Finasteride: Facts and Myths

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Abstract: Media reports, Internet sites and misinformation by alternative medicine practitioners recently contributed to a negative image associated with finasteride, leading to apprehension and concern among patients taking the medication. Frequently, even dermatologists seem to be hesitant to prescribe the drug for long periods, mistakenly fearing the occurrence of long-term side effects. Finasteride, either alone or in combination with topical minoxidil, is an excellent option for men with androgenetic alopecia, reducing hair loss, and/or restoring hair growth in 9 of 10 patients. The drug can be taken at any time of the day, with or without food. There are no reports of significant drug interactions or allergies. Because it is metabolized in the liver, the drug should be used with caution in patients with liver diseases, but there is no need to indicate liver function tests frequently yet.

Keywords: Androgenetic alopecia. Finasteride. Adverse effects. 5 alpha-reductase. Androgens.

INTRODUCTION

The association between male pattern baldness and testosterone was first observed by Hippocrates, who reported that young eunuch men had no hair loss. Baldness also does not happen in men with genetic deficiency of 5-alpha-reductase II [1]. Both type I and type II of 5-alpha reductase convert testosterone into dihydrotestosterone (DHT) [1]. Type I is predominant in the skin, including the hair scalp, whereas type II is present in the hair follicles and in the prostate [1]. Meanwhile, there is a decrease in the serum and hair scalp levels of DHT, while there is an increase in testosterone levels in hair scalp.

Finasteride is a synthetic 4-azasteroid compound, derived from the 3-oxo-5 alpha-steroid, a specific inhibitor of the enzyme 5 alpha-reductase II. It has been investigated since the early 1980s, and its mechanism of action is not limited to a simple enzyme inhibition [2]. Finasteride has no hormonal action *per se*, but significantly decreases the levels of DHT in the hair follicle and in the bloodstream. In addition, it does not act as an androgenic, estrogenic, anti-estrogenic or progestogen hormone. Rather, it could be defined as anti-androgen [2]. In men aged 60 years or older, finasteride has no effect, because the enzyme 5-alpha-reductase is not as active as in youth [1].

The drug is absorbed from the gastrointestinal tract and metabolized by the liver, and excreted *via* urine and feces, with a half-life of five to six hours. It should be used with caution in patients who have liver diseases. However, drug interactions of clinical significance were not observed [1].

DIHYDROTESTOSTERONE (DHT) LEVELS AND FINASTERIDE

Niiyama *et al*. [3] stated that finasteride decreases serum DHT levels by 60% to 70%, since it inhibits the enzyme 5-alpha-reductase II. According to the authors, 30% to 40% of patients did not respond to medication, probably due to the action of the enzyme 5 alpha-reductase I on testosterone.

The use of finasteride in men with androgenic alopecia (AA) has been approved by the Food and Drug Administration (FDA) in December 1997, at doses of1 mg/day, butit was not approved for women, due to potential teratogenicity. In this dose, within 24 hours, finasteride lowers DHT levels by 65%and increases the estradiol and testosterone by 15% [2].

Drake *et al*. [4] studied 135 men with alopecia, divided into four groups. A group of 34 patients was administered orally with 0.2 mg per day of finasteride. A second group of 33 patients used finasteride 1 mg/day. Another group of 35 patients used finasteride5 mg/day and a last group of 33 men used placebo. The study scope was to measure the levels of DHT in hair scalp, through biopsy obtained after 42 days of treatment. Patients who used finasteride 5 mg/day had decreased levels of DHT by 65 ± 3%. In the group using 1 mg/day, the reduction was 57 ± 4%. On the other hand, in the group using 0.2 mg/day, the reduction was 54 ± 4%. In the placebo group, there was an increase of 5.4 ± 12% in the levels of DHT in the hair scalp. The authors concluded that, in high

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dosages, around 5 mg/day, DHT inhibition was higher than in the other groups, while in the dosages of 0.2 mg/day and 1 mg/day, the results seemed to be very similar.

