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A Review Article On "Alopecia: Treatment And Their Side Effects"

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Abstract:

Alopecia, a condition characterized by hair loss, affects millions of people worldwide and can have significant physical and emotional consequences. This paper explores various treatments for alopecia, focusing on both their effectiveness and the potential side effects associated with each. Current treatment options include topical solutions such as minoxidil, oral medications like finasteride, and corticosteroid injections, which aim to reduce hair loss or promote regrowth. While these treatments are widely used, they are not without risks, including scalp irritation, hormonal changes, and long-term dependency. The paper also discusses the side effects that can arise from these treatments. While traditional options like minoxidil may cause irritation or unwanted hair growth in other areas, newer treatments like Janus Kinase (JAK) inhibitors carry risks of immune suppression. Personalized treatment approaches are crucial, as different individuals respond differently to each therapy, and side effects can vary significantly. The research highlights the need for continued exploration of safer and more effective therapies for alopecia. Although advancements in medical science offer hope for better treatments, managing side effects remains a critical aspect of improving patient outcomes. This paper aims to provide a comprehensive overview of current and future treatments for alopecia, emphasizing the importance of balancing treatment effectiveness with the minimization of side effects. In addition to these established therapies, newer approaches like platelet-rich plasma (PRP) therapy, and stem cell treatments are gaining attention for their potential to offer more effective solutions. PRP involves using the patient's own blood to stimulate hair growth, while JAK inhibitors target autoimmune pathways responsible for certain types of alopecia. Stem cell therapies are being explored for their regenerative properties, with the potential to repair damaged hair follicles. However, these emerging treatments are still in development stages and require further clinical trials to fully understand their effectiveness and safety.

Keywords: Alopecia, Types of Alopecia, Hair loss Treatments, Hair Transplantation, minoxidil, finasteride, Platelet-Rich plasma, Immunotherapy, Stem cell therapy.

1. INTRODUCTION

Alopecia is a condition, which results in loss of hair from one's head or other body parts where hair is naturally supposed to be found. The distressful condition causes low self-esteem affecting patients psychologically and socially. There are diverse categories of alopecia but the commonest are androgenic alopecia (common baldness), alopecia areata and chemotherapy induced alopecia. Causes of the conditions are many including stress, heredity, hormonal, nutrition, some sickness as well as certain medications like those prescribed for cancer [1,2]. Although the FDA sanctioned only two serendipitous drugs (finasteride and minoxidil) for the management of alopecia, there are many unapproved medications which are claimed to reverse the condition. [3]

Hair is an essential part of the body, derived from the ectoderm of the skin, and acts as a protective appendage. It is considered an accessory structure of the integument, along with sebaceous glands, sweat glands, and nails. Hair is also classified as an epidermal derivative, as it originates from the epidermis during embryological development. This vital structure plays a key role in protecting the body and enhancing appearance [4]. Each hair grows in three cyclic phases:

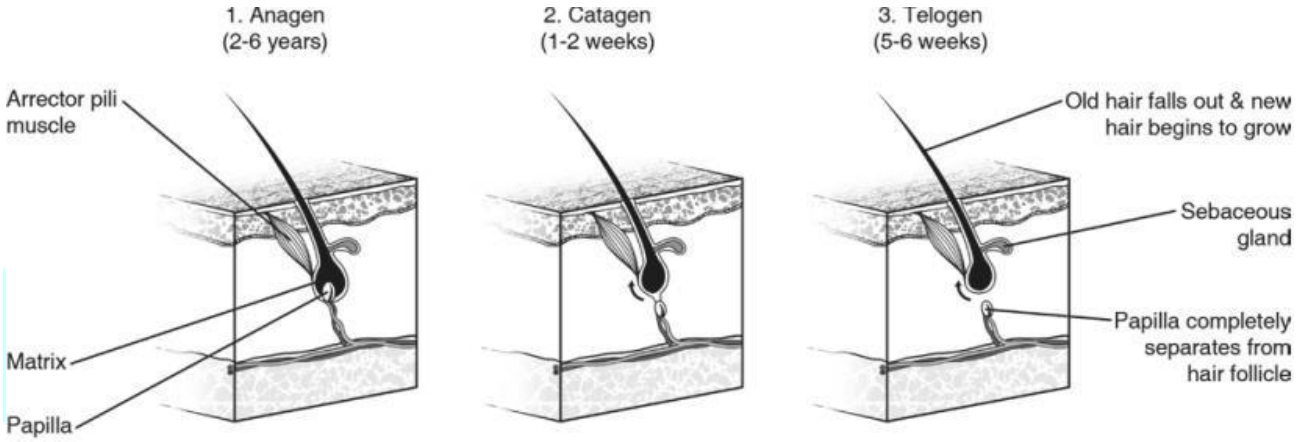

Fig: Hair growth cycle [5]

Anagen (Growth phase) – The anagen phase can be short as 2 years to as long as 6 years. Approximately 80 % of hair is usually in anagen phase.

