our knowledge, no complete summary about finasteride treatment in postmenopausal women and the optimal conditions for greater effectiveness of the drug has yet been presented. Therefore, in this systematic review, we tried to evaluate the effect of finasteride treatment, administered orally or topically, in women with FPHL in different age groups and with different underlying conditions (hormonal or nonhormonal). For this purpose, we reviewed relevant clinical trials available in the scientific databases.

Materials and methods

The present systematic review is comprehensively evaluates single or combination therapy involving oral or topical treatment with finasteride for hormonal and nonhormonal hair loss in women from 1999 to 2020. The finasteride therapy was studied by examining the dosage used and the side effects. A comprehensive search of the PubMed/MEDLINE, Embase, PsycINFO, TRIP Cochrane, and Cochrane Skin databases was performed, according to predetermined clinical endpoints.

The clinical examination of the topical and oral use of finasteride in women with alopecia and hair loss constituted the main body of the selected articles. The articles that were used for this systematic review included clinical trials, retrospective, prospective, double-blind, and randomized studies.

Inclusion criteria were at least 1 group treated with finasteride, the coverage of results related to the effectiveness of finasteride, and the use of in vivo therapy only. Exclusion criteria were articles written in the language other than

English, articles that were designed as nonoriginal or that were not trials, or studies on finasteride that did not concern the treatment of alopecia in women.

To collect information regarding finasteride treatment, the following key words were searched in the desired databases: "hormonal and nonhormonal hair loss", "single therapy", "combination", "oral finasteride treatment", "topical hair loss", etc. Electronic search was conducted on 380 articles. Of these, 260 articles were removed after reviewing the title or abstract, since they were unrelated to the topic of the research, and 87 review studies were excluded. Finally, the full texts of 33 original articles were reviewed and 14 clinical trials that met the inclusion criteria were selected. Figure 1 depicts the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) chart of evaluated studies.

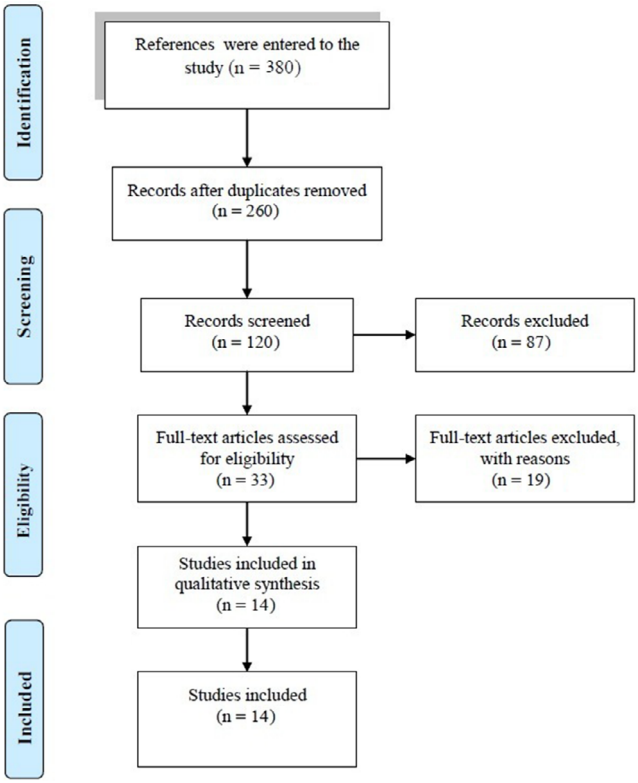

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart of studies evaluated for this systematic review

Screening and data extraction

Two authors trained in performing systematic reviews and database searching conducted the search strategy. In the first stage, the titles and abstracts of the articles were reviewed; in the next stage, two authors independently reviewed the full text of the articles. After preparing a list of titles and summaries of studies, articles were evaluated in terms of various methodological aspects, including sampling methods, reliability of the tools used and the objectives of the study. Finally, a set of articles appropriate in terms of topic coverage and content structure was included in the article.

Results and discussion

Out of 33 reviewed articles, 14 articles were included in the study based on the inclusion/exclusion criteria. A summary of the results of the 14 original trials that were reviewed is given in Table 1.