Dallob *et al*. [5] analyzed 27 male patients with AA. They treated eight patients with finasteride, 1 mg/day; nine other patients used placebo, and ten were in the control-group, not treated. The age of patients ranged from 35 to 55. The purpose of the study was to assess the levels of testosterone and DHT in the hair follicle and plasma after 28 days of treatment. Hormones were measured on the hair scalp after biopsies and in the blood. After 28 days, the patients who used finasteride had decreased DHT levels from 6.4 ± 1.07 pmol/g to 3.62 ± 0.38 pmol/g, and plasma concentration fell from 1.36 ± 0.18 pmol/g to 0.46 ± 0.10 pmol/g. The finasteride did not affect testosterone levels in the skin and in the plasma as well. In the placebo and control groups there were no changes in levels of testosterone and DHT. The authors concluded that finasteride at a dosage of 1 mg/day decreases the levels of DHT in the hair scalp and plasma.

Roberts *et al*. [6] conducted a study to identify the optimal dosage of finasteride in 693 patients with androgenetic alopecia. The men were evaluated with ages varying from 28 to 36 years old, and they were divided into four groups to use finasteride in the following dosages: 0.01 mg/day, 0.2 mg/day, 1 mg/day, 5 mg/day and placebo. Placebo and finasteride were administered orally. With 0.01 mg/day, there was no therapeutic response, while in the group using finasteride at 0.2 mg/day, there was good response regarding the reduction of the hair loss, and the volume of hair increased too. In groups taking finasteride 1 and 5 mg/day, response was better than in the other groups, but without significant differences between them, thus the authors concluded that the best dosage for the use of finasteride could be 1 mg/day. This latter study has shown thatlowering DHT levels locally and in the plasma might not be enough, as also demonstrated by Drake *et al*. [4] previously. Clinical experience has shown that although DHT levels, both locally and in the plasma, reduce similarly with finasteride dosages of 0.2 and 1 mg/day, the clinical effect of 1 mg/day is higher.

Finasteride is contraindicated in women of child bearing age (Pregnancy Category X), unless they are using contraceptive methods regularly. This is due to the fact that, if a pregnancy takes place, the drug can cause feminization in male fetuses. However, men can keep using the medication, even if their wives get pregnant. Minimal amounts of finasteride are found in the seminal fluid, but with no consequence to the fetus, if the pregnancy happens while he is taking the drug [2]. Besides the risk of birth defects, a previous report [1] has failed to prove the effectiveness of finasteride in the treatment of female androgenetic alopecia. There are no studies on the use of finasteride in children.

INFLUENCE OF HORMONE LEVELS

Camacho *et al*. [7] conducted a study in 2008 which investigated the influence of finasteride 1 mg daily on hormone levels and on hair growth in men of different ages, and with different degrees of alopecia. Two hundred and seventy men aged 14-58 years, with male pattern AA and score III-VI in the Hamilton-Norwood scale, were treated with finasteride, 1 mg/day. Steroid hormones (free testosterone, 5α-dihydrotestosterone, DHEAS, δ4-androstenedione, 17OH-progesterone), PSA and changes in trichogram were determined at baseline and at 6 and 12 months after treatment. Patients were matched for age (older or less than 26 years). In the group of patients ≤ 26 years, high levels of 5α-dihydrotestosterone have been found at the beginning of the treatment, but there was a decrease of 50% between the baseline and the 12th month. This decrease ran in parallel with an improvement of alopecia and increased anagen hairs in trichogram. At 1 year, PSA levels decreased by 20%, mainly in patients older than 26 years. The conclusion was that high levels of 5α-dihydrotestosterone, in patients under 26 years at the start of treatment, could be a predictor of good response to treatment with finasteride, 1 mg/day. The most important androgen is 5α-DHT, due to its ability to address the follicular target organs.

The trichogram performed 6 months after the beginning of treatment, showed that patients under 26 years of age have more anagen hairs compared to patients over 26 years. In patients older than 26 years, the levels of 5α-DHT did not change significantly during treatment and improvement of alopecia was much slower than in the younger group. In conclusion, it was emphasized in this study that patients aged less than 26 years, with high levels of 5α-DHT at the start of treatment, had an excellent response with finasteride 1 mg/day. The decreased levels of 5α-DHT in patients aged ≤ 26 years are associated with a clinical improvement of alopecia. This improvement is more impressive in the first 6 months of treatment. Patients over 26 years of age should always be analyzed by laboratory tests before starting the treatment to check the levels of PSA levels or other hormonal changes.