Catagen (Involution) – In the catagen phase, the growth activity increases, and hair moves to the next phase, catagen phase is between 1-2 weeks [5].

Telogen (Resting phase) – The telogen phase is a state at which the hairs move into resting state. This phase lasts for 5-6 weeks. In general, 50-100 hair at random is shed every day. An increase of more than 100 hair per 6- constituents a state of hair loss or alopecia, albeit it could be temporary [6].

. There are many types of treatments on Alopecia but Hair transplant surgery and Platelet-Rich Plasma (PRP) Therapy, these two are the most common treatments. Hair transplantation is a surgical procedure that moves hair follicles from a donor area, usually the back of the scalp, to balding or thinning spots [7]. There are two primary techniques for this: Follicular Unit Transplantation (FUT), which involves removing a strip of skin with hair, and Follicular Unit Extraction (FUE), where individual hair follicles are extracted one by one. Both methods provide natural and permanent hair growth but may have minor side effects, such as swelling or scarring. This procedure is commonly used to treat pattern baldness in both men and women [8]. In addition to surgical options, Platelet-Rich Plasma (PRP) therapy is a popular non-surgical treatment that uses a patient's own blood. This blood is enriched with concentrated platelets, which help promote healing and tissue regeneration. During hair restoration, PRP is injected into the scalp to stimulate hair growth and strengthen thinning hair. It is an effective, natural procedure that requires minimal downtime and is frequently used to address conditions like androgenetic alopecia, or pattern baldness. The side effects of PRP are generally mild and can include temporary tenderness or swelling of the scalp [9,10].

2. TYPES OF ALOPECIA

Alopecia can manifest in various forms, each linked to different underlying causes. The most common types include androgenetic alopecia, alopecia areata, chemotherapy-induced alopecia (CIA), anagen effluvium, telogen effluvium, traction alopecia, and trichotillomania. This condition is generally categorized into two main types: scarring alopecia, which results from inflammatory responses that damage hair follicles, and the more prevalent non-scarring alopecia, which can be triggered by factors such as hormones, medications, nutritional deficiencies, and certain health conditions.[11]

2.1 Androgenic alopecia

Androgenetic alopecia, commonly known as male or female pattern baldness, is a widespread form of hair loss that affects both genders, although it is more prevalent in men. In men, this condition is characterized by a receding hairline and thinning at the crown, while women typically experience diffuse thinning of the hair on the scalp without a pronounced hairline recession [12].

Fig: Androgenic alopecia [12]

The primary driver of this condition is the male sex hormone testosterone, which is metabolized into dihydrotestosterone (DHT) by the enzyme 5-alpha reductase. Approximately 10% of the testosterone in the body is converted to DHT. This potent androgen is responsible for accelerating hair loss, as it binds to androgen receptors in hair follicles with a higher affinity than other androgens. This means that DHT binds more easily and lasts longer on these receptors—53 minutes compared to testosterone's 35 minutes [13,14]. The interaction between DHT and hair follicle receptors leads to progressive shrinkage and weakening of the hair follicles, ultimately resulting in follicle destruction. This process shortens the anagen (growth) phase of the hair cycle while prolonging the telogen (resting) phase, leading to fewer and finer hairs over time. Research indicates that androgenetic alopecia affects approximately 70% of men and about 40% of women at some point in their lives. Interestingly, men who do not experience significant baldness typically have lower levels of 5-alpha reductase enzyme activity. Moreover, studies show that Caucasians are more likely to be affected by this condition compared to other ethnic groups. Overall, androgenetic alopecia represents a significant health concern, not just because of its impact on appearance but also due to its psychological effects on those affected. The prevalence of this condition across different genders and races underscores the need for ongoing research and effective treatment options [14]. Prevalence of this condition across gender and race are depicted on Table 1