Among the selected articles, 4 were randomized control, 5 were uncontrolled prospective, 4 were retrospective studies, and 1 was a case report.

The quality of the articles was assessed using the Cochrane Risk of Bias 2 tool (https://methods.cochrane.org/risk-bias-2). According to this tool, only 1 study had a risk of bias in 5 areas, 2 studies had a risk of bias in 3 areas, and 1 had a risk of bias in 2 areas. Other studies had unclear risk of bias in 4 areas, namely selection bias, performance, reporting, and types of bias.

Out of the 14 chosen articles, 10 (3 randomized control, 3 uncontrolled prospective and 4 retrospective studies) reported a high rate of alopecia recovery in women taking finasteride. In 2 prospective articles and 1 retrospective article included, the rate of improvement after the treatment period was high. Two articles reported a reduced rate of recovery after the treatment.

The criteria for reviewing the results of articles were as follows: articles in which the improvement rate or the percentage of patients reporting improvement was more than 50% were considered articles with high recovery, articles with an improvement rate of less than 50% were considered articles with great improvement, and articles in which there was no significant difference between the treated group and the control group were considered articles with a decrease in recovery.

In this study, data on 735 postmenopausal patients with FPHL aged 21–65 years and treated with finasteride were analyzed. After reviewing the articles, it was concluded that in 50% of cases treated with finasteride, significant and high efficacy were observed, in 25% of them partial to moderate efficacy was seen, and in 25% no efficacy was observed; also, only in one of the 14 articles, no improvement in hair thickness and growth was observed. In 25% of the articles, in addition to finasteride, other medications such as estradiol and minoxidil were used to enhance the efficacy of the treatment. The lowest dose of finasteride was 1 mg/day and the maximum dose was 5 mg/day. The minimum duration of treatment was 3.5 months and the maximum duration was 12 months.

Based on the results of 4 clinical trials included in Table 1, the treatment with 5 mg oral finasteride per day can be considered an effective and safe therapy for normoandrogenic women with FPHL.[29–31]

Overall, the reviewed articles showed that hair loss and hair growth problems were reduced after the topical administration of finasteride. The use of topical finasteride gives promising results.

Other studies provide similar data. In a systematic study, Lee et al. showed that topical finasteride treatment

Table 1. Findings of studies related to single or combination therapy with oral or topical finasteride

