International Journal of Dermatology, Venereology and Leprosy Sciences

E-ISSN: 2664-942X
P-ISSN: 2664-9411
www.dermatologypaper.com
Derma 2024; 7(1): 10-20
Received: 05-11-2023
Accepted: 11-12-2023

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Female pattern hair loss

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DOI: https://doi.org/10.33545/26649411.2024.v7.i1a.169

Abstract
Female Pattern Hair Loss (FPHL) is the predominant hair loss condition among women. The etiology of this phenomenon is polygenic and multifactorial. Yet no treatment is satisfactory.

Keywords: Female pattern hair loss (FPHL), hair loss condition, etiology

Introduction

Hair cycle

The hair follicle (HF) represents a dynamic complex little organ [1] that once developed it undergo lifetime cyclical transformations categorized by episodes of speedy growth (Anagen), transformation (Catagen), relative quiescence (Telogen), and shedding (EXOGEN) [2] (Figure 1).

Habitually, hair cycling is not synchronous; in other words, the approximately 100,000 hairs roughly an individual's head grow independently for the seek of prevention of the occurrence of mass shedding of hair. Intrinsic or extrinsic factors may cause synchronization of the HF by persuading a premature transition from anagen phase to the telogen one so, manifest hair loss 2-4 months later take place. Hormones, drugs, growth factors, and the seasons are some of these contributory factors [3].

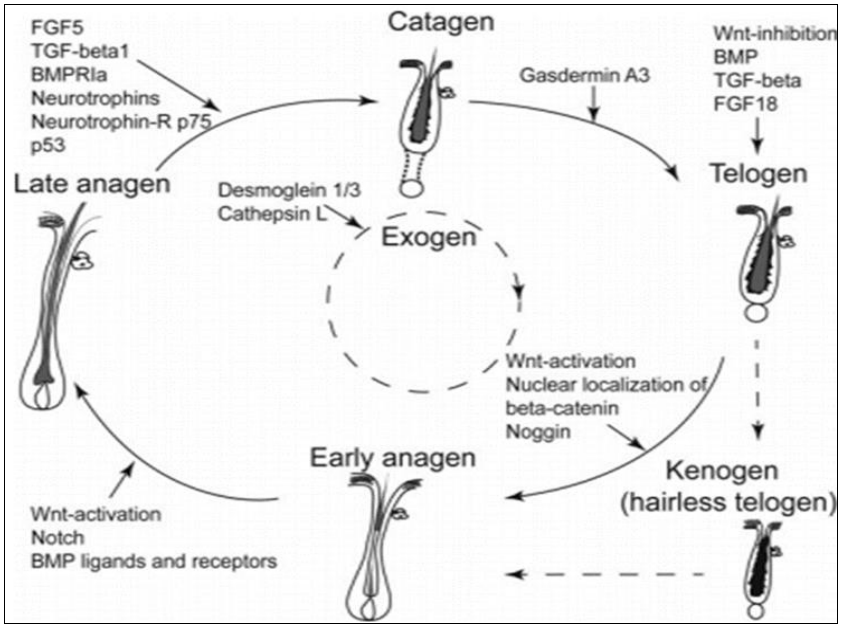

Fig 1: Key stages of the hair cycle [4]

- **FGF5:** Fibroblast Growth Factor 5.
- **TGF-eta 1:** Transforming Growth Factor beta -1.
- **BMPRIa:** Bone Morphogenetic Proteins Receptors Inhibitors a.

- **P53:** P53 gene.
- **Wnt-activation:** Wnt- pathway activation.
- **Wnt-inhibition:** Wnt-Pathway inhibition.
- **BMP:** Bone Morphogenetic Proteins.
- **FGF18:** Fibroblast Growth Factor 18.

Anagen

During this growth stage that lasts from 2 to 6 years hair grows at a rate of approximately 0.3 mm/day, or 1 cm each month. The maximum achievable hair length is determined by the duration of the anagen phase, which varies depending on the kind of hair and its location. At any one moment, almost 90 percent of hair follicles on the scalp are in the anagen phase [3].

Throughout the anagen, matrix cells that are quickly proliferating, also called transit-amplifying cells, undergo differentiation as they travel upwards from the hair bulb. This process results in the formation of one of the six layers of the HF and the hair shaft [5].

Catagen

As the number of rapidly dividing matrix cells decreases, the HF undergoes the catagen phase, in which the bottom part of the HF regress and hair growth stops. The regression is caused by the programmed cell death of the lower HF, resulting in the formation of a strand of epithelial cells termed the hair club. This strand climbs upwards till reaching the upper, non-cycling part of the HF, bringing the dermal papilla near to the bulge of the HF. The duration of this phase on the human scalp is around three weeks [5].

Telogen

The telogen phase is sometimes referred to as the quiescence or resting phase. It occurs after the catagen phase and has a duration of 2 to 3 months on the scalp [6, 7].

EXOGEN

The EXOGEN phase of the HF, which involves the shedding of telogen hair, occurs simultaneously with the conclusion of the telogen phase. In a typical scalp, around 90-95% of the hair follicles are in the anagen phase, while the remaining 5-10% are in the telogen phase. On a daily basis, around 100-150 hairs are lost. Only a limited number of HF will develop in the transitional or catagen phase. The biological clock that regulates the transition from the anagen phase to the catagen/telogen phase is an intricate phenomenon, the underlying molecular mechanisms of which are now being revealed [8].