Table 1 Prevalence of androgenic alopecia across different races[14]

Race	Male (%)	Female (%)
African	14.5	3.5
Caucasian	79.9	45.0
Asian	60.0	---
Chinese	21.4	6.0

2.2 Alopecia areata

Alopecia areata is a non-scarring autoimmune disorder that leads to hair loss on the scalp and other areas of the body. The exact cause of this condition remains unclear, although some studies suggest it may be an organ-specific immune response mediated by T lymphocytes targeting hair follicles. Other theories propose that genetic predisposition and environmental factors could trigger the condition. Alopecia areata is characterized by the sudden appearance of small, round bald patches, primarily on the scalp, although these patches can expand if the condition is not effectively managed.[15]

Fig: Alopecia areata in Men & Women [15]

Alopecia areata affects both men and women, especially children and adolescents. In severe cases, it can progress to alopecia totalis, causing complete scalp hair loss. Fortunately, it does not permanently damage hair follicles, allowing hair regrowth once the immune system is balanced. Treatments like corticosteroids, minoxidil, and immunosuppressants have limited success, often leading to frustration. However, emerging therapies like Janus kinase (JAK) inhibitors show promise. Psychological support is crucial due to the emotional impact of visible hair loss. More research is needed to better understand and treat alopecia areata effectively. [16].

2.3 Anagen effluvium

Anagen effluvium is a condition characterized by the shedding of hair that is in the anagen (growth) stage, leading to what is known as anagen arrest. Similar to chemotherapy-induced alopecia, this condition can be triggered by chemotherapy or other medications.

Fig: Anagen effluvium [17]

When anagen hair is lost, it results in a prolonged telogen (resting) phase that lasts for the duration of the treatment being administered. Additionally, the excessive use of certain medications, such as blood thinners, hormonal birth control pills, diuretics, and specific acne treatments, has been linked to the onset of this disorder. While anagen effluvium is often reversible, allowing for hair regrowth within a few months

after stopping the triggering medication, there are instances where the condition may become permanent. This potential for irreversible hair loss can significantly impact a patient's mental well-being, leading to anxiety, depression, and a diminished sense of self-esteem. The psychological toll of losing one's hair can be profound, as many individuals associate their hair with personal identity and attractiveness. In many cases, patients experiencing anagen effluvium are unaware of the exact medications causing their hair loss, which can add to their distress. [18,19] Healthcare providers should discuss potential side effects of medications, including hair loss, with patients before treatment begins. Supportive care like counselling and support groups can help individuals cope with the emotional impact of hair loss. Patients can explore options like wigs, hats, and scarves to manage their appearance and boost confidence. Treatments for hair regrowth, such as minoxidil, may also be considered, though their effectiveness varies. Ongoing research into anagen effluvium could lead to better treatments in the future. Raising awareness among both healthcare providers and patients can foster better understanding and support for those dealing with hair loss.[20]

2.4 Telogen effluvium

Telogen effluvium refers to a non-scaring form of hair loss that occurs when hair follicles are prematurely pushed into the inactive telogen stage of the hair growth cycle. This condition is commonly observed in older individuals, as well as in those experiencing significant physical or emotional stress. It can also be associated with hormonal imbalances, such as those seen in thyroid disorders.

Fig: Telogen effluvium [21]

The severity of hair loss experienced in telogen effluvium is often proportional to the intensity and duration of exposure to the triggering factor rather than the nature of the trigger itself. There are different types of telogen effluvium: acute telogen effluvium typically lasts for less than six months, while chronic telogen effluvium persists for longer than six months. Chronic repetitive telogen effluvium is characterized by multiple episodes of hair loss over time.[21] Telogen effluvium causes noticeable thinning or shedding, often increasing anxiety about appearance. It typically resolves once the underlying cause, such as childbirth, surgery, severe illness, or weight loss, is addressed, allowing hair to regrow over time. Nutritional deficiencies, especially in iron or protein, can also trigger this condition. Managing stress through relaxation techniques and maintaining a balanced diet rich in essential vitamins and minerals can support hair health and recovery. For chronic cases, consulting a dermatologist for treatment options, like topical solutions or supplements, may be necessary. Raising awareness and educating individuals about telogen effluvium helps in early detection and proactive management. [22]