Author, year and study type	Title	Population/age	Dosage/method/duration of use	Results
Price et al.[2] 2000 RCT	Lack of efficacy of finasteride in postmenopausal women with AGA	137 postmenopausal women with AGA 41–60 years	1 mg of finasteride or placebo daily; the effectiveness was evaluated by counting the scalp hairs, evaluating the photos taken by an expert panel and by histological analysis of the scalp biopsy specimens	after 1 year of treatment, there was no significant difference in hair number change between finasteride and placebo groups; both treatment groups had a significant reduction in the number of hairs in the anterior/anterior (anterior/middle) area of the scalp during the 1-year study period; the evaluations showed no improvement in the process of hair thinning, increased hair growth, or improved hair appearance in people treated with finasteride compared to the placebo group; in postmenopausal women with AGA, taking 1 mg of finasteride per day for 12 months does not increase hair growth and does not slow the progression of hair thinning
Carmina and Lobo[13] 2003 RCT	Treatment of hyperandrogenic alopecia in women: Fertility and sterility	48 hyperandrogenic premenopausal women with FPHL 25 ±2 years Ludwig scores I–III	finasteride 5 mg/day vs CPA with EE vs flutamide 250 mg/day vs none; the experiment period was 12 months	flutamide significantly decreased Ludwig scores; no significant changes in Ludwig scores and clinical evaluation in finasteride group
Oliveira-Soares et al.[29] 2013 uncontrolled prospective	Finasteride 5 mg/day treatment of patterned hair loss in normo-androgenetic postmenopausal women	40 postmenopausal women with normal menopause and AGA	5 mg of oral finasteride faily for 18 months; the effectiveness was assessed by patient satisfaction and global photo evaluation	after 6 months, 22 patients showed significant improvement, 12 showed moderate improvement and 6 did not show any improvement; according to the evaluation of the photos, 8 patients did not show improvement, 16 cases showed moderate improvement and 16 cases showed significant improvement in the 6th month; slight improvements were observed over time from 6 to 12–18 months; decreased libido was observed in 4 patients and an increase in liver enzymes was observed in 1 patient; older patients showed less positive response
Yeon et al.[31] 2011 uncontrolled prospective	5 mg/day finasteride treatment for normoandrogenic Asian women with FPHL	87 women with FPHL during pre- and postmenopause	5 mg of oral finasteride daily for 12 months	after 12 months, 70 patients (81.4%) had recovered, 10 patients showed moderate and 4 patients showed significant improvement; 13 patients (15.1%) stayed unchanged and 3 patients (3.3%) had a low exacerbation; 4 patients (4.6%) had mild side effects that disappeared quickly
Suchonwanit et al.[33] 2019 RCT	Efficacy of topical combination of 0.25% finasteride and 3% minoxidil versus 3% minoxidil solution in FPHL	30 postmenopausal women with FPHL	each participant was randomly administered 0.25% topical finasteride with 3% topical minoxidil or 3% topical minoxidil solution for 24 weeks	after 24 weeks, hair density and diameter had increased in both groups, and finasteride/minoxidil was significantly superior to minoxidil solution in terms of hair diameter; no systemic side effects have been reported; serum dihydrotestosterone levels in the finasteride/minoxidil group decreased significantly from the beginning; topical combination of 0.25% finasteride and 3% minoxidil may be a promising option in the treatment of FPHL with an additional benefit in increasing hair diameter; it may be absorbed through the skin, thus it should be used only in postmenopausal women
Iorizzo et al.[35] 2006 uncontrolled prospective	Finasteride treatment of FPHL	38 women with FPHL 21–48 years	2.5 mg of finasteride daily and 3 mg of oral contraceptive drug, containing drospirenone and 30 µg of ethinylestradiol; the experiment period was 12 months	62% of patients showed improvement after taking 2.5 mg of finasteride daily while taking contraceptives; further studies are needed to understand which hair loss pattern responds best to this treatment

Table 1. Findings of studies related to single or combination therapy with oral or topical finasteride – cont.

