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REVIEW

Use of 5-Alpha Reductase Inhibitors in Dermatology: A Narrative Review

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ABSTRACT

Finasteride and dutasteride are 5-alpha reductase selective inhibitors (5ARIs). They were introduced as therapeutic agents for the treatment of benign prostatic hyperplasia in 1992 and 2002, respectively; finasteride has also been approved for the treatment of androgenetic alopecia since early 2000. These agents inhibit the conversion of testosterone (T) to 5α-dihydrotestosterone (5α-DHT), limiting steroidogenesis and playing a crucial role in the physiological function of the neuroendocrine system. Therefore, it has been proposed that blocking androgen synthesis with the use of 5ARIs would be beneficial in the treatment of various diseases related to states of hyperandrogenism. This review describes the dermatological pathologies in which 5ARIs have been used as part of the treatment, evaluation of the efficacy, and knowledge of the safety profile. Specifically, we discuss the application of 5ARIs in androgenetic alopecia, acne, frontal fibrosing alopecia, hirsutism, and the implications of adverse events associated with its use to inform about the applications of 5ARIs in general dermatology practice.

Keywords: Alopecia; Finasteride; Dutasteride; 5-Alpha reductase inhibitors; Dermatology

Key Summary Points

5α-Reductase inhibitors (5ARIs) have shown efficacy in reducing hair loss and stimulating hair growth in men with androgenetic alopecia.

5ARIs are effective in women with hyperandrogenism and alopecia, with evidence also supporting their use in normoandrogenic postmenopausal women.

Topical formulation of 5ARIs reduces unwanted side effects and may improve patient adherence to treatment.

The application of 5ARIS for pharmacological treatment of acne vulgaris, hirsutism, and frontal fibrosing alopecia is promising, but requires further evaluation.

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INTRODUCTION

The 5-alpha reductases (5α-Rs) are a group of enzymes that are present in various organs and tissues. Their primary role is to convert steroid precursors produced by the gonads, adrenals, and central nervous system (CNS) into neuroactive steroids and functional hormones. The 5α-R family consists of five enzymes, including three main isotypes (5α-R 1, 2, and 3) associated with steroidogenesis, and two *trans*-2,3-enoyl-CoA reductases (TECR and TECR-like) with less understood functions. The substrates for 5α-R include progesterone (PROG), corticosterone, deoxycorticosterone (DOC), cortisol, and aldosterone. The products of this conversion process are 5α-dihydro-derivatives, such as 5α-dihydroprogesterone (5α-DHP), 5α-dihydrodeoxycorticosterone (5α-DHDOC), 5α-dihydrotestosterone (5α-DHT), 5α-dihydrocortisol, 5α-dihydrocorticosterone, and 5α-dihydroxyaldosterone [1]. This enzyme converts testosterone to dihydrotestosterone (DHT), which amplifies androgen effects in certain tissues. DHT has a stronger impact on the androgen–androgen receptor complex than testosterone. 5α-Reductase inhibitors (5ARIs) act by blocking DHT production from adrenal and gonadal sources, leading to a substantial reduction in serum (around 70%) and prostate DHT levels (approximately 90%) [2]. Finasteride and dutasteride are the most commonly prescribed 5ARIs, which act by inhibiting 5α-R type 2, primarily. Dutasteride provides roughly threefold higher inhibition of type 2 5α-reductase compared to finasteride, and 100 times stronger inhibition for the type 1 5α-reductase enzyme [3]. Applications of 5ARIs in clinical practice have been primarily focused on the treatment of benign prostatic hyperplasia; however, application of these medications has since expanded to other fields, including dermatology for which it is commonly prescribed as treatment for androgenetic alopecia. Nevertheless, its applications in other dermatological conditions are not widely discussed. In this narrative review, we provide an overview of androgen metabolism in the skin and the pharmacological implications of 5α-Rs inhibition in dermatological conditions. Particularly, we focus our evaluation on androgenetic alopecia in men and women, acne, frontal fibrosing alopecia and hirsutism, as well as the adverse events that are associated with use of 5ARIs to promote a wider application in general dermatological practice.