2.5 Traction alopecia

Traction alopecia is primarily caused by tension and stress placed on the hair follicles, resulting in hair breakage and loss. This condition is particularly common among middle-aged women, who often strive to maintain a polished appearance through various hairstyles. Styles that involve tight braids, ponytails, or updos can pull on the hair and lead to significant strain over time. Additionally, frequent use of chemical treatments, such as hair bleaching and dyeing, can weaken the hair and exacerbate the risk of traction alopecia. This condition can affect individuals from diverse cultural backgrounds, as it is closely linked to personal hair care practices and styling choices. While it is most prevalent in women, men can also

experience traction alopecia, especially if they adopt similar hairstyles that place undue stress on their hair.

Fig: Traction alopecia [22]

The damage is usually concentrated around the hairline and areas where tension is applied most, leading to thinning and bald patches. Traction alopecia can be prevented by adopting safer hairstyling practices. For example, individuals can opt for looser hairstyles or take breaks from tight styles to give their hair follicles time to recover [22,23]. To manage traction alopecia, reducing the frequency of chemical treatments and using protective styles that minimize tension are key. Early intervention is crucial; individuals noticing thinning or bald patches should immediately modify their styling habits. Consulting a dermatologist or trichologist can help identify effective treatments, such as topical solutions or supplements. Education on proper hair care and awareness of the risks of certain hairstyles can prevent traction alopecia. If caught early, the condition can be reversed, but chronic tension can lead to permanent hair loss. Promoting self-acceptance and prioritizing hair health over trends fosters healthier habits and a positive self-image.[24]

2.6 Trichotillomania

Trichotillomania alopecia is a condition characterized by the compulsive urge to pull out one's hair from the scalp or other areas of the body, leading to noticeable hair loss and damage. This behavior is often seen in children and individuals with underlying psychological conditions. In many cases, those affected may not even realize they are engaging in this behavior, and it can be triggered by stress, anxiety, or boredom [25]. Trichotillomania, a hair-pulling disorder, can cause emotional distress and social embarrassment, impacting self-esteem and body image. Though commonly seen in children, it can persist into adulthood, requiring more intensive treatment, such as cognitive behavioral therapy (CBT) to address underlying triggers. In children, the condition may resolve as they mature, but supportive environments and guidance from caregivers are crucial. Engaging in activities like crafts or using fidget toys can help reduce hair-pulling. Treatment options include mindfulness, habit reversal training, and in some cases, medication. Support groups also provide a helpful space for sharing experiences and finding support. [24,26]

2.7 Cicatricial Alopecia

Cicatricial alopecia, or scarring alopecia, is a group of hair loss disorders characterized by permanent destruction of hair follicles and scar tissue formation in the scalp. It can result from inflammatory diseases, autoimmune responses, infections, trauma, or burns. Unlike non-scarring alopecia, it involves inflammation that irreversibly damages hair follicles, leading to permanent hair loss. Symptoms often include redness, itching, and pain, significantly affecting quality of life. Common variants include lichen planopilaris, central centrifugal cicatricial alopecia, and discoid lupus erythematosus. Diagnosis involves clinical examination and scalp biopsy. Treatment options include anti-inflammatory medications, corticosteroids, and sometimes hair transplants. Early intervention is crucial to manage symptoms and slow progression. The emotional impact of visible hair loss can lead to self-esteem issues, making supportive care and counseling essential. Ongoing research aims to improve understanding and treatment of this challenging condition. [27,28].