Author, year and study type	Title	Population/age	Dosage/method/duration of use	Results
Kohler et al.[39] 2007 retrospective	Effect of finasteride 5 mg (Proscar) on acne and alopecia in female patients with normal serum levels of free testosterone	12 women (6 with acne and 6 with alopecia)	5 mg of oral finasteride daily for 12 months	9 out of 12 patients who received treatment had significantly reduced symptoms and an improved mental state than before receiving finasteride; the other 3 patients did not receive finasteride at all and did not report any change in acne/alopecia; further evaluation is needed to clarify more accurate indications for prescribing finasteride in women with acne and alopecia
Verdonschot et al.[40] 2014 retrospective	The effectiveness of finasteride and dutasteride used for 3 years in women with AGA	120 women with FPHL 16–84 years	finasteride 1.25 mg/day or dutasteride 0.15 mg/day; the experiment period was 3 years	improved hair thickness in 81.7% of patients in finasteride group and in 83.3% of patients in dutasteride group; improved hair density from GPA in 68.9% of patients in finasteride group compared to 65.6% of patients in dutasteride group
Won et al.[41] 2018 retrospective	Clinical efficacy of oral administration of finasteride at a dose of 2.5 mg/day in women with FPHL	112 women in the pre- and postmenopausal period with FPHL 25–65 years	finasteride 2.5 mg/day; the duration of the review period was 12 months	using global photographs, it was found that 33 cases (29.5%) of the 112 studied patients showed a slight improvement, 73 cases (65.2%) showed a significant improvement, while in 6 cases (5.4%) no changes were recorded; finasteride has a better effect on hair growth when patients have lower Ludwig scores and are of older age
Rossi et al.[44] 2020 retrospective and single-blind	Efficacy of topical finasteride 0.5% vs 17α-estradiol 0.05% in the treatment of postmenopausal FPHL	119 women	subjects were divided into 2 groups: the 1st group consisted of 69 women treated with 0.5% finasteride and 2% minoxidil; in the 2nd group, 50 women were treated with 0.17% estradiol and 2% minoxidil	the efficacy of finasteride and 17α-estradiol was statistically significant at the 6, 12 and 18 months; the effect of topical finasteride was significantly greater than the 17α-estradiol solution in the 6-, 12- and 18-month studies; the highest improvement after 12–18 months was observed with the topical application of finasteride; topical 0.5% finasteride in combination with 2% minoxidil could be a valid treatment option for menopausal FPHL, which shows higher efficacy than topical 17α-estradiol with 2% minoxidil at 6, 12 and 18 months of follow-up
Camacho-Martinez[58] 2009 RCT	Finasteride for hair loss in women	137 postmenopausal women with normal serum testosterone 41–60 years	patients were divided into 2 groups and received 5 mg of finasteride (67 people) or placebo (70 people) for 12 months	doses used are 5 mg/week to 5 mg/day, for periods of 6 months to more than 2 years; finasteride at different doses was well tolerated with the side effects of the treatment; finasteride could cause changes in male fetuses and it is important to control consumption in pregnant women
Boychenko et al.[59] 2012 case report	Finasteride in the treatment of female pattern (androgenic) alopecia	one 44-year-old woman with androgenic alopecia	1.25 mg of oral finasteride daily for 3.5 months	hair loss has been significantly reduced and excess hair growth has been reported without side effects
Trüeb[60] 2004 uncontrolled prospective	Finasteride treatment of patterned hair loss in normoandrogenic postmenopausal women	5 postmenopausal women without clinical symptoms or high blood pressure	2.5 or 5.5 mg of oral finasteride daily; the effectiveness was evaluated at 6, 12 and 18 months	oral finasteride at a dose of 2.5 mg/day or more may be effective in treating hair loss in postmenopausal women in the absence of clinical or laboratory symptoms; finasteride treatment with all evaluation methods, improved scalp hair
Kim et al.[62] 2012 uncontrolled prospective	Efficacy of finasteride 1.25 mg on FPHL	18 postmenopausal women with normal androgen, iron, ferritin levels, and thyroid function tests at baseline	the study was performed for 28 weeks with a minimum dose of 1.25 mg of finasteride daily	after 28 weeks of treatment, phototrichogram evaluation showed a 5.87% increase in hair density and an 11.8% mean increase in hair thickness that was not statistically significant; 1.25 mg daily dose of finasteride administered for 28 weeks showed measurable efficacy in FPHL patients but did not show objective clinical efficacy; a dose higher than 1.25 mg/day, more patients and longer duration of treatment are required to confirm the effect of this clinical trial on normoandrogenic FPHL

RCT – randomized controlled trial; FPHL – female pattern hair loss; AGA – androgenetic alopecia; CPA – cyproterone acetate; EE – ethinyl estradiol; GPA – global photographic assessment.

significantly reduced hair loss and hair growth problems. The authors stated that the initial results regarding the use of topical finasteride are limited but safe and promising. However, continued research on drug delivery, ideal topical concentrations and frequency of use, side effects, and use for other alopecia helps to elucidate the full extent of the topical use of finasteride.[32]

Systemic pharmacodynamic evaluation of oral finasteride

Experts have been studying the effects of finasteride on FPHL for many years. In 2000, Price et al. in a 1-year study on the effectiveness of finasteride (1 mg/day) in 137 postmenopausal female patients with AGA concluded that taking 1 mg of finasteride per day had low efficacy and did not increase hair growth and diameter. Further research should be performed in this regard.[2]

There is a lot of clinical evidence regarding the therapeutic effects of finasteride and its important and effective role in the treatment of female pattern baldness.[2,33,34] However, a small percentage of studies have reported lack of efficacy of finasteride treatment; for instance, a 1-year study showed that finasteride had no significant effect on the treatment of postmenopausal women with alopecia.[13]