FINASTERIDE AND SPERM COUNT

There is little evidence that finasteride has a negative effect on the number or on the spermatozoon morphology. In a comprehensive, double-blind, placebo-controlled study, 181 men diagnosed with androgenetic alopecia were randomized to receive finasteride 1 mg or placebo for 48 weeks. The study has not found any significant effects on sperm concentration, total number of sperm per ejaculation, motility or on spermatozoa morphology. The authors concluded that testosterone, not DHT, is primarily responsible for the regulation of spermatogenesis, maturation of spermatozoon and seminal fluid production in the testicles, epididymis and seminal vesicle [8]. Another study [9] demonstrated a significant difference in the number of spermatozoa (34%) after 26 weeks of daily use of 5 mg of finasteride, but the change has become smaller and was no longer significant after 52 weeks and at 24 weeks thereafter. There were no morphological changes in sperm [9].

One very small study [10] analyzed the sperm of three men who were taking finasteride (1 mg/day) for five years. Using transmission electron microscopy, the survey found morphological changes in sperm, compatible with necrosis. One patient presented azoospermia, and the other two presented normal concentrations of spermatozoa, despite severe reduction in motility. After a year of stopping treatment, the tests were repeated and there was a return to normal values. There are also two cases reporting severe azoospermia, which resulted in infertility [11].

These studies led us to question whether patients and partners are having difficulty conceiving. Withdrawal of finasteride in these situations could, theoretically, enhance semen parameters and help the couple, avoiding more aggressive fertility treatments.

SIDE EFFECTS OF FINASTERIDE

The main side effects of the medication reported in men were as follows [12-14]: decreased libido (1.8%), erectile dysfunction (1.3%), decreased ejaculation volume (0.8%), ejaculation dysfunction, hypersensitivity reaction, gynecomastia, severe myopathy, and acute pancreatitis. Altomare *et al*. [15] described 19 patients (14 men and 6 women, with a mean age 28 years old), who developed moderate to severe depression after using finasteride. Some other isolated studies reported the occurrence of depression in patients using finasteride. This side effect needs to be further investigated, but should be considered in patients with a history of severe depression.

Mondaini *et al*. [16] investigated a "nocebo" phenomenon (which happens when an adverse effect is not caused by the pharmacological action of a drug, but the patient's awareness about this adverse effect) with finasteride. They tested this hypothesis in 120 patients using finasteride for treatment of benign prostatic hyperplasia (BPH), which randomly were assigned to groups that were or were not informed about the side effects of medication. After 6 and 12 months, the group that was informed about these effects reported a higher incidence (43%) of sexual side effects than the control group, which was not informed (15%). Thus, it leads them to the conclusion that, sometimes, sexual side effects have more to do with a psychological cause than with a pharmacological cause.

SIDE EFFECTS RELATED TO SEXUAL FUNCTION

Media reports, Internet sites and misinformation by alternative medicine practitioners recently contributed to a negative image associated with finasteride, leading to apprehension and concern among patients taking the medication. Frequently, even dermatologists seem to be hesitant to prescribe the drug for long periods, mistakenly fearing the occurrence of long-term side effects. When they do occur, side effects of finasteride are usually transient and can be solved with medication withdrawal.

Androgens, especially testosterone, increases libido. Any drug that interferes with the action of androgens can be therefore associated by patients to sexual impotence. However, the precise role of androgens in penile erection needs to be fully elucidated. Even a person with low testosterone levels can achieve erection Besides androgens, visual, olfactory, tactile, auditory impacts and imaginative stimuli may directly affect libido. Penile erection is mainly under the control of the parasympathetic nervous system [17].

Sexual side effects of finasteride occur in about 2.1% to 3.8% of cases [18-21]; erectile dysfunction is the most frequent adverse reaction, accompanied by ejaculatory dysfunction and loss of libido [14,18-21]. It was observed that these effects occurred early in the treatment and disappeared with the withdrawal of the drug or soon after a long period of continuous use of the drug. The only causal association between

finasteride and sexual adverse effects is a decrease in the ejaculatory volume due to the predominant action of DHT on prostate [22].

