

Dutasteride for Androgenetic Alopecia: Review Article

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ABSTRACT

Background: The disorder known as androgenetic alopecia (AGA), which is androgen-mediated, is characterised by a gradual loss of apparent scalp hair density. Dihydrotestosterone (DHT), which causes hair follicles to gradually shrink and thin out, targets genetically susceptible hair follicles. Hair loss, which typically starts at the hairline on both sides of the forehead, eventually causes the hair on top of the head to fall out. Dutasteride, a dual 5ARI, has been utilised in the clinic to treat AGA, demonstrating a unique mechanism and potent therapeutic impact. For patients with AGA, dutasteride could be an alternate therapy.

Objective: This article aimed to highlight the dutasteride for androgenetic alopecia.

Methods: PubMed, Google scholar and Science direct were searched using the following keywords: Dutasteride, Hair loss and Androgenetic alopecia. The authors also screened references from the relevant literature, including all the identified studies and reviews, only the most recent or complete studies were included.

Conclusion: Dutasteride is now becoming popular treatment option in AGA, due to its good response for treatment Androgenetic alopecia.

Keywords: Dutasteride, Hair loss, Androgenetic alopecia.

INTRODUCTION

The most frequent cause of patterned hair loss in susceptible men and women is androgenic alopecia (AGA). AGA is a polygenetic, complex illness that affects 40–50% of Caucasian women and 80% of Caucasian men throughout life⁽¹⁾. Men's predominance in Asian and African populations has decreased to approximately 14%⁽²⁾.

The most typical kind of hair loss in males is known as male androgenetic alopecia (AGA). More than 90% of all male instances of alopecia are due to it⁽¹⁾. When males who are genetically prone to it are exposed to androgens, it happens. AGA may have an adverse effect on a patient's quality of life and may hinder their capacity for lead fulfilling social and professional lives⁽³⁾. AGA may also result in indirect physical injury, such as sunburn, from exposure to UV radiation and hair loss⁽³⁾. Additionally, hypertension, hypercholesterolemia, and myocardial infarction may all be made worse by AGA⁽⁴⁾. The only therapies approved by the FDA are topical minoxidil and oral FIN, although their effectiveness is only moderate (40–60%)⁽⁵⁾.

Circulating androgens, microinflammation, and endocrine abnormalities are some of the factors that contribute to the multifactorial, polygenetic condition known as AGA⁽⁴⁻⁶⁾. It drastically lowers quality of life and frequently causes mental suffering. Fundamentally, the 5- α -reductase (5 aR) enzyme's Dihydrotestosterone (DHT) that is produced via the local and systemic conversion of testosterone, is the primary pathogenic mechanism for AGA.

Three isoenzymes, types I, II, and III, make up 5 aR⁽⁹⁾. The key locations for type I are hair follicles, sweat glands, and sebaceous glands, whereas the primary sites for type II are the prostate and the male genitalia, including the inner root sheath of hair follicles^(10, 11). Type III has been discovered in the mammary

gland, brain, dermis, and epidermis, among other places, but its purpose is still unknown⁽¹²⁾. When DHT binds to the androgen receptor, the hormone-receptor complex triggers the genes that cause the massive, terminal hair follicles to gradually diminish. The vellus hairs that are the signature of AGA are produced as a result of shorter anagen and smaller matrix sizes in succeeding hair cycles⁽¹²⁾. Finasteride is less effective than dutasteride, a second-generation 5 aR inhibitor, which only reduces DHT blood levels by 70%, because it has the ability to block both type I and type II isoenzymes⁽⁷⁾.

At 0.5 mg per day, dutasteride, an inhibitor of type I and type II 5 alpha-reductase, is approved for the treatment of symptomatic BPH. It is 100 times more potent than finasteride in inhibiting type I 5 alpha-reductase, while it is roughly three times as effective at inhibiting type II 5 alpha-reductase⁽¹³⁾. Finasteride lowered serum DHT by 70% at a dose of 5 mg/d, but dutasteride reduced blood DHT levels by more than 90% at a dosage of 0.5 mg/d^(13,14). Despite only having a license to treat symptomatic BPH, dutasteride has been tested for the treatment of AGA. Dutasteride has been shown in trials to dramatically enhance scalp covering, minimise additional hair loss, and boost patient satisfaction when taken as the main medication for the treatment of AGA⁽¹⁵⁾.