In a 2006 study of finasteride doses, Iorizzo et al. stated that it was unclear whether the achieved success was due to higher doses of finasteride (2.5 mg instead of 1 mg) or its association with oral contraceptives containing drospirenone (with antiandrogenic properties). Further studies are necessary to understand which hair loss pattern responds best to this treatment.[35] Two-thirds of women treated with finasteride experience hair regrowth. Finasteride is aimed at controlling hair loss, not at its definitive treatment, thus a continuous administration of the drug is indicated for better results.[34] In men, however, better therapeutic responses have been seen.[36,37] One study has shown that finasteride has a positive effect in 90% of men with male pattern baldness. After 5 years of treatment, 48% of men showed increased hair growth, 42% did not show any hair loss, and the remaining 10% experienced hair loss. In contrast, 6% of men treated with placebo reported increased hair growth and 19% did not report any new hair loss, while the remaining 75% continued to lose hair.[38]

In parallel with the Iorizzo study, Kohler et al. conducted a retrospective study with the use of questionnaire on 12 female patients in 2007.[39] In patients who received the treatment, the symptoms significantly decreased and they reported an improved mental state. However, further evaluation is needed to elucidate more accurate indications for the administration of finasteride in women with acne and alopecia.[39]

Another study on oral finasteride in 87 normoandrogenic women with FPHL was conducted in 2011 by Yeon et al. In this study, in order to evaluate the clinical effect of 5 mg of oral finasteride in normoandrogenic Asian women with FPHL, 87 women were enrolled and followed up for 12 months. On initial visits, the average hair density was 90 ±22 cm^2 and the average hair thickness was 64 ±11 μm. After 12 months of treatment with finasteride, hair density increased significantly to 107 ±23 cm^2 and hair thickness increased significantly to 70 ±9 μm. In 70 cases (80.4%), an improvement was noticed. Thirteen (15.1%) patients did not notice any changes and 3 patients (3.3%) had a slight exacerbation. Four patients (4.6%) reported side effects, such as headache, menstrual irregularities, dizziness, and increased body hair growth. However, these side effects were mild and quickly disappeared. The results of the study indicated that the treatment with 5 mg of oral finasteride per day could be effective and safe for normoandrogenic women with FPHL.[31]

Two years later, Oliveira-Soares et al. conducted a study in 40 normoandrogenic postmenopausal women with AGA. The study was performed for 18 months, and patients were given 5 mg of oral finasteride daily. After 6 months, 22 patients noticed a significant improvement, 12 showed a moderate improvement and 6 did not show any improvement. According to the evaluation of the photos, 8 patients did not show any improvement, 16 patients showed a moderate improvement and 16 cases showed a significant improvement after 6 months. A decrease in libido was reported by 4 female patients and an increase in liver enzymes was observed in 1 patient. Finally, it was shown that taking 5 mg of oral finasteride per day is very effective and can improve hair loss pattern in postmenopausal women.[29,40]

Five years later, a study was conducted by Won et al. in 112 pre- and postmenopausal women. A dose of 2.5 mg of oral finasteride per day was prescribed. The follow-up period of this study was 3 months and the patients who received other FPHL treatments, including topical minoxidil, were excluded from the study. Using photos taken at the end of the finasteride course, 33 cases (29.5%) showed a slight improvement, 73 cases (65.2%) showed a significant improvement, while in 6 cases (5.4%) no change was recorded. From these data, it was concluded that finasteride at a dose of 2.5 mg/day could be effective for the treatment of patients with FPHL and it is more effective for patients with lower Ludwig scores and older age.[41] Knowing more about promising treatments of AGA and its probable associations with metabolic syndrome and other dermatologic disorders[42,43] helps manage the disorder better, especially in challenging cases.

Present studies on the topical administration of finasteride in the treatment of AGA are limited to a small number of randomized controlled trials, prospective studies and retrospective medical records; thus, more extensive research is needed in this regard. General data from the studies evaluating the efficacy and safety of topical finasteride treatment in AGA show promising results compared to systemic subjects.