SEARCH METHODS

We searched Medline and Google Scholar for publications focusing on the use of 5ARIs in dermatological practice. We included the search terms "5-alpha reductase inhibitors" AND ("dermatology" OR "alopecia" OR "acne" OR "hirsutism") for articles up to May 31, 2023. Abstracts were screened and relevant articles which discussed evidence on the application of 5ARIs in the aforementioned dermatological conditions were selected for full review.

Compliance with Ethics Guidelines

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

ANDROGEN METABOLISM WITHIN THE SKIN

Genetic and non-genetic factors that increase the activity of steroidogenic enzymes are associated with hirsutism, acne, and alopecia. The skin can synthesize active androgens using DHEA-S as a precursor. This involves the desulfation of DHEA by steroid sulfatase (STS) and subsequent activation of enzymes like 3β-HSD (3β-hydroxysteroid dehydrogenase/$\Delta^{5\text{-}4}$ isomerase), 17β-HSD (17β-hydroxysteroid dehydrogenase), and 5α-reductase, which convert weaker androgens (e.g., DHEA) into more potent ones like DHT and testosterone [4]. Stronger androgens can be transformed into weaker steroids or metabolized through other pathways such as aromatase whose function is to convert androgens to estrogens, or 3α-hydroxysteroid dehydrogenase which creates

androsterone and androstanediol. Studies suggest that low enzyme activity is associated with less balding in the scalp. Patients with baldness have increased 3β-HSD activity in sebaceous glands and elevated 17β-HSD and 5α-reductase activity in frontal hair follicles.

Steroid hormones enter target cells through the plasma membrane and bind to intracellular androgen receptors (AR), influencing gene expression. Changes in AR conformation or expression are linked to conditions like androgenetic alopecia. Although single gene mutations such as AR abnormalities have been identified, they alone are insufficient to cause disease. Pathologies resulting from hyperandrogenism are believed to be polygenic or multifactorial. Recent research has identified hair follicle microinflammation as part of the pathogenesis spectrum contributing to these conditions [4].

"Microinflammation" refers to a slow process distinct from classic inflammatory scarring alopecia. The initial event is believed to occur near the infundibulum of the follicle. Possible cofactors like *Propionibacterium* sp., *Staphylococcus* sp., and *Malassezia* sp. contribute to a proinflammatory stress response, activating adhesion molecules in the capillary endothelium. Chemokines and adhesion molecules facilitate the migration of inflammatory cells across the endothelium, leading to enlargement of the follicular dermal sheath (perifollicular fibrosis). Other damage mechanisms involve keratinocytes responding to irritants, UV radiation, and pollutants, generating reactive oxygen species and releasing interleukin-1α (IL-1α). This cytokine may disrupt hair follicle growth in hair cultures. Microinflammation thus plays a role in the pathogenesis of certain hair disorders [4].

DERMATOLOGICAL USES OF 5ARIS

Androgenetic Alopecia in Men

Randomized controlled studies conducted since 1999 have demonstrated the effectiveness of 5ARIs in reducing hair loss and promoting hair growth in men with male-pattern alopecia. One study focused on determining the minimum dose of finasteride needed to significantly decrease DHT levels in both plasma and tissue. Men with androgenetic alopecia (AGA) underwent scalp biopsies before and after receiving daily doses of 0.01, 0.05, 0.2, 1, or 5 mg of finasteride or a placebo for 42 days. The results of this study justified the dosage range for subsequent clinical trials, establishing an effective and safe dose of finasteride between 0.2 and 5 mg for treating male-pattern alopecia [5].

In a phototrichogram study examined the effects of finasteride on the hair growth cycle, 212 men were randomly assigned to receive either finasteride or a placebo. The results indicated that a daily dose of 1 mg of finasteride over 48 weeks led to an increase in total hair count and improved the ratio of anagen to telogen hairs, promoting the transition to the anagen phase [6]. After verification of the efficacy of finasteride, long-term use of finasteride at a 1-mg dose proved to be safe and effective in treating male-pattern AGA. Evaluation techniques conducted over 1 and 2 years demonstrated significant improvement vs. placebo with a notable increase in hair count within a 1-inch circular area on the bald vertex scalp. Patient self-assessment confirmed that finasteride treatment effectively reduced hair loss, stimulated hair growth, and enhanced the appearance of hair loss [7].