Etiology and pathophysiology

The underlying mechanisms of FPHL are still not fully understood, and there are very few options for therapy that have strong scientific evidence to support their effectiveness. This makes managing FPHL a difficult task.

The development of FPHL is intricate, including several genes and factors, and is most likely initiated by a genetic predisposition and environmental influences [9]. Initially, it was thought that androgens were the cause of FPHL, which is why it is referred to as androgenic alopecia [10]. This concept has been disputed due to the existence of studies documenting women with FPHL who are unresponsive to androgens. Therefore, in this particular group of individuals, the occurrence of FPHL is attributed to causes unrelated to androgens [9]. Polygenic vulnerability and persistent low-grade inflammation in the scalp may contribute to or cause loss of hair in FPHL [10].

In hair shaft biopsies of FPHL, there is often indication of a micro folliculitis around the hair bulge of the miniaturized hairs. This observation is absent around the terminal hairs, indicating that inflammation is a contributing factor in FPHL [11].

The rise in FPHL with age, particularly in postmenopausal women, indicates a potential preventive effect of estrogen. In addition, it was shown that young women had significantly elevated amounts of cytochrome p-450 aromatase, an enzyme that has the ability to convert testosterone into estrogen, in both frontal and occipital follicles compared to males. The observed elevation in aromatase levels seems to have a beneficial effect in preventing hair loss in women [12].

Hair cycle changes

Female Pattern Hair Loss is characterized by the gradual shrinking of HF and the transformation of terminal HF into vellus-like ones. These follicles, resembling vellus hair, have a shorter hair growth cycle due to a decrease in the anagen stage, resulting in the creation of short and thin hair shafts. In contrast to males, women do not experience uniform and strong miniaturization, resulting in the absence of full areas of baldness, unless in very rare instances that have been overlooked and left untreated [13].

Additionally, the process of miniaturization may result in a mild-to-moderate infiltration of lymphohistiocytic inflammation in the peri-infundibular area. The term "micro-inflammation" is utilized to distinguish this infiltration from the inflammation that takes place in scarring alopecia [13] (Figure 2).

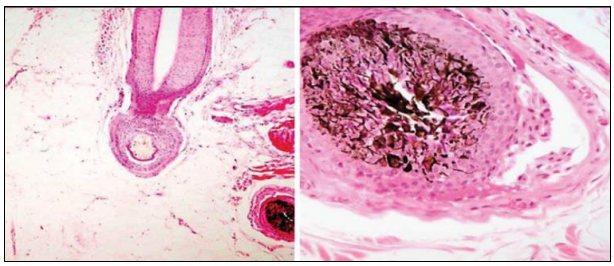

Fig 2: A. Catagen hair with miniaturization×40. B. Follicular bulb with melanic pigment casts and a peribulbar lymphocytic inflammatory infiltrate. Original magnification×60 [14]

The pathogenesis of these changes are

Androgens

Androgen has a recognized impact on the development of both scalp and body hair [15]. Dihydrotestosterone (DHT) is a very powerful androgen that is produced by the metabolic conversion of testosterone by the 5α-reductase enzyme [15].

Dihydrotestosterone has a higher affinity for androgenic receptors in HF compared to testosterone. This leads to the activation of genes involved for the progressive conversion of terminal HF into miniaturized HF as illustrated in [16] (Figure 3).

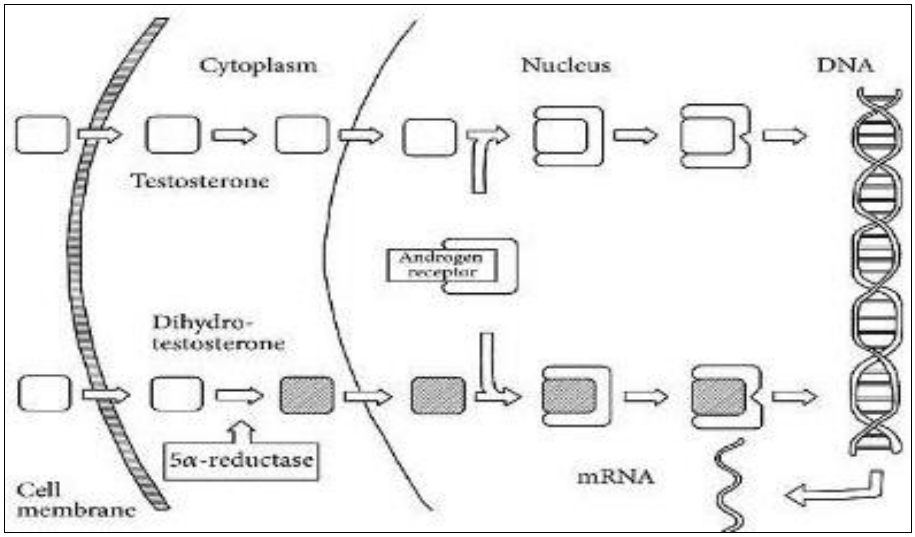

Fig 3: Schematic of the general mechanism of androgens action [12]

Testosterone and DHT attach to the androgenic receptor inside the cell. After the hormone has attached, the compound will attach to the DNA, modifying the expression of certain genes that rely on androgens.