Comparative evaluation of systemic pharmacodynamics of finasteride with other substances

Numerous studies have been performed to compare the performance of finasteride with other substances in improving hair loss pattern in women. For instance, in a double-blind randomized controlled trial by Suchonwanit et al. in 2019, the efficacy of a topical combination of 0.25% finasteride and 3% minoxidil compared to 3% minoxidil solution in hair loss in 30 postmenopausal women was examined. To determine the efficacy of the treatment, hair density and diameter were measured, and evaluations were performed at 1, 8, 16, and 24 weeks; side effects and serum DHT levels were also assessed. Finally, it was concluded that hair density and diameter increased in both groups, and finasteride/minoxidil was significantly superior to minoxidil solution in terms of improving hair diameter. No systemic side effects were reported. However, serum DHT levels in the finasteride/minoxidil group decreased significantly from those reported at baseline.[33]

Additionally, in a study by Rossi et al., 0.5% topical finasteride showed a significantly higher efficacy in the treatment of FPHL in postmenopausal women compared to 17α-estradiol 0.05%.[44] In that study, 119 postmenopausal female patients were examined. The patients were divided into 2 groups; the 1st group consisted of 69 women treated with 0.5% finasteride and 2% minoxidil, and the 2nd group of 50 women were treated with 17α-estradiol 0.17% and 2% minoxidil. Photographs were taken at the beginning and at 6-, 12- and 18-month follow-ups. Improvement was statistically significant at 6 and 12–18 months for both finasteride and 17α-estradiol groups. The efficacy of topical finasteride was significantly higher than that of the 17α-estradiol solution in the first 6 months and at 12–18 months of follow-up. In general, the highest improvement rate was observed after 12–18 months of topical finasteride treatment.[40]

Mechanism of action of finasteride

Finasteride stimulates the growth of fresh hair at the molecular level. It is a synthetic azasteroid with high potency as a noncompetitive and selective inhibitor that irreversibly inhibits the activity of an enzyme that converts the male sex hormone (testosterone) to its active form in the hair follicle.[44] Testosterone affects the skin, hair follicles, prostate gland, and skin sebaceous glands.[39] Hair follicle tissues are sensitive to a special form of testosterone called DHT. Testosterone is converted to DHT by an enzyme called 5α-reductase. Finasteride inhibits the action of this enzyme and prevents the conversion of testosterone to DHT. The α-reductase includes 2 types, namely type 1 and type 2. Type 1 is more common in adipose tissue, and type 2 is more common in hair follicles and prostate tissue.[45] People with normal or high levels of type 2 enzyme have high levels of normal DHT and are more likely to loose hair. Finasteride inhibits type 2 of this enzyme, lowers DHT levels and reduces the risk of male PHL.[46] The plasma half-life of this drug is 8 h and its biological effects last longer.[21]

Although preliminary results regarding the use of topical finasteride are limited, studies have shown that it may be safe for use in patients wishing to prevent systemic side effects.[39]

Finasteride significantly reduces the DHT levels in the blood and scalp, which is thought to be the effect of the drug. Taking 1 mg of finasteride per day reduces blood DHT levels by up to 70% and increases blood testosterone levels by about 10%, which is within the normal range. Patients who used this drug regularly experienced hair growth and thickening of their hair strands, resulting in a high hair density.[39] In various studies, doses of 2–5 mg finasteride demonstrated a positive effect on the treatment process.[29,30,35,41] The results showed that taking finasteride in the form of a 5-milligram tablet per day, with food or alone, had good efficacy.[31] Finasteride should be taken regularly to achieve the desired result, and taking more than the desired dose does not increase the effect of the drug and could cause side effects.[29]

It is important to note that finasteride only controls the complication and could not be used as a short-term treatment. If finasteride administration is stopped, the DHT hormone, which causes hair loss, returns to a high level after a while. Therefore, to maintain low DHT levels, daily administration of finasteride should be continued.[40]

Finasteride and 5α-reductase

In various studies, the α-reductase has been mentioned as an effective enzyme in the process of hair loss. The 5α-reductase is an enzyme that converts testosterone into a more active form, DHT. If the level of this enzyme increases, more testosterone is converted to DHT and as a result, more hair loss occurs. The 5α-reductase enzyme has 2 types; type 1 is found mostly in the sebaceous glands, which naturally make the skin slippery and sticky, and type 2 is more common in the genitourinary tract and hair follicles. Type 2 of enzyme is more important in hair loss.[45] Finasteride is a selective inhibitor of the 2nd type of 5α-reductase. It appears to act on the 5α-reductase enzyme in hair follicles and inhibit the production of DHT.[37]