2.8 Alopecia universalis

Alopecia universalis is an advanced form of alopecia areata, an autoimmune disorder characterized by the complete loss of all body hair, including scalp, eyebrows, eyelashes, and body hair. This condition occurs when the immune system mistakenly attacks hair follicles, leading to hair loss in patches and eventually resulting in total hair loss. Alopecia universalis can affect individuals of any age, gender, or ethnicity, though it often emerges during childhood or adolescence. The exact cause of this condition remains unclear, but genetic predisposition, environmental triggers, and other autoimmune factors are believed to play a role in its development. Patients with alopecia universalis may experience additional symptoms, such as changes in nail texture, where nails can become pitted, ridged, or brittle. The emotional impact of losing all body hair can be profound, leading to feelings of anxiety, depression, and social withdrawal. Because alopecia universalis can occur suddenly and unpredictably, it can be particularly distressing for those affected. Diagnosis typically involves a thorough clinical examination, patient history, and sometimes a biopsy to confirm the absence of hair follicles. While there is currently no cure for alopecia universalis, various treatment options aim to manage symptoms and promote hair regrowth. These treatments can include topical corticosteroids, intralesional corticosteroid injections, immunotherapy, and systemic medications like corticosteroids and JAK inhibitors.[29] The effectiveness of treatments for alopecia universalis varies, and hair regrowth is not always permanent. Emotional support through counseling and support groups is essential in helping individuals cope with the psychological challenges of complete hair loss. Ongoing research aims to better understand the immunological causes and develop more effective therapies to improve patients' quality of life. Many individuals adapt to their condition by embracing their appearance and finding self-acceptance. Strategies like wearing wigs, hats, or makeup can help in social settings, and a sense of community often develops among those affected. Despite its challenges, alopecia universalis can foster personal growth, resilience, and a stronger sense of identity.[30]

2.9 Chemotherapy induced alopecia

Chemotherapy-induced alopecia is the hair loss that occurs as a result of cancer treatment with chemotherapy drugs. These drugs target rapidly dividing cells, a hallmark of cancer cells. However, they also affect other fast-growing cells in the body, including those in hair follicles, leading to hair loss. Hair follicles have a high turnover rate, meaning they regularly produce new cells to grow hair. Chemotherapy disrupts this process by damaging the hair matrix cells, which are responsible for producing the hair shaft. The severity of hair loss depends on the type of chemotherapy, dosage, and the individual's biological response. Some chemotherapy agents cause more hair loss than others, and in some cases, it may only thin hair rather than causing complete baldness. Alopecia usually begins a few weeks after starting chemotherapy, and the hair can fall out in clumps or gradually. It affects the scalp most commonly but can also involve hair loss from eyebrows, eyelashes, and other body areas. Hair loss is generally temporary, and regrowth typically starts after treatment is completed. The new hair may initially be different in texture or color but usually returns to its. original state over time.

Fig: Chemotherapy induced alopecia [31]

Chemotherapy-induced alopecia can vary in pattern and extent, depending on the individual and the

treatment regimen. In some cases, cooling caps are used during chemotherapy to reduce blood flow to the scalp, potentially minimizing hair loss. Emotional and psychological impacts are often significant, as hair loss can affect a person's self-image and confidence. Patients are usually advised about the possibility of alopecia before starting treatment, allowing them time to prepare emotionally or explore options like wigs, scarves, or hats. Overall, while distressing, the condition is temporary, and hair typically regrows after chemotherapy ends.

3. TREATMENTS FOR ALOPECIA (Hair Loss)

3.1 Medication for Alopecia (hair loss)

Hair loss treatments vary depending on the cause and severity of the condition. Common medications for hair loss include:

3.1.1 minoxidil

Minoxidil is a widely used, FDA-approved topical medication for the treatment of androgenetic alopecia (pattern hair loss) in both men and women. Initially developed as an oral medication for hypertension, due to its potent vasodilatory effects, minoxidil was discovered to have a side effect of promoting hair growth, leading to its reformulation as a topical solution. The precise mechanism by which minoxidil promotes hair growth is not fully understood, but it is believed to work by increasing blood flow to the scalp. This enhanced circulation delivers more oxygen and nutrients to hair follicles, thereby stimulating their growth. Minoxidil is also thought to prolong the anagen (growth) phase of the hair cycle, while shortening the telogen (resting) phase, resulting in increased hair density and length over time. Minoxidil is available in 2% and 5% concentrations, typically as a liquid solution or foam. The 5% concentration is generally recommended for men, while women are more commonly prescribed the 2% solution, although higher concentrations can be used in more severe cases. The medication is applied directly to the scalp once or twice daily, depending on the formulation and the severity of hair loss. Clinical studies have shown that minoxidil is most effective in treating hair thinning at the vertex and mid-scalp areas, with approximately 40% of men and 20-30% of women experiencing noticeable hair regrowth after three to six months of consistent use. However, the benefits of minoxidil are usually seen only with continued application. Discontinuation of the medication often results in the resumption of hair loss within several months. For optimal results, minoxidil can be combined with other therapies, such as finasteride (a DHT-blocking medication used primarily for men) or low-level laser therapy, which can improve outcomes in cases of more severe hair loss. Despite its limitations, minoxidil remains one of the most reliable and accessible treatments for androgenetic alopecia. However, as a long-term commitment is necessary to maintain results, patients must be prepared for ongoing use. This makes it a key component in the management of hair loss, especially for those seeking a non-invasive solution [31,32].