Similar results were demonstrated in a multicenter study with a double-blind, randomized, placebo-controlled design which examined the efficacy and tolerability of finasteride in men aged 41–60 with vertex male-pattern hair loss. Through the use of global scalp photographs, patient self-evaluations, and clinical assessments by researchers at various time points, the study concluded that a 1-mg dose of finasteride significantly improved hair growth on the scalp compared to placebo. These positive changes were observed at 6 months and were sustained for the entire 24-month duration of the study [8]. Subsequent studies have tested the efficacy of finasteride in different doses. A study in 414 Japanese men with male-pattern hair loss compared the efficacy of different doses of finasteride. The participants were randomly assigned to receive finasteride 1 mg, finasteride 0.2 mg, or a placebo once daily for 48 weeks. Efficacy

was assessed through comprehensive photographic evaluation, patient self-assessment, and investigator assessment. After 48 weeks, 58% of men in the finasteride 1 mg group, 54% in the finasteride 0.2 mg group, and 6% in the placebo group showed improvement based on global photo evaluations. However, all efficacy measures favored the 1-mg dose, suggesting that a daily dose of 1 mg is the ideal choice [9].

Prior studies confirmed blocking type 2 alone prevented testosterone conversion and provided benefits in patients with AGA. Dutasteride's introduction led to the hypothesis that dual inhibition of 5α-reductase type 1 and 2 would enhance the efficacy of male-pattern AGA treatment. In a randomized study by Olsen et al. in 2006, 416 men with AGA were given dutasteride (0.05, 0.1, 0.5, or 2.5 mg), finasteride (5 mg), or placebo daily for 24 weeks. Three clinical parameters were assessed: hair count, changes in global photographs, and self-evaluations related to various aspects of hair loss. Finasteride demonstrated superiority across all three parameters. After 24 weeks, the percentage of subjects with over 10% increased hair count was 0%, 17%, 38%, 48%, and 56% for placebo, dutasteride at doses of 0.05, 0.1, 0.5, and 2.5 mg, respectively; and 41% for finasteride. Photographic analysis showed a higher percentage of moderate or greater hair growth in the vertex and frontal regions for patients receiving dutasteride at doses of 0.5 mg and 2.5 mg compared to finasteride. Self-assessment indicated that only the dutasteride 2.5 mg and finasteride 5 mg groups consistently demonstrated significantly better results than the placebo group for all questionnaire parameters. These findings suggest that finasteride is more effective than dutasteride in treating AGA on the basis of the evaluated clinical parameters [3].

Oral 5ARIs are effective in treating AGA but may cause unwanted side effects, leading to poor long-term patient tolerance. Recent studies have explored topical treatments as an alternative. Both oral and topical 5ARI administration significantly lower DHT plasma levels, with the topical solution reducing DHT by approximately 68–75% and the oral form by approximately 62–72%. This evidence highlights the comparable efficacy of topical treatment in reducing DHT levels, offering a potential option for patients who struggle with the adverse effects of long-term oral therapy [10]. In a 24-week study involving 323 adult male patients with AGA, three treatment groups were compared: topical finasteride with oral placebo, topical placebo with oral placebo, and topical placebo with orally administered finasteride. The study aimed to measure the target area hair count (TAHC). The results showed that the topical finasteride group had significantly better results compared to the placebo group. Efficacy was similar between topical and orally administered finasteride, but the topical group had lower peak plasma finasteride concentrations and less initial reduction in serum DHT concentration [11].

Treatments to evaluate synergy efficacy have also been reported: one study compared the efficacy of topical 0.25% finasteride mixed with 3% minoxidil versus 3% minoxidil alone in men with AGA. Forty-eight men were randomized into two groups and evaluated at week 24. Combination therapy demonstrated effectiveness in improving hair density and hair diameter, indicating its efficacy for both parameters [12]. A systematic review of 33 randomized controlled trials published in 2020 concluded that topical finasteride is a promising therapeutic option for AGA in men [13].