Vaughan *et al*. [23] observed 71 patients with benign prostatic hyperplasia treated with finasteride, 5 mg/day, for seven to eight years. The drug was well tolerated and no major side effects were observed. Some adverse effects in the sexual sphere were observed only in the first year of treatment. A comprehensive review of a total of 73 articles on medical therapies for benign prostatic hyperplasia (BPH) was conducted focusing on the effects of different pharmacological agents on sexual function. The analysis showed that finasteride is rarely associated with ejaculation (2.1 to 7.7%), erection (from 4.9 to 15.8%) and libido disorders (3.1 to 5.4%) [18].

Two trials conducted in 1998 and 1999 have shown that the incidence of side effects of finasteride therapy was comparable to that observed with placebo, and there was no evidence of dose-dependency or increased incidence of long-term treatment (> 12 months) [14,19]. In addition, side effects in patients have disappeared, even when they continued to take finasteride over time.

A long-term study showed that sexual side effects related to the drug, such as decreased libido, erectile dysfunction and ejaculatory disorders, occurred in < 2% of men [20]. These side effects disappeared not only in all men who stopped the drug because of the side effects but also in most of those who continued therapy. The incidence of side effects of finasteride was comparable to those of placebo, both at 1 year and at five years. The incidence of each side effect decreased to ≤ 0.3% after the fifth year of treatment with finasteride.

A large prospective study with 17,313 patients was conducted to investigate the effects of finasteride and other variables on sexual dysfunction as part of the analysis of the Prostate Cancer Prevention Trial (PCPT). Sexual dysfunction was assessed in 17,313 subjects who received finasteride 5 mg over a period of seven years. Finasteride only slightly increased sexual dysfunction, even at a dose of 5 mg (which is higher than 1 mg administered for hair loss), and the impact decreases over time. The authors concluded that the effect of finasteride on sexual functioning is minimal for most men and should not affect the decision to prescribe or take finasteride [24]. A recent review of available literature has also come to similar conclusions [25].

However, more recent studies have documented notorious findings. A study conducted by Irwig *et al*., [26] which was widely reported in the lay press, showed results after conducting standardized interviews with 71 healthy men, aged between 21-46, who reported sexual side effects associated with the use of finasteride (decreased libido, problems with ejaculation and orgasm), persisting for at least three months after medication discontinuation. The average number of sexual intercourses per month decreased and the incidence of sexual dysfunction increased after the use of finasteride ($p < 0.0001$). The mean duration of finasteride use was 28 months and the average duration of sexual side effects was 40 months from the date of medication discontinuation. However, there are many limitations in the study, such as the small number of patients, selection bias, recall bias, lack of previous data on the use of finasteride, besides the fact that no serum hormonal analysis has been made.

An important study previously conducted by Mella *et al*. [27] was a systematic review of 12 randomized controlled trials that evaluated the efficacy and safety of finasteride therapy for a total of 3927 male patients. Moderate quality of evidence was observed for an increase of erectile dysfunction (RR, 2:22; IC 95%, 1.03-4.78) and a possible increased risk of sexual disorders (RR, 1:39; IC 95%, 0, 99-1.95). However, the risk of treatment discontinuation due to adverse sexual effects was similar to that of placebo (RR, 0.88; IC 95%, 0.51-1.49).

A number of isolated reports on cases of the effects of low doses of finasteride on the DNA of sperm, motility and sperm counts have also been published [28,29]. The patients studied were under the investigation for oligospermia and infertility when these findings were discovered. All parameters improved significantly after treatment discontinuation.

Traish *et al*. [30] conducted a review of various published studies and concluded that changes in sexual function, such as erectile dysfunction and decreased libido, were actually reported by a subset of men receiving finasteride, raising the possibility of a causal relationship. The review suggested discussion with patients on the potential sexual side effects and possible alternate treatments before administration of the drug.