3.1.1.1 Side Effects:

Minoxidil is generally well-tolerated, though some users may experience mild side effects such as scalp irritation, itching, redness, or dryness. A less common but notable side effect is hypertrichosis, where excessive hair growth occurs in unintended areas, such as the face or neck. Systemic absorption is minimal, but in rare cases, individuals may experience dizziness or hypotension. The drug’s effectiveness tends to plateau after one year, and it works best when used in the early stages of hair thinning. It is less effective in treating areas that are completely bald.[32]

3.1.2 Finasteride

Finasteride is an FDA-approved oral medication primarily used to treat androgenetic alopecia (male pattern baldness) in men. It is also used to treat benign prostatic hyperplasia (BPH), or an enlarged prostate. The drug works by inhibiting the activity of 5-alpha-reductase, an enzyme responsible for converting testosterone into dihydrotestosterone (DHT), a more potent androgen. Elevated DHT levels are strongly

associated with the miniaturization of hair follicles in androgenetic alopecia, leading to thinner and shorter hair over time and eventually, hair loss. By lowering DHT levels in the scalp, finasteride helps to reverse or slow this process, promoting hair regrowth and halting further hair thinning. Finasteride is typically prescribed in a 1 mg daily dose for hair loss, while higher doses (5 mg) are used to treat BPH. Clinical trials have shown that finasteride can significantly reduce DHT levels in the scalp by up to 60- 70%, which helps to preserve hair density and stimulate regrowth, particularly at the crown and mid-scalp areas. The drug is less effective for hair loss at the frontal hairline, but many users still report some improvement in this region. The benefits of finasteride become apparent after about three to six months of continuous use, with maximal effects observed after one year. Importantly, if treatment is stopped, hair loss will typically resume within 6 to 12 months, as DHT levels return to their pre-treatment levels. One of the major advantages of finasteride is its ability to not only halt hair loss but also promote the regrowth of lost hair in a significant portion of users. Studies have shown that about 80-90% of men taking finasteride experience a noticeable reduction in hair loss, and up to two-thirds report significant hair regrowth. This makes it one of the most effective treatments available for androgenetic alopecia, especially in combination with other therapies like minoxidil or low-level laser therapy. Despite its efficacy, finasteride does come with potential side effects, particularly because it interferes with hormone pathways. The most reported adverse effects are sexual in nature, including reduced libido, erectile dysfunction, and decreased semen volume. These side effects occur in a small percentage of users—typically around 1- 2%—but they are usually reversible upon discontinuation of the drug. However, some users have reported persistent sexual side effects even after stopping finasteride, a condition referred to as post-finasteride syndrome (PFS).[33] While rare, this syndrome has raised concerns about the long-term safety of the drug, although extensive research has not definitively established a direct causal link between finasteride and these lasting effects. In addition to sexual side effects, some men report mood changes, including depression or anxiety, though these are less common. Finasteride is typically contraindicated for women, especially those who are pregnant or may become pregnant, as the drug can cause developmental abnormalities in male foetuses. However, some studies have explored the use of finasteride in postmenopausal women with female pattern hair loss. While results are less consistent than in men, some women have experienced modest improvements in hair density, though its use in this population remains off-label and is less widely recommended than in men. Basically, finasteride offers a long-term, non- invasive solution to managing androgenetic alopecia. Given that the drug's effects are contingent on continuous use, it is generally recommended as part of a sustained treatment plan for men who wish to preserve their hair. Many dermatologists and hair loss specialists suggest combining finasteride with topical minoxidil, as the two medications target hair loss through different mechanisms, potentially leading to better overall outcomes. Another advantage of finasteride is its relatively low cost and ease of administration, as it is taken once daily in pill form. This convenience, coupled with its strong efficacy profile, has made it a cornerstone treatment for men with androgenetic alopecia. It is crucial for patients considering finasteride to have a thorough discussion with their healthcare provider about the potential benefits and risks, as well as the importance of monitoring for side effects during treatment. For most men, the risk-benefit ratio is favourable, with the majority experiencing significant preservation or regrowth of hair with minimal adverse effects. [33,34]