Androgenetic Alopecia in Women

As a result of the proven results in men with AG in 2000, the safety and effectiveness of finasteride, a treatment for AGA, were evaluated specifically in postmenopausal women. The trial involved 137 women without clinical or biochemical evidence of hyperandrogenism, who were randomly assigned to receive finasteride 1 mg/day or a placebo for 12 months. Results showed that finasteride did not promote hair growth or slow down hair thinning [14]. However, subsequent studies have aroused controversy by demonstrating the efficacy of finasteride in the treatment of AGA in normoandrogenic women. Oliveira-Soares et al. evaluated the efficacy and safety of finasteride

5 mg/day for 18 months in 40 normoandrogenic postmenopausal patients. Patient satisfaction and global photographic assessment were used to assess efficacy, revealing significant subjective and photographic improvements at months 6, 12, and 18. This study, though limited by its subjective assessment and lack of a placebo group, supports the potential benefits of finasteride [15].

Later, four case reports demonstrated that finasteride could improve the pattern of hair loss in women with hyperandrogenism. Two cases showed increased hair growth within 6–-12 months, while the other two cases experienced a halt in hair loss progression after 6–9 months. The difference in outcomes may be attributed to the longer duration (24–-30 months) and higher dosage (1.25 mg/day) of finasteride prescribed in this series compared to the trial conducted by Price et al., which used lower doses and treated patients for only 1 year. These findings suggest that finasteride improves hair loss in women with hyperandrogenism but does not have the same effect on postmenopausal women, supporting the idea that different types of female hair loss have varying underlying causes [16].

The effectiveness of 5ARIs in women with AGA remains a subject of debate. To assess the efficacy of antiandrogenic therapies in women with AGA and hyperandrogenism, a study was conducted involving 48 premenopausal women with female-pattern AGA. Out of these women, 21% had mild hirsutism and 42% experienced menstrual irregularities. Twelve women were not included in any treatment group, while the remaining 36 women were randomly assigned to one of three treatments for 1 year: cyproterone acetate (50 mg) with ethinyl estradiol, flutamide (250 mg), or finasteride (5 mg) daily. The treatments were evaluated using Ludwig's classification, self-evaluation scale, and investigator evaluation. After 1 year, only flutamide demonstrated a significant but modest reduction in Ludwig scores, indicating slight improvement in alopecia. Cyproterone acetate and finasteride did not show effectiveness in treating AGA. These findings suggest that among the three treatments, only flutamide at a dose of 250 mg per day yielded noticeable results in reducing hair loss in women with hyperandrogenism and AGA after 1 year of treatment [17]. On the other hand, a retrospective cohort study evaluated the effectiveness of finasteride and dutasteride on hair loss in women with AGA. The study included 120 patients who took finasteride 1.25 mg or dutasteride 0.15 mg daily for 3 years. Both treatments were found to halt the progression of AGA and improve the condition in 68.9% and 65.6% of cases, respectively. However, the study has limitations: it does not specify the presence of clinical or serological hyperandrogenism in the women, premenopausal women received combined treatment with unspecified contraception, and there was no comparison with a placebo as a result of the study's methodology [18].

Despite this, on the basis of evidence indicating that orally administered finasteride may be effective in treating women with AGA, the use of a topical formulation has been proposed to minimize unwanted effects. A prospective study was conducted in 30 postmenopausal women with AGA to explore the use of topical finasteride in combination with minoxidil for treatment. The participants were randomly assigned to receive either a topical 0.25% finasteride combined with minoxidil 3% or minoxidil 3% alone for 24 weeks. Hair density and diameter were measured to assess efficacy. The study found that the combination therapy was effective in improving both hair density and diameter, suggesting that topical finasteride combined with minoxidil can be a viable option for treating AGA in women [19].

Few studies have evaluated the efficacy and safety of 5ARIs in women with or without hyperandrogenism; the available studies have used various treatment regimens and have yielded different results. Therefore the benefit of 5ARI usage is currently still uncertain.