In view of the conflicting data and the continuing importance of the subject, the International Society of

Hair Restoration Surgery (ISHRS) created a study group on the controversies and adverse effects of finasteride in order to evaluate the published data and make recommendations. The group published its initial update on the subject as follows:

> "To date, there is no data from numerous double-blind placebo controlled studies conducted regarding the use of finasteride 1 mg/day for treatment of androgenetic alopecia, which has shown the link between the drug and long-term sexual side effects. The reports of these effects come from a variety of inconsistent sources, like some internet sites that attract individuals who claim to have sexual and psychological problems related to the medication. While the erection disorders after discontinuation of finasteride continue being reported in areas of post-marketing surveillance, the incidence of the problem remains unknown. Long-term sexual side effects seems to be a rare event and it is necessary to determine if recent reports represent a true causal relationship or are simply a coincidence, for example, related to other factors such as the high incidence of sexual dysfunction in the general population and/or nocebo effect. Besides, there is little data available about the medical and psychological status of these patients to exclude other potential causal factors.
>
> At present time, the mechanism of interaction between the brain, the metabolism of 5α-reductase and hormones on sexual dysfunction is speculative and poorly understood. Clearly, this is a complex issue that overlaps with other medical fields such as endocrinology, urology and psychiatry. More research is needed to assess the true incidence of these side effects, to determine if there is true causal relationship and identify patients at risk.
>
> Millions of patients have benefited and still benefit from the use of finasteride, with no side effects or minimal and reversible side effects. It is extremely important for the medical community to analyze carefully the reports available and conduct further studies, so that accurate information may be given to our patients and to enable them to make informed choices about the use of the drug."

Thus, evidences available on safety of the drug may be considered questionable, and certainly cannot be ignored. The matter needs further research and more systematic documentation.

There is no doubt that, for the layman, the chance of sexual impotence while taking a medicine for hair loss is frightening, although, theoretically, this risk is minimal. The drug inserts mention the possibility of this side effect and the patient is often unable to distinguish between real contingent risks. Several websites provide a very unfavorable opinion about the side effects of finasteride, contrary to the scientific evidence available. Many blogs discuss these side effects and individual and anecdotal experiences are highlighted and are often documented in an exaggerated and sensationalist manner. Any patient who reads these comments can become understandably apprehensive, and therefore tends to discontinue treatment, or in some cases does not start treatment at all. Losing sexual power to gain hair is not an attractive proposition, although this possibility is remote.

FINASTERIDE AND CANCER

Development of breast cancer in some men who have used finasteride [2] should be taken into consideration as a relevant side effect. Since finasteride has gained ground in the treatment of androgenetic alopecia in women, so far there is no report on the onset of breast cancer in women who have used finasteride. Lee and Ellis [31] emphasize the fact that finasteride produces an imbalance in the association between androgens and estrogens, because the drug inhibits the formation of DHT, a far more potent androgen than testosterone. This imbalance can lead to the formation of gynecomastia and breast cancer in men. The authors report that, in the Prostate Cancer Prevention Trial, 4.5% of men taking 5 mg of finasteride per day developed gynecomastia and, according to the study Medical Therapy of Prostatic Symptoms, of the 1,554 men who used finasteride 5 mg a day, four (0.255%) developed breast cancer, i.e., 200 times more than expected in men who did not use the medication.

Green *et al*. [32] reported the cases of two men who used finasteride 5 mg per day and developed breast

cancer. One of them, aged 59, developed intraductal carcinoma after 35 days of drug administration. The other, aged 63, developed the same type of cancer after a year and a half on the drug. These data deserve to be taken into account, and women who use finasteride should undergo breasts periodic evaluation.

Thompson *et al*. [33] observed a group of 18,882 men over 55 years, without prostate disease confirmed by digital rectal examination and by prostatic specific antigen (PSA) dosage, which used finasteride 5 mg/day or placebo for preventing the onset of prostate carcinoma. After seven years, 9,060 patients concluded the experiment. In the group that used finasteride, 803 (18.4%) of 4,368 patients developed prostate cancer. In the placebo group, 1,147 (24.4%) of 4692 patients developed prostate cancer. The drug proved to be effective in preventing prostate carcinoma, since it reduced the prevalence of cancer in 24.8% compared to the estimated rate for the period; however, one fact caught the attention of researchers: Gleason tumor grades 7, 8, 9, or 10, which is a prostatic carcinoma of high malignancy, was more common in the group using finasteride: 280 (6.4%) of 4368 patients against 237 (5.1%) of 4692 patients in the placebo group. This fact demonstrates that although finasteride can reduce the prevalence of prostate cancer, the development of tumors of high malignancy becomes more frequent. Although the study has been conducted in patients older than those who usually take finasteride, the results are remarkable. These worrying findings about the increase in Gleason score have limited its use as a chemoprophylactic agent.