3.1.2.1 Side Effects:

Finasteride, when used as a medication for hair loss, can cause a range of side effects, though they are generally uncommon and occur in a small percentage of users. The most frequently reported side effects are sexual in nature, including decreased libido, erectile dysfunction, and reduced ejaculate volume. These sexual issues affect about 1-2% of men using the medication and typically resolve after discontinuation, though some users report persistent sexual dysfunction, a condition referred to as post-finasteride syndrome (PFS). In rare cases, psychological side effects like depression and anxiety have been noted. Some men may also experience physical changes such as breast tenderness or enlargement (gynecomastia), rashes, or mild swelling in the hands or feet. Testicular pain has also been reported in isolated cases. Additionally, there is concern about the drug's impact on fertility, as it may reduce sperm count or semen quality, though these effects are usually reversible. Finasteride is contraindicated for women, particularly during pregnancy, as it can cause severe birth defects in male foetuses.[33]

3.1 Hair Transplantation

Hair transplantation is a popular surgical procedure designed to address hair loss caused by various forms of alopecia, including androgenetic alopecia, alopecia areata, and scarring alopecia. This technique involves relocating hair follicles from a donor area, typically the back or sides of the scalp, to areas experiencing thinning or balding. The primary aim of hair transplantation is to create a natural-looking hairline and restore volume in balding regions. The two most common methods of hair transplantation are Follicular Unit Extraction (FUE) and Follicular Unit Transplantation (FUT). [34]

3.1.1 Follicular Unit Extraction (FUE):

Follicular Unit Extraction (FUE) is a modern, minimally invasive hair transplantation technique used to treat hair loss by individually harvesting hair follicles from a donor area, typically the back or sides of the scalp, and transplanting them to areas of thinning or balding. Unlike the older Follicular Unit Transplantation (FUT) method, which involves removing a strip of scalp tissue and dissecting it into individual follicular units, FUE extracts each follicle directly from the scalp using a specialized micro-punch tool, usually between 0.6 to 1.0 mm in diameter. This process leaves tiny, circular scars that are less visible than the linear scar associated with FUT, making FUE more popular for individuals who prefer to wear their hair short.[35] The FUE procedure begins with the surgeon shaving the donor area and applying local anaesthesia. Each follicular unit, containing one to four hairs, is carefully extracted and stored in a solution to preserve its viability. Once the required number of grafts is collected, the recipient site is prepared by creating tiny incisions or slits where the follicles will be implanted. The surgeon meticulously places each graft into these incisions, ensuring the direction, angle, and density of the transplanted hairs match the surrounding natural hair for a seamless appearance.

Fig: Follicular Unit Extraction (FUE) [36]

One of the key advantages of FUE is that it is less invasive than traditional methods, with a faster recovery time, minimal discomfort, and less noticeable scarring. The risk of complications, such as infection or excessive scarring, is relatively low. However, FUE is a more time-consuming and labour- intensive procedure compared to FUT, as the extraction of each follicle must be done individually, often requiring several hours or multiple sessions, depending on the extent of hair loss. The technique is highly skill-dependent, requiring an experienced surgeon to ensure optimal results. Although FUE offers a more natural and aesthetically pleasing outcome, it is important to note that, as with all hair transplantation methods, it does not prevent future hair loss, and some patients may require additional treatments over time to maintain density. [36]

3.1.2 Follicular Unit Transplantation (FUT):

Follicular Unit Transplantation (FUT), also known as the strip method, is a widely used hair transplantation technique for treating hair loss. It involves surgically removing a strip of scalp, typically

from the back or sides of the head (the donor area), where hair is genetically resistant to balding. This strip of tissue is then dissected under a microscope into individual follicular units, which are naturally occurring groups of one to four hairs. These follicular units are carefully preserved before being transplanted to the recipient area, where the hair is thinning or balding. [36]

Fig: Follicular Unit Transplantation [37]