Testosterone is also involved in reducing adipose tissue. High levels of testosterone may reduce the scalp's ability to regulate follicular acidity. It has been shown that older women respond less positively to finasteride treatment.[33] This is because, in young people, the follicles inside the scalp are covered with a layer of fat. Young skin can also retain water better. When this water is lost, the scalp compresses the follicles, causing them to shrink. As the follicles try to maintain their state, excess enzyme activity

occurs in that area. Converting more testosterone to DHT increases erosion and causes hair loss. More DHT production and male pattern hair loss may one day lead scientists to finally succeed in discovering male pattern baldness treatment.[46]

New generation of 5α-reductase inhibitors

In addition to finasteride, another new drug called dutasteride has been discussed in several studies. It is a new generation of 5α-reductase inhibitors (5-ARIs). It inhibits both types I- and II-α-reductase isoenzymes, and is 3 times more potent than finasteride in inhibiting type I enzymes and 100 times more potent in inhibiting type II enzymes.[47] Dutasteride is not currently approved by FDA for females, but it can be used as an adjunctive therapeutic agent.[48] A study in 416 men with AGA reported that taking 2.5 mg of dutasteride per day was much more effective than 5 mg of finasteride in increasing hair growth and improving the appearance of skin.[49] In a single-case study of a 46-year-old woman with FPHL who had a low response to minoxidil and finasteride, a clinical improvement was reported after 6 months of 0.5-mg daily dutasteride treatment.[50] These data support the efficacy of dutasteride; however, broader studies are needed and certain situations like pregnancy planning, contraception, normal basic laboratory data, etc. should be considered.

Follow-up time

Dihydrofinasteride reduces testosterone in the scalp by 64% and serum by 68%. After 12 months of administration, the number of full and thick hairs on the scalp increases and the number of thin hairs decreases. Finasteride could effectively stop the hair miniaturization and initiate hair regrowth. The finasteride pill is taken daily and its effects appear within 4–6 months. Usually, after 24 months, the maximum effect occurs. The efficacy of finasteride lasts as long as the drug is administered. Finasteride can be taken with food or on an empty stomach.[51] The administration for at least 12–18 months has a positive effect on hair loss[29] and 1 year of treatment or more (about 2 years) showed better results.[14] However, during the first 6 months, the existing hairs become a little thinner. Sometimes the reason for this is that hair loss is progressing and the effect of finasteride has not yet begun, while in some cases it is due to the loss of a series of miniature hairs, which leave space for new and healthy hair growth. Therefore, short and thin hairs will be lost, and thick and healthy hairs will replace them.[44]

Side effects

Finasteride, like all drugs, is associated with possible risks and side effects. Studies by Oliveira-Soares et al. showed that side effects such as decreased libido in 4 patients and increased liver enzymes in 1 patient were observed.[29]Another study showed that 4 female patients (4.6%) experienced side effects (headache, menstrual irregularities, dizziness, and increased body hair growth). However, these side effects were mild and disappeared after a while.[31] In another study, finasteride was well tolerated at different doses, although some side effects were observed. This study states that finasteride can alter and increase female characteristics in male fetuses by affecting fetal hormones. Therefore, finasteride should be eliminated before pregnancy, and women in childbearing age should employ safety precautions when taking finasteride.[30]

In another study on women with a pattern of hair loss, the findings showed that treatment with finasteride had acceptable results, hair loss was significantly reduced and excess hair growth was reported without any side effects.[25] In men, the findings show that very few men face side effects while taking the drug; about 2% experience decreased sexual potency or ejaculation problems, decreased semen volume, and erection problems. Unfortunately, some individuals have also experienced aggression and mild depression.[52]

The findings of studies related to single or combination therapy with oral or topical finasteride have been summarized in Table 1.