Patients taking finasteride usually have levels of PSA (prostate specific antigen) decreased by approximately 50%. This was revealed by a study of 355 men, aged between 40 and 60 years, who were stratified into age groups and randomized in a ratio of 4:1 for finasteride 1 mg/day or placebo. Patients aged between 40 and 49 years presented a decrease of 40% in PSA levels on average, and patients between 50 and 60 years had a decrease of 50%. This is consistent with the recommendation that the levels of PSA should be doubled in patients using finasteride 5 mg/day in order to estimate the correct level.

A study [34] showed that finasteride did not induce morphological changes in prostate carcinoma. Pathologists could not distinguish histopathological differences amid carcinomas in the group using finasteride and groups on placebo. Similar histological findings are seen in tissues undergoing androgen deprivation therapy. Changes may be due to the loss of glandular luminal spaces (luminal collapse) and the manifestation of cellular infiltrates, which can simulate high-grade malignant carcinoma.

Mathematical models have examined the role of biases as an explanation for the increased number of cases of high-grade malignant cancers in patients using finasteride. Due to the fact that finasteride decreases prostate volume, the relative size of biopsy site increases. This can also increase biopsy sensitivity and the probability of diagnosing a high-grade malignant disease earlier. Serfling *et al*. [35] demonstrated that a 25% reduction in prostate volume (as it happens during treatment with finasteride) can improve the detection of cancer at 23%. In fact, Kulkarni *et al*. [36] not only found an increased occurrence of high-grade malignant cancers among men with small prostates, but also the same occurrence in radical prostatectomy specimens. The combination of these studies demonstrates that our patients are not at risk when we prescribe finasteride.

RESULTS OF TREATMENT: HAIR COUNT

Kaufman *et al*. [19] evaluated, for one year, 1,553 men aged 18 and 41 years with androgenetic alopecia at the vertex who used finasteride at 1 mg/day. Among these patients, 1,215 continued treatment for another year. The therapeutic effect of finasteride was observed after the third month. At the beginning of the treatment, there was on average 876 hairs per area of 2.54 cm/diameter circle. After a year of treatment, there was a mean increase of 107 hairs per area, and after two years, 138 hairs per area. In the placebo group there was no improvement at that time, and androgenetic alopecia continued progressing. Besides the improvement in hair counts, there was also a decrease in the hair loss and an improvement of hair volume.

Van Neste *et al*. [37] evaluated 212 men with androgenetic alopecia (AA) with ages varying from 18 to 40 years, and 106 of them took finasteride 1 mg/day, and 106 placebo for a period of 48 weeks. At the beginning of treatment and after 24 and 48 weeks, a delimited area of the hair scalp was photographed, and anagen hairs were counted within a 1 cm^2 circle. In patients who used the medication at the beginning of treatment, the average amount of hair was 200 ± 5.2 hairs by 0.5 cm^2, and 124.4 ± 4.9 (62%) were in the anagen phase. The anagen/telogen ratio was 1/7.4 ±

5.4 hairs per cm^2, and 142.5 ± 5.4 (68.5%) were anagen. The anagen/telogen ratio became 2/3.3 ± 0.20. In the placebo group, the amount of hairs was on average 195.8 ± 5.4 hairs per cm^2, and 195.8 ± 5.4 (60%) were anagen. The anagen/telogen ratio was 1/5.7 ± 0.13. After 48 weeks of treatment, the total amount of hairs was on average 186.2 ± 5 hairs per cm^2 (square inch), and 110.2 ± 4.7 (59%) were in the anagenphase. Anagen/telogen ratio was 3 ± 0.13. This study has shown that finasteride not only increases the amount of hair, but also improves its appearance.

Leyden *et al*. [14] studied 326 men with moderate hair thinning in the frontal region, although 50% of patients also had hair thinning in the vertex region. The objective of the study was to evaluate the effect of finasteride in the frontal region, different from study by Kaufman *et al*., [19] which evaluated the vertex. A group of 166 patients used finasteride 1 mg/day and one group of 160 patients was on placebo. Initially a hair count per square centimeter was performed in the frontal region in both groups, resulting in 211 ± 4 hairs per square centimeter in the group using the medication, and 219 ± 5 in the control group. After a year of treatment there was an increase of 9.6 ± 1.5 per square centimeter in the group on finasteride, while in the placebo group the hairs decreased 2 ± 1.5. Among patients taking finasteride, 50% noticed increased hair volume and 70% reported a decrease in hair loss.