The distribution of hair loss, which usually does not affect the back of the head, indicates variations in the susceptibility of scalp HF to androgens. Several writers have postulated that the development of FPHL may involve a similar mechanism, which is further supported by the discovery that women with excessive levels of androgens may have FPHL at an earlier age [12].

Genetic factors

There is less knowledge on the influence of genetic variables in FPHL. Several individuals observed a higher occurrence of balding among the immediate male relatives of 56 women experiencing hair loss compared to women without any family history, indicating a shared genetic effect. Conversely, research including twins in older women did not find any indication of a genetic factor in hair thinning. However, there was a significant inherited impact on fronto-temporal recession. Empirical evidence indicates that early-onset FPHL is hereditary. However, studies have shown that the degree of heritability is more strongly associated with male balding than with female pattern hair loss [17].

This genetic predisposition allows for the normal amounts of circulating androgen to have an effect on certain cells in the follicles. These cells are particularly sensitive because they attach to specific androgenic receptors within the cells. Alternatively, in certain instances, the development of FPHL may be influenced by a process that is not reliant on androgens [13].

Clinical features of female pattern hair loss (FPHL)

FPHL may manifest in three distinct patterns

1. The crown portion of the head is experiencing thinning hair, but the hairline at the front remains intact. Two scales, namely the 3-point Ludwig scale [21, 29] (Figure 4) and the 5-point Sinclair scale [11, 12] (Figure 5), are employed to characterize this pattern.
2. The core area of the scalp is becoming thinner and wider, causing the frontal hairline to recede. This is referred to as the Christmas tree pattern according to the Olsen scale (Figure 6).
3. Thinning hair due to receding hairline on both sides; measured using the Hamilton-Norwood scale.

All of these typical patterns avoid affecting the occipital region. The variations seen may be attributed to the embryological origin of the dermis in the respective locations. Avian embryology reveals that the dermis of the frontal/parietal scalp originates from neural crest cells, while the dermis of the occipital scalp originates from mesodermal cells [18]. (Figure 4).

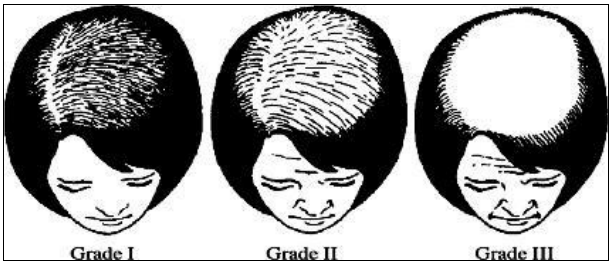

Fig 4: Ludwig scale [11, 12]

- **Grade I:** Noticeable hair thinning on the crown, with a restricted area in the front extending 1-3 cm below the frontal hairline.
- **Grade II:** There is a noticeable decrease in the density of hair on the top of the head, such as in the same region as Grade I.
- **Grade III:** Complete alopecia (Complete denudation) within the same region as Grades I and II (Figure 5).

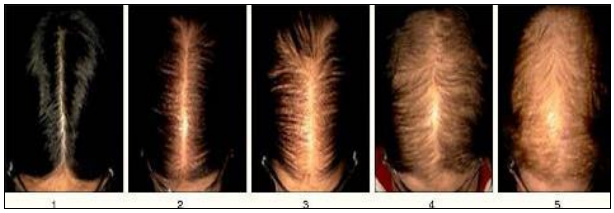

Fig 5: Sinclair Scale [11]

- **Grade 1:** is considered to be within the normal. This pattern is seen in prepubescent girls, but it is only observed in 45% of women who are eighty years old or

older.

- **Grade 2:** demonstrates an expansion of the center region.
- **Grade 3:** is characterized by a broadening of the middle section of the hair and a reduction in hair thickness on both sides of the middle area.
- **Grade 4:** indicates the appearance of a widespread hair loss on the upper part of the scalp.
- **Grade 5:** denotes significant loss of hair (Figure 5).

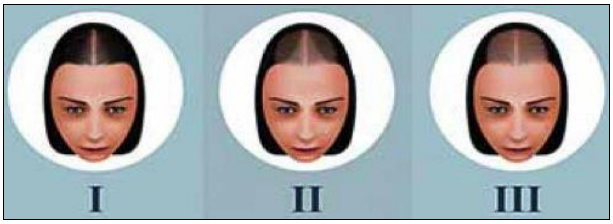

Fig 6: Olsen scale [11]

Olsen introduced a categorization system (figure 6) that resembled Ludwig's classification but included the emphasis on fronto-vertical alopecia, characterized by a triangular or "Christmas tree" pattern. Olsen noted that loss of hair in women may manifest as a discreet pattern of thinning that becomes evident when parting the hair along the midline. This pattern often involves a gradual reduction in the density of hair from the crown of the head to the front of the scalp, resembling a distribution of loss like a "Christmas tree". This pattern is seen in both the initial and later phases of hair loss.