Acne Vulgaris

Acne vulgaris is a multifactorial disease where excessive sebum production plays a central role. Sebum secretion by the sebaceous glands is accelerated by the conversion of testosterone to

DHT by type I 5α-reductase, which is strongly expressed in the sebaceous glands. Therefore, it has been proposed that type I 5ARIs have the potential to improve acne vulgaris [20]. There are few publications regarding the use of 5ARIs and patients with acne. In a 6-month clinical trial involving patients with moderately severe acne, the use of 5ARIs in combination with minocycline was investigated. The study included 182 patients who were randomly assigned to five treatment groups: group 1 received minocycline 100 mg twice daily, group 2 received compound A (5ARI type 1) 25 mg once daily, group 3 received a combination of minocycline and compound A, group 4 followed the same regimen as group 3, and group 5 received a placebo. The trial evaluated the change in inflammatory lesion counts, total lesions, and the assessment of acne by investigators, patients, and through facial photographs. The results showed that patients treated with minocycline alone and those receiving the combination of minocycline and a type I 5ARI experienced a significant improvement in their acne condition. However, there was no additional improvement observed for patients receiving the combination treatment compared to those on minocycline alone. The lack of enhanced improvement with the combination treatment could be attributed to the direct stimulation of sebaceous production by testosterone and the expression of type II 5α-reductase in sebaceous glands associated with acne follicles [20].

A retrospective study carried out in 2007 evaluated the subjective benefits of the use of finasteride (5 mg/day) in women who had normal levels of free testosterone and suffered from acne or alopecia, previously treated with antibiotics, isotretinoin, and/or or antiandrogens (cyproterone acetate + ethinyl estradiol or spironolactone). The study involved 12 patients, six with acne and six with alopecia. Nine of the 12 patients experienced significant improvements in their symptoms and reported an overall improvement in their well-being after undergoing finasteride treatment. In general, the treatment was well tolerated with only a few minor adverse effects observed. These findings support the hypothesis that excessive 5α-reductase enzyme activity in peripheral tissues may play a role in the development of acne and alopecia in women with normal free testosterone levels. However, the fact that three patients did not respond to finasteride suggests the involvement of alternative pathways in the development of these conditions [21]. It has been observed that patients with AGA treated with dutasteride, who obtained a beneficial effect on concomitant acne vulgaris, without the use of antibiotics and anti-acne cream, obtained a notable improvement between 3 and 5 months after the start. Dutasteride could be a new option for the treatment of male patients with AGA and acne vulgaris [22].

A recent clinical trial was conducted to compare the effectiveness of montelukast and finasteride in treating moderate acne vulgaris in normoandrogenic women. The trial was prospective, randomized, single-blind, and lasted for 12 weeks. The study included 65 participants who were randomly assigned to two groups. One group received montelukast orally at a daily dose of 10 mg, while the second group received finasteride orally at a daily dose of 2.5 mg along with a topical solution of clindamycin 2%. After the 12-week period, the results showed that 88.6% of the patients in the finasteride group and 79.6% of the patients in the montelukast group achieved almost complete clearance of their acne. On the basis of these findings, the study concluded that both treatments are effective in treating moderate acne in normoandrogenic women. However, it was observed that finasteride was more effective than montelukast in this particular study [23].

Androgen-mediated skin disorders (AMSD) in women, including acne, hirsutism, and female-pattern hair loss, probably share the same pathophysiology; however, this is not fully understood. Some affected women have no detectable endocrine abnormalities but have variable sensitivity to androgens. Although there is currently no formal recommendation for their use, it has been proposed that regardless of the hormonal status of the patient, women with AMSD may benefit from hormone modulation therapies, including 5ARIs [24].