The analysis of these two studies, assessing separately the frontal and vertex regions, has shown that finasteride stabilizes the process of hair loss in 83% of AA cases on the vertex, after two years of treatment, and 70% of cases of frontal region, after one year of treatment. Hair growth occurred on the vertex 61% of cases after two years, and in 37% on the frontal region after one year.

Whiting *et al*. [38] studied a group of 424 men with ages varying between 41 and 60 years, who had androgenetic alopecia and used finasteride 1 mg/day for two years. Finasteride has shown better efficacy in patients who had predominantly androgenetic alopecia on the vertex. The results were very evident in the first six months of treatment, and remained stable until the second year.

Finasteride has shown to be useful in fixing a hair transplant. A randomized, double blind study involving 79 men with AA treated with finasteride 1 mg/day or placebo, for four weeks before and 48 weeks after the hair transplant, showed that the treated group had a significant improvement compared with the group on placebo.

COMBINED TREATMENTS

Finasteride is an excellent option for men with AA, either alone, or in combination with topical minoxidil. It reduces the hair loss, and/or restores hair growth in 9 of 10 patients [39]. The drug can be taken at any time of the day, with or without food. There are no reports of significant drug interactions or allergies. The drug is metabolized in the liver, and therefore should be used with caution in patients with liver diseases, but there is no need to have liver function tests frequently. It is recommended to wait at least six to nine months for therapeutic results to show up; although the package inserts (leaflets) usually indicate three months.

Hugo Perez [40] has shown that the combination of finasteride with shampoo based on 2% ketoconazole is more effective than finasteride administered alone.

Arca *et al*. [41] used 5% topical minoxidil or finasteride 1mg/day orally in 65 male patients with moderate or severe AA, for a period of 12 months. Forty patients received finasteride and 25, minoxidil. Increase in hair volume was observed in 32 (80%) of patients in the group using finasteride versus 13 (52%) in the group receiving minoxidil. Both drugs have proven to be effective, but finasteride has shown to be more effective ($p < 0.05$).

FINAL CONSIDERATIONS

In view of all this, it is extremely important to properly advise and inform the patient, thus ensuring adherence to treatment and the effectiveness of therapeutic response. Particularly, the following points need to be addressed and highlighted:

1. The drug is probably the best available for the treatment of AA and the one approved by the regulatory agencies capable to attack the root of the problem.

2. Its effects are proven scientifically.

3. Several studies have demonstrated its safety over long duration of administration. The indicated dosage (1 mg) is considered low and the probability of this dose to cause side effects is minimal. Even in cases in which adverse reactions were reported, the changes reverted after cessation of use.

4. There are very few effective alternatives to finasteride, and therefore it is important that the patient does not stop treatment, unless when experiencing any side effects.

5. When in doubt, the patient should contact the doctor, informing him about any side effect presented.

6. Drug use is entirely voluntary, as male pattern baldness is just a cosmetic condition; it is up to the patient to decide whether or not to take finasteride.

7. The physician should provide full information about the drug, thus allowing the patient to make informed decisions.

8. It is prudent to avoid the indication to patients with a prior history of oligospermia and/or infertility, especially if they are newly married and are aiming to build a family.

Moreover, in patients who are anxious about side effects, it is worthwhile considering the administration of lower daily doses or staggered doses to enhance patient compliance to the treatment. As previously discussed, there is support for the initial administration of the schemes proposed. The plasma half-life of finasteride is 6 to 8 hours and tissues binding last from 4 to 5 days. An average dose of 0.2 mg/day is adequate to suppress the action on the hair scalp and the levels of DHT in serum. While 0.2 mg of finasteride per day can cause 55% DHT suppression, 5 mg achieved 69% DHT suppression.

Therefore, the drug may be initially administered at a 0.5 mg/day or 1 mg on alternate days, in order to gain the confidence and compliance of the patient by increasing the dosage to 1 mg/day, once the patient is comfortable and positive in relation to treatment.

CONFLICTS OF INTEREST

None.

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