- **Grade I:** Noticeable hair thinning on the crown.
- **Grade II:** There is a noticeable thinning of the hair on the top of the head, namely in the same region as Grade I.
- **Grade III:** Complete alopecia (Complete denudation) within the same region as Grades I and II [11].

Diagnosis of female pattern hair loss

Diagnosis of FPHL is usually straightforward from the history and examination of the hair and scalp [18].

Patient history

The patients often report experiencing persistent loss of hair with intermittent times of greater activity, notably in autumn and winter seasons. While a positive family history is more common, it is important to note that a negative family history doesn't always rule out the diagnosis. A comprehensive gynecological and obstetrical assessment should be conducted to rule out any underlying hormonal dysregulation that may be affecting the individual [19].

Physical examination

Scalp and Hair Scalp Examination

When examining the scalp and scalp hair, it is important to specifically look for patterns of hair loss and assess the thickness of the hairs in certain regions. Indications that align with FPHL involve the observation of hair loss at the front and/or top of the scalp, as well as the presence of thinner and shorter hairs, also known as vellus hairs [19].

Trichoscopy or scalp dermatoscopy

Trichoscopy, also known as scalp dermatoscopy, is a noninvasive diagnostic technique that is performed in a medical office. It is very beneficial for diagnosing and monitoring hair and scalp diseases [19].

Scalp follicular units (FU) typically consist of a maximum of four hairs. In a typical scalp, a single pore will produce a tuft of one main hair and 1-3 additional hairs. In FPHL, both the overall quantity of terminal hairs and the number of terminal hairs per FU decrease as the severity of the condition increases. Comparing the occipital scalp is crucial because telogen effluvium leads to a decrease in double and triple follicular units over the whole scalp [20].

In addition, the existence of short vellus hair measuring 0.03 mm on the frontal scalp is a significant indication of severe miniaturization and may be used as a valuable diagnostic clue for FPHL. Other signs of severe miniaturization include yellow dots, which are more common in individuals who suffer from severe FPHL, as well as pinpoint white dots and scalp pigmentation, which appear as a honeycombed-like pattern on the scalp exposed to the sun. The peripilar sign, which is something particular in the early stages of the disease, indicates perifollicular inflammation and is only visible in active and early diagnosed cases that are untreated. Focal areas of baldness, known as atrichia, can be observed in postmenopausal women. The diagnosis of FPHL can also be confirmed by calculating the ratio of terminal-to-vellus hair, with a ratio of 4:1 considered diagnostic of FPHL [20].

In 2009, Rakowska *et al.* [21] introduced major and minor diagnostic trichoscopic criteria for the identification of FPHL.

The major criteria consist of three characteristics: (1) there are more than four yellow spots present in the frontal region of the four images. (2) The average thickness of hair in the frontal area is lower contrasted to the occiput. (3) Over 10% of the hairs in the frontal area are thin, measuring less than 0.03 mm in thickness (Figure 7).

The minor criteria consist of three characteristics: (1) an elevated ratio of single-hair pilosebaceous units from the front to the back of the head; (2) the presence of vellus hairs; and (3) discolouration around the hair follicles. The diagnosis of FPHL is established when there are two main criteria present, or one major criterion together with two minor factors [21].

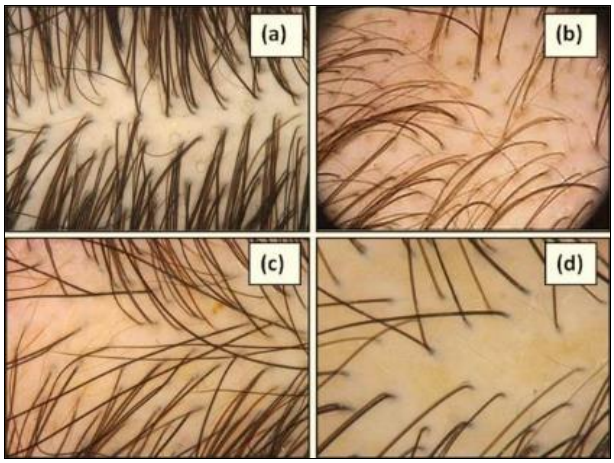

Fig 7: Scalp trichoscopy of female pattern hair loss [20, 22]

(a) and (b), Diagnosis is established by the existence of over 20 percent variety in hair diameter, indicating variability

and decrease in hair shaft caliber, especially in the frontal region of the scalp. This may be seen at standard magnification.
(b) Additionally, there are yellow dots exist, a decrease in the number of triple hair follicular units (less than 10% of all follicular units), and an increase in single hair follicular units (approximately 50%).
(c) The diagnosis is established by the existence of 10% (or more) short vellus hairs on the frontal area of the scalp when viewed at 20× magnification.
(d) This is a later stage of FPHL, characterized by a high proportion of single hair FU. There are also thin, short regrowing hairs on the frontal area of the scalp, which can be observed at standard magnification.

Scalp biopsy
It is widely considered to be the most reliable method for diagnosing FPHL. Nevertheless, the utilization of trichoscopy has led to a substantial decrease in the requirement for diagnostic scalp biopsy in FPHL. The diagnosis is established when the ratio of terminal to vellus-like hair is less than 3:1 (with a normal ratio being more than 7:1), and there are no other visible abnormalities. Histology may also determine the level of inflammation, that seems to affect the potential response to minoxidil treatment [19].