Frontal Fibrosing Alopecia

Frontal fibrosing alopecia (FFA) is considered a variant of lichen planopilaris (LPP). The pathogenesis is poorly understood, although it is known that an autoimmune reaction and hormonal influence play an important role in its pathogenesis. Treatment is often disappointing and there have been reports of cases of improvement or stabilization with various topical, intralesional, and systemic therapies, including 5ARIs. In 2014, a significant article on FFA was published, aiming to provide insights into its epidemiology, comorbidities, clinical findings, and therapeutic options. The study employed a multicenter and retrospective approach, involving 12 Spanish centers and a total of 355 patients diagnosed with FFA. The severity of FFA was classified into five degrees: I (< 1 cm), II (1–2.99 cm), III (3–4.99 cm), IV (5–6.99 cm), and V (> 7 cm). For statistical purposes, patients were grouped as having mild FFA (grades I and II) or severe FFA (grades III, IV, and V). The response to therapy was assessed on the basis of clinical notes and photographic evaluation, categorized into three outcomes: worsening (progression of hairline recession), stabilization (halt in hairline recession), or improvement (regrowth of hair on the hairline). The study's findings described the efficacy of various drugs, with antiandrogens being the most effective treatment compared to other systemic drugs like hydroxychloroquine, as well as topical treatments including minoxidil and topical or intralesional steroids. Finasteride was administered to 102 patients at a dose of 2.5–-5 mg/day, resulting in improvement in 47% and stabilization in 53% of patients. Dutasteride was used in 18 patients at a dose of 0.5 mg/week, leading to improvement in 44% and stabilization in 56% of patients [25].

A recent review on the treatment of FFA included 14 publications and focused on the efficacy of 5ARIs. The review analyzed a total of 270 patients, with 121 patients using finasteride and 149 patients using dutasteride. Results showed that 15.6% of patients experienced improvement or stabilization of the disease when treated with 5ARIs alone. Most patients received combination therapy with topical steroids, topical minoxidil 2%, topical pimecrolimus 1%, or intralesional triamcinolone acetonide. Some studies, classified as levels of evidence 2, 3, and 4, reported definitive hair growth, particularly in patients using daily dutasteride. These findings indicate that patients with FFA can achieve disease stability or slow down the progression with appropriate treatment [26].

In a retrospective observational study involving 224 patients (99.1% women, 0.9% men) with a mean age of 61.2 years, the effectiveness of dutasteride for the treatment of FFA was evaluated. The study had a median follow-up period of 24 months. Results showed that 66.1% of the patients received dutasteride, with varying weekly doses ranging from 1 to 7 capsules. Among the patients, 25% did not receive any systemic treatment, while the remaining patients received finasteride, hydroxychloroquine, doxycycline, or isotretinoin. The study concluded that dutasteride was the most effective therapy for FFA, with a dose-dependent response. The optimal dose was found to be 5–7 capsules of dutasteride 0.5 mg per week [27]. In light of the results in the studies presented above, a double-blind, randomized clinical trial should be considered to determine the efficacy of 5ARIs in the treatment of FFA.

Hirsutism

Hirsutism is the presence of excessive male-pattern body hair in specific areas. DHT plays a key role in the transition from fine hairs to terminal hairs in hirsutism. Around 80% of women with hirsutism have elevated androgen levels (hyperandrogenemia), while the remaining 20% are considered "idiopathic" with normal androgen levels but may have increased sensitivity to steroids or abnormal local androgen concentrations [24]. In 2018, the Endocrine Society updated the clinical practice guideline "Evaluation and Treatment of Hirsutism in Premenopausal Women." The guideline recommends initiating treatment for hirsutism with oral contraceptives in women who are not planning to become pregnant. If significant hirsutism continues after 6 months of

monotherapy with an oral contraceptive, the guideline suggests considering the addition of an antiandrogen, including 5ARIs [28]. A prospective, randomized, controlled clinical trial compared the efficacy and safety of finasteride in women with hirsutism. Fifty-six women with moderate or severe hirsutism were divided into two groups: group I received 2.5 mg of finasteride per day, and group II received 5 mg of finasteride per day orally for 1 year. Both groups showed improvement in hirsutism scores after 12 months of treatment. The percentage reduction in hirsutism scores was similar between the two groups. This study concludes that low doses of finasteride, both 2.5 mg and 5 mg, are safe and effective in treating women with hirsutism [29].

Barrionuevo et al. conducted a systematic review and meta-analysis to evaluate the efficacy of various treatment options for hirsutism. The review included 43 clinical trials. The findings indicated that finasteride, whether used alone or in combination with oral contraceptives, led to a significant improvement in hirsutism scores. Specifically, finasteride monotherapy resulted in a reduction of hirsutism scores by 1.48, while the combination of finasteride and oral contraceptives achieved a reduction of 1.64. These results highlight the effectiveness of finasteride in reducing hirsutism and support its use as a treatment option for women with this condition [30].