There are some other emerging and promising systemic drugs for male and female pattern AGA; one of them is oral minoxidil. In an original study with 30 cases of male pattern AGA who were treated with oral minoxidil 5 mg/day, total hair counts were significantly increased at weeks 12 and 24. Vertex area revealed 100% improvement with a 43% of excellent response. The frontal area also exhibited significant improvement; however, it was less pronounced than that in the vertex area. Safety profile was acceptable and the most common side effects were hypertrichosis (93%) and pedal edema (10%). Case selection is of extreme importance in this treatment, and patients with cardiovascular problems or significant hypertension may not be good candidates for this therapy.[53] In another 6-month trial, the authors suggested that 1.25 mg daily low dose of oral minoxidil can be considered an effective therapeutic option for male pattern AGA with an acceptable safety profile, and higher doses (2.5–5 mg/day) may be beneficial in resistant cases.[54] In another study in 148 women with FPHL, oral minoxidil was used at the dosage of 0.25–2 mg/day (median: 1 mg/day) for a mean duration of 9 months, and 85% of patients received oral minoxidil in combination with other drugs. About 80% of patients experienced a clinical improvement (in 65% of cases this improvement was slight), and patients with more advanced stages of alopecia experienced a more visible clinical improvement. There was no statistically significant difference in the effectiveness or safety of the drug in terms of dosage or age.[55]

In a systematic review that evaluated the efficacy of oral minoxidil on nonscaring alopecia (including AGA and alopecia areata), the authors found that oral minoxidil

usually has been used in the range of 0.25–5 mg/daily/twice daily. Acceptable clinical improvement has been shown in 61–100% and 18–82.4% of patients with AGA and alopecia areata, respectively. This therapy also had promising results in FPHL, chronic telogen effluvium, monilethrix, and permanent post-chemotherapy alopecia. Although this regimen has been considered safe, hypertrichosis and postural hypotension were among the most common side effects. In addition to efficacy and safety, oral minoxidil resulted in better compliance than the topical form.[56] In a review study encompassing 634 cases, oral minoxidil has been used as the primary treatment for hair loss. The most common condition among studied patients was AGA, but alopecia areata, telogen effluvium, permanent chemotherapy-induced alopecia, lichen planopilaris, loose anagen syndrome, and monilethrix were other conditions that required treatment. There are not enough high-level evidence studies using standardized objective measurements which compare the efficacy and safety of different doses of treatment. Finasteride and dutasteride are usually used when there is a difficulty with the topical formula.[57]

It is of great importance to compare finasteride with oral minoxidil in future trials and review studies.

Limitations

There are less trial studies on the use of finasteride in women than in men, and there are a few well-designed prospective clinical trials concerning the use of topical finasteride. Moreover, in this systematic review, we only included trial studies, the number of which is limited. There is a need for further trial studies in this field.

Conclusions

Various drugs, including topical minoxidil, oral finasteride and oral antiandrogens, are widely used for treating FPHL. Studies have shown that different doses of finasteride are effective in controlling FPHL in postmenopausal women and in the women in reproductive age. Administration of the drug should be continued for at least a year until the hair density reaches the desired level. To increase the effectiveness of the drug, the usage of higher doses, such as 5 mg/day, provided that there is resistance in patients or side effects, is recommended. As it is not very effective in women over 70 years of age, this drug can be recommended for younger age groups. Dutasteride, a new generation of 5α-reductase inhibitors, is also being discussed for treatment, and the use of this drug could be considered in certain situations. The current systematic review has shown that finasteride can be a very effective treatment for FPHL. In the reviewed articles, the effectiveness of the drug reported for topical and oral use was between 15% and 65.2%. In all reviewed articles, side effects were either not reported, observed in a low percentage (4.6%) of female patients or tolerable for them. The use of combination drugs such as topical estradiol and minoxidil could increase the effectiveness of the drug. It was also found that topical finasteride is more effective than other topical formulas used.

The FDA has not yet approved the use of finasteride in the treatment of hair loss in women due to its effect on female hormones and the growth of external genitalia in male fetuses. However, due to its low side effects, the present findings recommend it for nonpregnant women, considering the specific conditions and risk factors such as pregnancy and hormonal diseases.

It is recommended that future studies maximize therapeutic trials and evaluate the efficacy and side effects of this treatment in patients with FPHL.

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