Laboratory tests
Measurements may be taken for serum ferritin, serum vitamin D, and thyroid-stimulating hormone levels. Women with FPHL were found to have substantially decreased levels of ferritin and vitamin D contrasted to the control group [23].
The consensus among professionals is that a comprehensive endocrinological examination is not required for every woman. A study will be conducted on women with FPHL who exhibit symptoms of androgen excess, such as hirsutism, acne, irregular menstrual cycles, and galactorrhea, to investigate the hyperandrogenic condition [23].

Differential diagnosis
Differential diagnosis of a diffuse alopecia with the FPHL involves.

Telogen effluvium (TE): Clinically there is a history of stressful condition in previous 3 months as: exams, labour, lactation surgical operation or severe medical illness, hair falling is evident & affects the whole scalp. By dermoscopy: peripilar brown halo, focal atrichia, pilosebaceous single and double hair units, honeycomb pigmentation, white dots, short vellus hair, reduced hair density with existence of empty follicles. On trichoscopy, telogen effluvium is a disease of exclusion.

In FPHL: Clinically patients complaint is hair thinning not hair loss mainly affecting the vertex. By dermoscopy: there was a variation in the thickness of the hair shaft of over 20%, and over 10% of the hair examined was short and lacked pigmentation, known as hypopigmented vellus hair. The study revealed a proportion of single hair units, which refers to hair follicles containing one or two hairs instead of three or more. Additionally, yellow spots were seen, which are empty follicular openings filled with keratin and sebum. Furthermore, the peripilar sign was present, indicating perifollicular hyperpigmentation related to perifollicular inflammation. We must put in mind that chronic TE may be a prodromal for FPHL [24]. Dermoscopic comparison between FPHL and TE shown in (Figure 8 & 9).

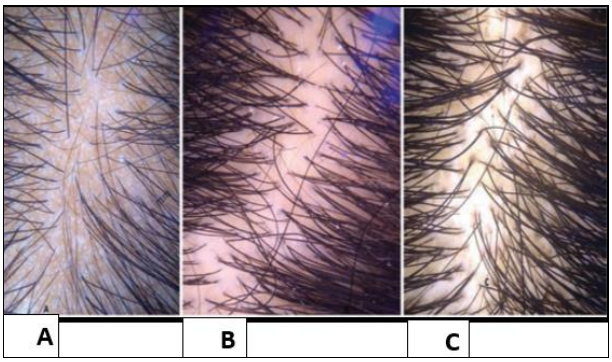

Fig 8: Comparative dermoscopic picture showing hair diameter diversity [24] over frontal area in, A): Female Androgenetic Alopecia, B): Telogen effluvium, C): control (magnification x10)

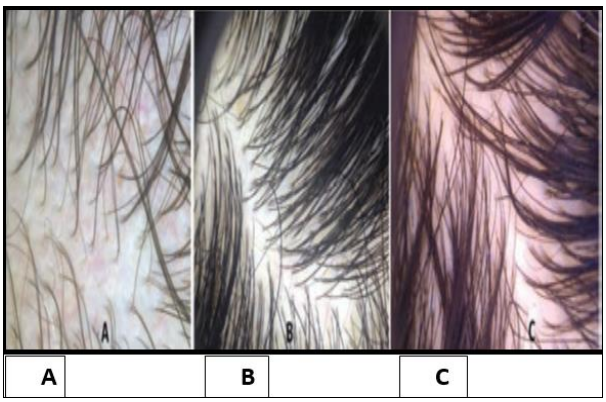

Fig 9: Comparative dermoscopic picture showing hair diameter diversity [24] over occipital area in, A): Female Androgenetic Alopecia, B) Telogen effluvium, C): control (magnification x10)

Cicatricial alopecia: In pattern distribution(History of trauma or chronic inflammation, scarring is evident clinically, no active hair follicles by dermoscopy and dermoscopic findings differ according to the cause as post-traumatic and scalp DLE (Figure 10) each has its special trichoscopic features [25].

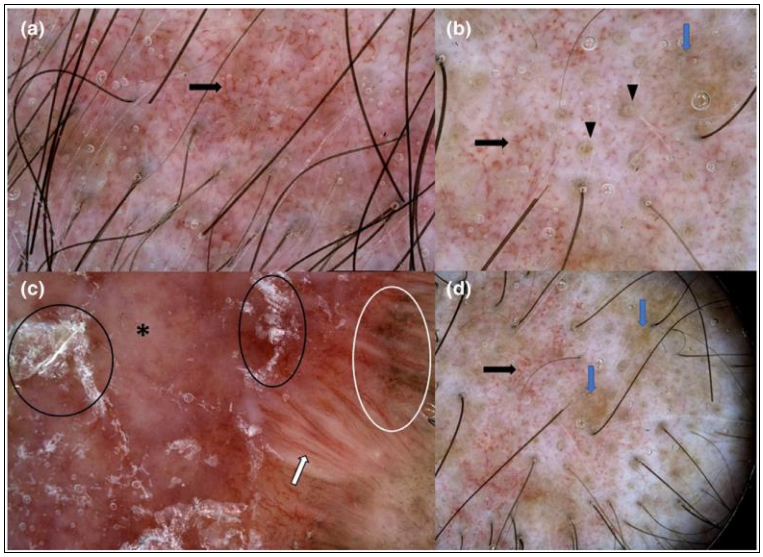

Fig 10: (a) (b) (c) (d) Demoscopic findings in scalp discoid lupus erythematosus [25]

- Thin arborizing vessels (black arrows) large yellow dots (black arrowheads).
- Speckled yellow-brown pigmentation (Blue arrows) white scales (Black circles).
- Peripheral pigmentation (White circle) hairpin vessels (White arrow) pink-white background (Black asterisk).