Adverse Effects and Toxicity

Post-Finasteride Syndrome and Other Reproductive Adverse Effects in Men and Women

The use of 5ARIs for AGA or benign prostatic hyperplasia has been linked to serious adverse effects in men. These effects, including sexual, physical, and mental symptoms, can occur during treatment and persist after discontinuation, leading to a condition called post-finasteride syndrome (PFS). A review by Traish aimed to analyze the scientific evidence supporting the relationship between 5ARI use and adverse effects. The review found multiple studies of varying statistical quality, but overall concluded that there is indisputable evidence linking 5ARI use to serious adverse effects. Reported symptoms include loss or reduction of libido, erectile dysfunction, orgasmic disturbances, depression, anxiety, and suicidal ideation. Generally, these symptoms improve after discontinuing the drug, but patients with epigenetic susceptibility may experience persistent effects regardless of age, drug dosage, or duration of use [31, 32].

The study conducted by Wu et al. aimed to analyze adverse effects reported in the US Food and Drug Administrations (FDA) Adverse Event Reporting System (FAERS) from 2004 to 2014 in patients with alopecia treated with minoxidil and/or finasteride. The analysis revealed that a significant proportion of adverse effect reports (48.2% and 97.1%) for minoxidil and finasteride, respectively, were from men. The ten most commonly reported adverse events were identified for both male and female patients using minoxidil or finasteride. In both genders, finasteride use showed a notably negative impact on the reproductive system. Men commonly reported sexual adverse effects such as ejaculation disorder, decreased or lost libido, decreased semen volume, and sexual dysfunction. Additionally, psychiatric adverse effects including anxiety, depression, and cognitive impairment were reported. Women also reported reproductive toxicity effects, with fetal toxicity and induced abortion being the most frequently reported, followed by miscarriage, cervical stenosis, and endometrial hypertrophy [33]. Nonetheless the FDA warns about possible adverse effects of finasteride use. As for the sexual effects in men, the FDA states that a direct causal relationship with the drug cannot be established. The FDA highlights a clinical trial that found a decrease in the prevalence of prostate cancer with finasteride treatment, but a significant increase in the risk of high-grade prostate cancer. For women of reproductive age, pregnant women, or nursing mothers, the FDA prohibits the use of finasteride because of the risk of male fetal genital malformation; therefore, specific adverse effects in women are not mentioned [34, 35].

Safety

Efficacy of 5ARIs for multiple trichological conditions has been demonstrated in various studies; however, their side effects limit medical prescription, as well as therapeutic adherence by patients. Therefore, treatment guidelines have been created to facilitate medical practice. The Indian Association of Dermatologists, Venereologists and Leprologists (IADVL) recommends caution when prescribing 5ARIs to patients with a history of low sperm count or infertility, particularly if they plan to have children. Lower doses should be prescribed to minimize side effects, ensuring that a daily dose of 0.2 mg adequately suppresses DHT effects on the skin and scalp. Although the 5α-reductase type II enzyme complex has a short half-life of 4–15 h, it takes around 30 days for it to regenerate. Starting treatment with a short-term daily dose of 0.5 mg, gradually increasing if tolerated without adverse effects, is one proposed approach. For women with AGA, using reliable contraception and conducting a pregnancy test before initiating finasteride treatment are advised because of the potential risk of fetal malformation. Adhering to these guidelines ensures the safe and appropriate use of 5ARIs while considering individual patient characteristics and reproductive factors [36].

CONCLUSIONS

Acne, male- and female-pattern AGA, FFA, and hirsutism are complex conditions that share a common underlying mechanism involving androgenic hormones. In the management of these diseases, 5ARIs play a significant role due to their antiandrogenic effects and favorable safety and efficacy profiles. Further research should investigate topical application of 5ARIs in dermatological conditions to assess its impact on patient adherence and adverse effects. Overall, incorporating 5ARIs into daily clinical practice within dermatology should be considered to improve patient outcomes.

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