The class of medications known as 5-alpha-reductase inhibitors includes dutasteride that inhibits 5-alpha-reductase enzyme activity. Dihydrotestosterone (DHT), an androgen hormone that has been associated to male pattern hair loss, cannot be produced by your body when you take this family of medications. The development of male sex traits including body and facial hair depends heavily on DHT. The end outcome of this is thin hair, a receding hairline, and hair loss around the crown (top of head). The most prevalent kind

of baldness, male androgenetic alopecia, may benefit from dutasteride, according to recent studies ⁽¹⁶⁾.

Pathophysiology of Androgenetic Alopecia (AGA)

AGA's pathogenesis is diverse and extremely complex. This disorder is influenced by a wide range of variables, including genetics, endocrine problems, circulating androgens, medicines, nutrition, and microinflammation in each person's hair follicles ⁽⁸⁻¹⁰⁾. Although the method of inheritance is uncertain, multiple gene polymorphisms have been discovered in AGA. Literature has linked mutations in 5 α -reductase, aromatase, oestrogen receptor, and other genes ^(9, 11-14). The greatest link between the development of AGA and genetic changes in androgenic receptors is made, though. These modifications enhance the expression of androgenic receptors, particularly in the regions of the frontal and vertex ⁽¹⁵⁾, which explains the pattern of hair loss ⁽¹⁶⁾.

Diagnosis of Androgenetic Alopecia

The Norwood scale can be used to identify the typical male pattern hair loss, however a differential diagnosis is necessary to accurately assess this issue. Strong indicators of this disorder include a family history of baldness and the shift of thick, long, pigmented vellus hairs to thinner, shorter, and non-pigmented vellus hairs ⁽¹⁷⁾. Trichoscopy can be helpful to assess the change in hair diameter ⁽¹⁸⁾, and the appearance of erythema and inflammation on the scalp should also be taken into consideration ⁽¹⁷⁾. AGA is frequently connected to female conditions such polycystic ovarian syndrome, congenital adrenal hyperplasia, and others that affect hormone metabolism ⁽¹⁹⁾. The physical exam is the primary tool for diagnosing AGA, however various laboratory tests may support the evaluation of the patient. When hormone problems are suspected, measurement of thyrotropin levels and testosterone metabolism might be helpful in correlating AGA with those conditions ⁽¹⁷⁾. AGA may also be impacted by alterations in the metabolism of iron and nutritional deficits ⁽¹⁷⁾.

Dutasteride and the management of AGA

Since treating AGA involves managing a complicated pathophysiology, halting development and further thinning are the primary objectives. Additionally, there are only two FDA-approved treatments: minoxidil, a vasodilator that may cause undesired hair growth, and finasteride, a type II 5 α -reductase inhibitor with well-documented sexual side effects ⁽²⁰⁾. Due to its capacity to block both kinds 1 and 2 of the enzyme, dutasteride, a second-generation 5 α -reductase inhibitor, is more effective than finasteride. This results with a 90% reduction of DHT serum levels compared to a 70% drop with finasteride ⁽²¹⁾. The first brief studies contrasting finasteride and dutasteride appeared in the 2000s ⁽²²⁻²⁴⁾. Dutasteride 2.5 mg is more effective than finasteride 5

mg for 24 weeks in males with AGA, according to research by **Olsen *et al.*** ⁽²²⁾. Dutasteride 0.5 mg was in a similar way, also more effective than finasteride 1 mg ⁽²⁴⁾.

Long-term research also revealed dutasteride to be safe and effective. A six-month phase III trial of AGA patients receiving 0.5 mg/day of dutasteride revealed tolerance and an improvement in hair growth ⁽²³⁾. Recent research by **Chung and colleagues** ⁽²⁵⁾ showed that using dutasteride for more than 6 years increased total, terminal, and vellus hair counts in male AGA patients ⁽²⁵⁾.

