**Finasteride and Dutasteride in the Treatment of Androgenetic Alopecia: Risk or Benefit?**

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**Abstract**

Androgenetic alopecia, also known as male pattern hair loss or female pattern hair loss, is the most common form of alopecia worldwide and occurs due to an excessive response to androgens. Its etiology is chronic and influenced by genetic and environmental factors. For these reasons, this condition can be extremely difficult to treat. The main form of treatment currently involves the use of finasteride or dutasteride, which have the ability to inhibit the enzyme 5-alpha-reductase, responsible for the conversion of testosterone into DHT, and consequently prevent the progression of androgenetic alopecia. Concurrently with the dissemination of this treatment, various concerns have arisen regarding the potential side effects caused by this class of medication, particularly impairments in sexual function and possible psychological disorders observed in a portion of users. With the emergence of new methodologies aiming at the treatment of androgenetic alopecia, there is much debate in the scientific community about whether the use of finasteride and dutasteride is the best way to treat this condition. In this article, we will discuss how 5-alpha-reductase inhibitors act in the treatment of androgenetic alopecia, focusing on their risks and benefits.

**Keywords:** Androgenetic alopecia; Finasteride; Dutasteride; Side effects.

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**1. Introduction**

Androgenetic alopecia is a very common chronic dermatological condition associated with genetic predisposition and characterized by progressive hair loss and thinning. Its incidence is more commonly observed in males after puberty. The mechanism involves the action of dihydrotestosterone (DHT), a sexual hormone that comes from the transformation of testosterone by the enzyme 5-alpha-reductase [1]. In men, hair loss typically occurs as a recession of the frontal hairline associated with thinning at the vertex of the scalp. In women, it presents with hair loss at the vertex of the scalp [2]. Besides the physical impact, alopecia causes enormous emotional distress and reduces the quality of life of individuals, leading to other subsequent diseases [3].

The hair growth cycle consists of four distinct phases: anagen or growth; catagen or involution; telogen or rest; and exogen or shedding. About 90% of follicles are in the anagen phase, where they remain for a period of two to seven years. In androgenetic alopecia, there is a shortening of the anagen phase, leading to abnormally short and thin hair strands. There is a replacement of terminal hairs by vellus and intermediate hairs, contributing to the thinning of the strands and the hair loss process [1].

One of the most recommended treatments for androgenetic alopecia is the use of 5-alpha-reductase inhibitors. The most well-known are finasteride and dutasteride. Finasteride's mechanism of action is based on the selective competitive inhibition of the type 2 5-alpha-reductase enzyme, preventing the conversion of testosterone into its more potent form, dihydrotestosterone (DHT), thus reducing its serum levels [4]. Although therapy based on
oral finasteride is well tolerated, its prolonged use in some patients shows sexual and mental adverse effects such as erectile dysfunction, loss of libido, and an increase in depression cases [5]. The topical use of finasteride offers greater safety to patients, with enzyme inhibition only occurring in the scalp, thus drastically reducing systemic effects [6].

Dutasteride has a very similar action to finasteride but can inhibit both type 1 and type 2 isoenzymes of 5-alpha-reductase. This inhibition has been proven to be more potent in reducing serum DHT levels compared to finasteride. Considering the clinical outcome of both drugs in the treatment of androgenetic alopecia, in some cases, better results may be observed with dutasteride-based therapy [7]. Within this context, the aim of this work is to correlate the therapeutic effect of finasteride and dutasteride in the treatment of androgenetic alopecia with their risks and adverse effects.

2. Methodology

A search was conducted on PubMed using the following keywords: androgenetic AND alopecia AND finasteride OR dutasteride. Studies were excluded if they addressed alopecia areata and if they were published in a language other than English. A total of 15 studies were selected after the search process, dating from 1992 to 2022. Articles that emphasized the therapeutic efficacy and adverse effects involving 5-alpha-reductase inhibitors were selected.

2.2 Development of PLGA nanoparticles with finasteride

The therapeutic efficacy of finasteride is extremely well-established, having been used as a treatment for androgenetic alopecia since 1997. Its effects increase over time; therefore the therapeutic response is seen in the long term [8]. A large study involving more than 3,000 men with androgenetic alopecia showed that 11.1% of the patients experienced significant hair growth using finasteride, 36.5% had moderate growth, and 39.5% did not achieve satisfactory growth over a period of 3 years [9]. The results generated using oral finasteride are superior at the vertex of the scalp when compared to the frontal and centroparietal region. Studies show that in patients over thirty years old, there is more significant hair growth compared to those under thirty [8]. In postmenopausal women, it can be used off-label in doses between 2.5 and 5 mg once a day [10].