Alopecia areata: (Diffuse or incognita):(history of stress or autoimmune disease, eye, dental or ENT troubles, the pattern of hair loss, dermoscopic finding of alopecia areata:" black dots (Figure 12), vellus hair, white dots, honeycomb pigmentation, circular hair, coudability sign, yellow dots (Figure 11), tapering hair (Figure 13) or exclamation mark (Figure 14), pili bifurcate like features and broken hairs (Figure 15): (Is evident & not that of FPHL). Dermoscopic findings in alopecia areata are demonstrated below (figures 11-115) Dermoscopy is an effective adjunctive technique that aids dermatologists in diagnosing scalp diseases [26].

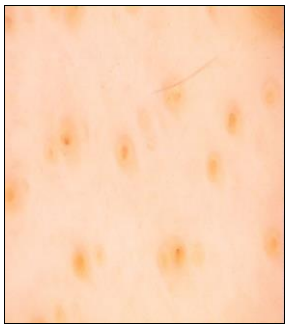

Fig 11: Yellow dots in alopecia areata [26]

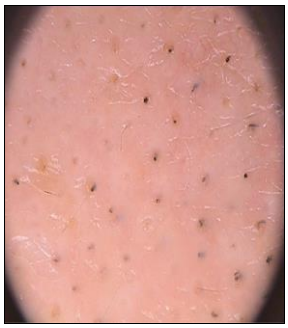

Fig 12: Black dots in alopecia areata [26]

Fig 13: Tapering hairs in alopecia area [26]

Fig 14: Exclamation mark in alopecia area [26]

Fig 15: Broken hairs in alopecia area [26]

Treatment of FPHL

Therapeutic options exist for FPHL, while a permanent solution does not yet exist. It is very important to know Yet, no treatment is satisfactory for patients nor physiacins in most of cases. Treatment options for women with FPHL are either topical or systemic [27]. It includes.

Medical treatment

First-line treatment (Androgen-independent medications).

- Minoxidil.
- Aminexil.

Second-line treatment (Androgen-dependent medications).

- 5-alpha-reductase inhibitors.
- Estrogen and oral contraceptive.
- Androgen receptor blockers.

Others

1. Prostaglandin Analogs: (PGE2).
2. Platelet-rich plasma (PRP).
3. Lasers and Light Treatments:

- Low level laser therapy(LLLT)
- Fractional lasers.

1. Threads.
2. Mesotherapy.
3. Herbal & natural therapy.
4. Cosmetic aid (camouflage).
5. Surgical treatment.

- Hair Transplantation.
- scalp reduction

Medical treatment

First-line treatment (Androgen-independent medications)

A. Minoxidil: (Will be discussed in details later on)

B. Aminexil

Aminexil, a derivative of minoxidil, can be found in shampoo and vial forms. However, it has not received approval from the U.S. Food and Drug Administration (FDA) or the European Medicines Agency (EMA) [28].

Aminexil is generally recognized as a very popular hair growth stimulant. The management of androgenetic alopecia included the utilization of Aminexil nanostructured lipid carrier, which was created using the pre-emulsion ultrasonication process. It is characterized by being more effective and less side effects than minoxidil but it is very expensive and most of patients can't afford its coast specially in long term therapy that must be followed in androgenetic alopecia [28].

Second-line treatment (Androgen - dependent medications)

5-alpha-reductase inhibitors

Mechanism of action

5-alpha-reductase inhibitors prevent the conversion of testosterone to DHT, resulting in androgens that have less binding affinity to their receptors. Finasteride is an inhibitor of the enzyme 5-alpha-reductase type II. While it has been authorized by the FDA for treating male androgenetic alopecia, it does not have FDA approval for treating FPHL. Finasteride is highly teratogenic and has been shown to induce feminization of male fetuses, along with sexual side effects, headache, depression, nausea, and hot flushes [29].

Dose

A research using modest dosages (1 mg daily) shown no statistically significant advantage in the first group. Nevertheless, the administration of a daily 2.5-mg dosage of finasteride in conjunction with an oral contraceptive pill resulted in hair loss improving for 62% of individuals within the second group. In the third group of the trial, it was seen that administering a daily dosage of 5 mg of finasteride for a duration of 12 months resulted in a notable augmentation in both hair thickness and density. Finasteride is categorized as pregnancy category X [29, 30].