Side effect of Dutasteride Treatment

Chills, cold sweats, and lightheadedness or dizziness after rising up from a laying or seated posture are the most typical adverse effects that may need medical care. Bloating, edoema, and unexpected weight gain or decrease are possible additional less typical negative effects. Some people who take dutasteride may get a severe allergic response that results in a rash and swelling of the face, tongue, or throat. Additionally, it can be linked to a higher risk of prostate cancer in its advanced stages. There have also been reports of erectile dysfunction, reduced sex drive, and ejaculatory issues. Unusual sleepiness, back discomfort, headaches, and stomach aches are rare adverse effects ⁽²⁰⁾.

Libido:

One of the side effects that was documented in at least three out of five trials examining oral dutasteride was libido. Following at least 24 weeks of medication, a non-significant rise in the proportion of diminished sexual desire was seen in the dutasteride group compared to the placebo group. No studies using intralesional therapy showed side effects related to libido ⁽²⁶⁾.

Erectile Dysfunction:

In four of the five trials evaluating oral dutasteride, there was a non-significant rise in the proportion of erectile dysfunction in the dutasteride group compared to the placebo group after at least 24 weeks of treatment. No research on intralesional treatment revealed erectile dysfunction-related negative effects ⁽²⁶⁾.

Ejaculatory Dysfunction:

After using oral dutasteride for at least 24 weeks, there was a non-significant rise in the percentage of ejaculation dysfunction when compared to placebo. 4 out of the 5 trials examining oral dutasteride reported ejaculation dysfunction. There are no known adverse effects of intralesional treatment related to ejaculatory dysfunction ⁽²⁶⁾.

Efficacy of dutasteride in treatment of AGA

AGA, a complicated genetically inherited multifactorial skin condition, is characterised by a gradual loss of visible terminal hair ⁽²⁷⁾. The key pathogenic component of AGA is DHT, which shrinks hair follicles and changes terminal hair into vellus hair ⁽²⁸⁾.

DHT is the main androgen implicated in the pathogenic phase of male AGA, and 5 α R may convert testosterone

to it ⁽²⁹⁾. As a result, blocking 5 α R activity becomes a crucial AGA therapeutic strategy. As two different types of 5 α RI, dutasteride and finasteride have both demonstrated some curative results in clinical settings. One study found that when compared to finasteride, dutasteride can block type 1 5 α R by a factor of 100 and around three times the ability to inhibit type 2 5 α R. After examining the two drugs' mechanisms of action, it was shown that when treating AGA, dutasteride may be more beneficial than finasteride ⁽³⁰⁾.

Numerous studies have documented how well dutasteride works for AGA patients ⁽²⁷⁻³⁰⁾. Both investigator evaluation and patient self-assessment questionnaires revealed that dutasteride significantly improved hair growth when one of the 17 pairs of identical twins with AGA received 0.5 mg/d for 12 months while the other received a placebo ⁽³¹⁾. Dutasteride significantly and dose-dependently increased hair growth in patients with AGA in a phase II, double-blind, placebo-controlled, 24-week research ⁽²²⁾. This study showed that after 12 and 24 weeks, dutasteride at a dosage of 0.5 mg/d significantly improved hair growth compared to the control. This outcome was, at the very least, comparable when finasteride was administered at a 5 mg/d dosage. In terms of stimulating hair growth in 12 and 24 weeks, dutasteride medication at a dosage of 2.5 mg/d surpassed finasteride treatment. However, when compared to finasteride at a dose of 5 mg/d (4%), sexual dysfunction associated with dutasteride, including decreased libido (13%) dramatically increased, and vice versa ⁽³¹⁻³³⁾.

Dutasteride medication at a dose of 0.5 mg/d was beneficial in improving the appearance of scalp hair in Korean men, according to research by **Jung et al.** ⁽³⁴⁾ by increasing hair density and thickness. Previously, these guys had not shown a clinically significant improvement in their hair growth in response to the conventional finasteride therapy. 77.4% of the patients showed a substantial improvement in the overall photographic evaluation after taking dutasteride for six months. When compared to post-finasteride therapy, hair density and thickness considerably increased in phototrichogram evaluation by 10.3% and 18.9%, respectively.

CONCLUSION

Dutasteride is now becoming popular treatment option in AGA, due to its good response for treatment Androgenetic alopecia.

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