Dutasteride is considered a second-generation 5-alpha-reductase inhibitor, succeeding finasteride. Due to its more potent effect in inhibiting serum DHT levels, some cases may observe better clinical results [7]. Studies report that dutasteride reduces DHT levels by 90%, while finasteride reduces them by only 70% [11]. A meta-analysis showed that 0.5 mg per day of dutasteride was significantly superior when compared to 1 mg per day of finasteride, considering hair count at 24 weeks of treatment [12]. It is evident that there is ample evidence confirming the therapeutic efficacy of 5-alpha-reductase inhibitors in patients with androgenetic alopecia. However, there is much debate in the scientific community about whether the benefits of these drugs outweigh their risks, given the side effects that manifest during and after treatment.

Regarding the adverse effects of 5-alpha-reductase inhibitors, there is a significant emphasis on side effects related to sexual function, documented in up to 38% of patients. Among these, the most observed was erectile dysfunction, followed by loss of libido [13]. Androgens are well known for their sexual functions in men. This raises the issue related to the decrease in DHT levels and sexual dysfunction. If these symptoms occur, discontinuation of the medication should be considered [14]. Finasteride has the ability to cross the blood-brain barrier and consequently inhibit the production of DHT in the central nervous system. However, it is not possible to say that this mechanism alone can lead to sexual dysfunctions, as it involves a multifactorial disease that includes various psychogenic and organic factors [15].

Another commonly observed effect is gynecomastia in men using finasteride and dutasteride. These medications, by inhibiting 5-alpha-reductase, lead to an increased conversion of testosterone into estradiol via the aromatase enzyme in peripheral tissues. Increased levels of estradiol also contribute to the emergence of events related to sexual function [16]. Regarding prostate cancer, it is not possible to verify an increase in its incidence in users of finasteride or dutasteride. However, several studies have shown that the population diagnosed with prostate cancer using finasteride had higher Gleason score ratings (between 7-10), indicating more aggressive carcinomas [17-18].

On the other hand, it was concluded that the use of finasteride 5 mg per day, used in patients with benign prostatic hyperplasia, is associated with a reduction in the incidence of prostate adenocarcinoma. This reduction occurs only in low-grade carcinomas, i.e., those
with a Gleason score of 2-6 [18]. Psychiatric effects such as depression and other mood disorders may manifest in patients using 5-alpha-reductase inhibitors long-term. In a study, 128 men with androgenetic alopecia who started treatment with 1 mg of finasteride were later evaluated on depression and anxiety scores. There was a small but significant increase compared to the placebo group. In these cases, discontinuation of treatment is indicated.

The mechanism by which 5-alpha-reductase inhibitors can cause depression involves the reduction of neurosteroids in the brain. This alteration was detected in users of finasteride and dutasteride, even after discontinuation of the medication. Neurosteroids are primarily responsible for the central modulation of mood disorders and anxiety [19]. In women, certain precautions must be taken when prescribing 5-alpha-reductase inhibitors. These medications can cause congenital defects in the male fetus, especially abnormal external genital development such as hypospadias. Due to this, they are contraindicated during pregnancy. Generally, there is a preference for therapy based on Minoxidil in women [20].

5. Conclusion

Given the information presented, it is possible to conclude that 5-alpha-reductase inhibitors are generally well-tolerated and show significant results in a large majority of patients. Regarding their side effects, no evidence was found correlating an increased incidence of prostate cancer. Sexual effects such as erectile dysfunction are frequently found, and if there is a significant impact on the patient’s sexual life, discontinuation of the treatment should be considered. Studies related to depression are still vague, being a multifactorial condition, but discontinuation of treatment is also advised. In women, there is a preference for other medications such as Minoxidil, and its use in pregnant women is prohibited.

In terms of efficacy, the results are usually significant when considering hair count and the permanent stabilization of hair loss. Therefore, it is crucial to carefully verify the aspects of each patient, such as personal history and acquired diseases, to assess whether treatment with 5-alpha-reductase inhibitors is indicated or not for each case.

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References