Dutasteride is a medication that inhibits the activity of 5-alpha-reductase enzymes, specifically both type I and type II enzymes. When contrasted to finasteride, this substance is three times more effective at inhibiting type II enzymes and 100 times more effective in inhibiting type I enzymes. Dutasteride lacks FDA approval for treating FPHL, and current trials mostly concentrate on male patients, however they provide encouraging results about the effectiveness of the inhibitor [31]. Dutasteride is categorized as pregnancy category X due to its teratogenic effects and is expected to have a similar theoretical risk of breast cancer as finasteride [30, 31].

Androgen receptor blocker

1. Spironolactone: (Will be discussed in details later on)

2. Cyproterone acetate

Mechanism of action

It works in several ways. It not only effectively prevents DHT from attaching to its receptors in target tissues, but it additionally has progestogen-like action, which reduces testosterone levels by suppressing the production of LH and FSH via pituitary-mediated suppression [32].

Dose

The administration of cyproterone acetate as a combination therapy involves a dosage of 2 mg in oral contraceptives together with ethinyl estradiol up to 100 mg/day. This medication is often given on days five to 15 of the menstrual cycle [33].

Side effects

Important side-effects are depression, breast tenderness, weight gain, and loss of libido. Severe fetal affection and teratogenicity as cyproterone acetate is categorized as pregnancy category X [33].

Flutamide

Mechanism of action

This substance is an oral anti-androgen that works by competitively blocking the absorption of androgen and it's binding to the nucleus in certain tissues [32].

Dose

Research has shown that a daily dosage of 250 mg is beneficial in treating FPHL in women with excessive levels of androgens [32, 34].

Side effects

Flutamide has the potential to induce liver damage, hence it is advised to regularly monitor liver function tests while on therapy. Flutamide is categorized as pregnancy category D [32].

Estrogen and oral contraceptive drugs

Mechanism of action

The function of estrogens in human hair development is still unknown. The HF has distinct estrogen receptors, namely alpha and beta. The beta receptor is the predominant receptor found in the scalp, and it generally inhibits cellular activity in the HF [35].

There is a suggestion that persons who are genetically vulnerable to a certain illness may be more likely to acquire it if they have a low ratio of estrogens to androgens. Controlled trials investigating the effectiveness of topical estrogens for loss of hair have shown conflicting findings. Oral estrogen is of limited role in treatment of FPHL because of unwanted side effects of oral hormonal therapy as predisposition to cancer breast [35].

Dose

Topical estrogens that may be used include fulvestrant, which should be used twice daily, or topical estradiol valerate 0.03%, which should be applied once daily [35].

Others

1. Prostaglandin Analogs: (PGE2)

Latanoprost and bimatoprost were originally created as treatments for glaucoma. The unintended effect of these medications was the stimulation of eyelash development. A single research conducted on males shown that the application of latanoprost 0.1% resulted in an enhancement in hair density on the scalp as contrasted to both the initial state and a placebo. However, it is important to note that this study had a limited sample size of only 16 male participants, and the medicine was given to a tiny region of the scalp. However, it is important to be cautious since various categories of prostaglandins seem to have opposing effects on the hair follicle [32].

2. Platelet-rich plasma (PRP)

Platelet-rich plasma (PRP) is a concentrated form of platelets that is derived from the patient's own blood and suspended in a tiny amount of plasma. It promotes the renewal of the skin and hair follicles by containing a variety of growth factors and cellular adhesion molecules that speed the healing process [32].

Procedure and mechanism of action

PRP is obtained by centrifuging the patient's own blood. It includes growth factors that act on specific cells involved in wound healing. As a result, PRP plays a crucial role in tissue repair processes and promotes the healing and regeneration of soft tissues at different stages [33].

The PRP consists of about 20 different growth factors, including Vascular Endothelial Growth Factor (VEGF), Platelet-Derived Growth Factor (PDGF), and Transforming Growth Factor (TGF-β1). These substances control the movement of cells, their growth, the restructuring of the extracellular matrix (ECM), and the stimulation of blood vessel formation, which together provide a favorable environment for improved wound healing [33].

While there may be variations in the way studies are conducted, including differences in how patients are chosen and the treatment methods used, certain authors have observed that after undergoing five local treatments of 3 mL of PRP at intervals of 2 to 3 weeks, there were indications of regrowth. Histologic examinations revealed thickened epithelium, developed collagen fibers and fibroblasts, and enhanced blood vessels surrounding the hair follicles. It is considered as adjuvant method for treatment of FPHL with efficacy of about 5% [32, 33].

3. Lasers and Light Treatments

A. Low Level Laser Therap

It refers to photo-biomodulation using light of wavelength ranging usually from the red (600-700 nm) or infrared (700-1,000 nm) spectrum, at low power densities (<100 mW/cm^2) and fluences (0.04-50 J/cm^2) [36]. FDA has approved the first LLLT device for AGA treatment in 2007 [37], as it has a proliferative effect on different tissues and cells, including hair follicles [38]. This effect has been discovered when a paradoxical hair growth was noted in association with hair removal by laser devices or intense pulsed light of low fluency [36].

Low level laser therapy promotes the progression of telogen follicles into anagen follicles and lengthens the anagen phase. This alteration in hair cycle is pronounced as increased hair density and shaft diameter and decreased hair shedding [37]. The mechanism by which LLLT performs its effect on hair follicles is still not fully understood. It is assumed that red/infrared light is absorbed by cytochrome c oxidase, which in turn releases nitric oxide. This leads to generation of adenosine triphosphate and reactive oxygen species by the electron transport chain. Moreover, it induces transcription factors. Eventually, this leads to vasodilatation, proliferation of cells and modulation of growth phases of hair follicles [38]. Other studies showed that LLLT decreases PGE2 and increases the anti-inflammatory cytokines [39].

Standard protocol for LLLT in AGA treatment is under study, as there are different devices and methods. It is suggested that using red/infrared light at doses of 2-4 J/cm2 is appropriate for treating AGA [40]. A duration of 16 weeks by LLLT is proved to be sufficient to produce a clinical effect [39]. LLLT is generally well tolerated, with few infrequent side effects as acne, mild burning sensation, dryness of skin, headache, urticaria and mild scalp pruritis [41].

B. Fractional lasers

A recent modality of AGA treatment is different types of fractional laser; ablative CO_2 laser, ablative Erbium: YAG laser, non-ablative Erbium glass laser and non-ablative Thulium laser. Generally, fractional lasers act by increasing vascularity and stimulating the stem cells of hair follicles, which in-turn causes anagen phase induction. Its effect is augmented when combined with topical treatment [37, 42]. Pain, erythema, edema and scaling are side effects of treatment with laser [42].

4. Threads

Recently, Thread therapy is a frequently used technique in Korean medicine for cosmetic purposes, namely to reduce skin wrinkles. An implanted thread was shown to provide continuous stimulation, thereby aiding in the regeneration of connective tissue. Nevertheless, its contribution to hair growth remains unknown [43].

Monofilament threads show significant improvements in hair mass index or hair count in women with FPHL. The patient survey findings indicate that monofilament threads have a therapeutic benefit, as reported by individuals and

measured by hair count or hair mass index. They induce micro-trauma to the scalp that will improve scalp vascularity and stimulate hair growth. The treated cases showed improvement in hair loss, rate of hair loss, hair thickness and ease of managing \ styling hair. Also, hair felt coarser or heavier after treatment with monofilament threads [43, 44].

5. Mesotherapy

It includes: finasteride, dutasteride and stem cells. As regarding intradermal and topical application of finasteride 0.25% has promising results in enhancing hair growth with fewer side effects than when used orally, as it affects scalp and plasma DHT without affecting serum testosterone level [44].

As for the local application of dutasteride, different studies were done to evaluate its efficacy and safety. Intradermal injections and micro-needling showed an increase in hair and capillary densities [45]. In addition, a new technique has emerged using the nanostructured lipid carrier technology that facilitates the drug penetration through the skin [31]. More studies are still needed to reach the optimal treatment protocol of this technique for both finasteride and dutasteride [39]. The superiority of topical administration of dutasteride in terms of efficacy and sexual adverse effects is yet to be further studied before recommending it over the oral route [46].

6. Herbal therapy

The use of herbs is introduced to overcome the adverse effects associated with other lines of AGA treatment. Different types of herbs with different mechanisms of action. Some act by inhibiting 5-αR enzyme as green tea, saw palmetto, pumpkin seed and licorice. Others act by increasing the blood supply to the scalp or increase the follicular cells proliferation as rosemary and grape seed respectively [47].

7. Cosmetic aids

Camouflaging products conceal bare patches on the scalp and mask noticeable hair thinning. In addition, they provide elevation at the root of the hair strand, so enhancing its fullness. Commonly utilized products include scalp spray thickeners, hair building fibers, alopecia masking lotion, and topical shading. Keratin fibers, known as hair forming fibers, are offered in many natural hair shades [32].

8. Surgical treatment

Hair Transplantation

Hair transplantation is a viable therapy option for FPHL if the hair loss has been normalized in individuals who are at least 25 years old. The follicular unit transplantation is considered the gold standard procedure because to its superior results in terms of natural architecture and final appearance [13].

Side effects

Common local consequences of the operation include face puffiness, erythema of the scalp, formation of crusts, bleeding after surgery, infections, swelling, severe headaches, temporary numbness of the scalp, and aberrant scarring of the graft. The possibility of hair transplantation in FPHL is often disregarded and not preferred as much as in male androgenetic alopecia due to unsatisfactory outcomes in female instances [13].

Scalp reduction

Hair transplantation is more popular than this alternative. It entails the removal of the core scalp damaged by alopecia and the bringing together of hair-bearing skin in close proximity. Occasionally, it is carried done in combination with hair transplantation to enhance the aesthetic results [13].

Side effects

The drawbacks of this procedure become more pronounced over time and encompass reduced effectiveness caused by the uncertainty of future hair loss, heightened visibility of excision scars, potential gradual expansion of scars due to the stretching of nearby scalp skin, and the typical requirement for multiple scalp reductions to adequately treat hair loss [13].

Conclusion

According to the information that is currently available there are three FDA approved drugs for treatment of Female pattern hair loss: minoxidil, Low level Laser Therapy and finasteride.

Conflict of Interest

Not available.

Financial Support

Not available.

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How to Cite This Article
Elsaftawy REM, Hassan GFR, Mady OY, Gheida SF. Female pattern hair loss. International Journal of Dermatology, Venereology and Leprosy Sciences. 2024;7(1):10-20.