The FUT procedure begins with the surgeon applying local anesthesia to the donor area, followed by the excision of a thin strip of scalp, usually 1 to 1.5 centimeters wide. The wound is then sutured or stapled, leaving a linear scar that, while permanent, can often be concealed by surrounding hair. Skilled surgeons use a trichophytic closure technique, which helps minimize the appearance of the scar. Once the donor strip is removed, a team of technicians meticulously dissects it into thousands of tiny grafts, each containing individual follicular units. Meanwhile, the surgeon prepares the recipient area by making tiny incisions where the grafts will be implanted. These grafts are placed into the incisions, with careful attention to the natural hairline, direction, and angle of hair growth to ensure a natural-looking result. FUT offers several advantages, particularly for patients who require many grafts in a single session. Since a higher number of follicles can be harvested at once, FUT is often more efficient and cost-effective for extensive hair loss cases. Additionally, the survival rate of the grafts is slightly higher in FUT compared to FUE (Follicular Unit Extraction) because the follicular units are handled less during extraction. However, the main disadvantage of FUT is the linear scar it leaves in the donor area, which can be more visible, especially for individuals who wear their hair short. The recovery time is slightly longer compared to FUE, and there may be some temporary discomfort or tightness in the scalp where the strip was removed.[37]

3.1.3 Donor Site Preparation & Anaesthesia

In hair transplantation, donor site preparation involves selecting the area of the scalp where healthy hair follicles will be harvested, typically from the back or sides of the head. This area is carefully shaved to make the follicles more accessible for extraction. Local anaesthesia is then administered to numb the donor site and minimize discomfort during the procedure. Proper donor site preparation is critical to ensure an even extraction of follicles and to avoid over-harvesting, which can lead to visible scarring or thinning in the donor area.[37]

3.1.4 Preparation of Local Anaesthesia

Administering local anaesthesia is a key step in hair transplantation to ensure the patient remains comfortable throughout the procedure. The anaesthesia is usually injected into both the donor and recipient areas of the scalp to numb them, preventing pain during follicular extraction and implantation. Care must be taken to administer the correct dosage and ensure that it is evenly distributed. Improper administration can result in uneven numbing, causing discomfort or complications such as swelling or allergic reactions.[37]

3.1.5 Complications

Complications in hair transplantation can occur at various stages, from preoperative planning to post-surgical recovery. Some of the most common issues include infection, excessive bleeding, scarring, or poor graft survival. Other complications can involve an unnatural hairline appearance, inadequate hair density, or poor wound healing in both donor and recipient areas. In rare cases, nerve damage or allergic reactions to anaesthesia can occur. Addressing complications early with proper medical care is crucial to prevent long-term consequences. [37,38]

3.1.5.1 Complications in the Preoperative Phase

Preoperative complications typically involve patient-related factors such as underlying medical conditions, medications, or lifestyle habits that can affect the surgery's success. For example, patients with conditions like diabetes or those on blood thinners may be at a higher risk for bleeding or poor healing. Inadequate preoperative instructions regarding smoking, alcohol use, or medication cessation can also result in complications. Thorough preoperative assessments and patient education can help mitigate these risks.

3.1.5.2 Complications in the Surgical Phase

During the surgical phase, complications can include excessive bleeding, improper graft handling, or difficulty in graft extraction and implantation. If the grafts are not handled carefully, they may become damaged or die before being implanted, which affects the overall success of the transplant. Overharvesting from the donor area can also lead to visible scarring or thinning. Moreover, poor placement of the follicles in the recipient area can result in an unnatural hairline or uneven hair distribution.[38]

3.1.5.3 Post-Surgical Complications

Post-surgical complications include infection, swelling, and excessive scarring at the donor or recipient sites. Patients may also experience shock loss, where existing hair temporarily falls out due to trauma from the surgery. In some cases, there may be issues with graft survival, leading to uneven or patchy hair regrowth. Additionally, patients can develop numbness, itching, or discomfort in the treated areas. Proper post-operative care, including medication, wound care, and regular follow-ups, is essential to minimize these complications and ensure successful outcomes. [38,39]

3.1.6 Side Effects:

Hair transplantation is generally safe and effective but can have side effects that patients should be aware of. Common immediate effects include swelling, redness, tenderness, itching, and crusting in the donor and recipient areas, along with a feeling of tightness in the scalp. There is also a risk of bleeding and infection, though these complications are rare with proper care. Shock loss can occur, leading to temporary thinning or loss of existing hair in the transplant area, which usually regrows within a few months. Patients may experience numbness or altered sensation in the scalp, especially in the donor area, which typically resolves over time. The Follicular Unit Transplantation (FUT) method can leave a linear scar, while the Follicular Unit Extraction (FUE) technique may result in tiny, scattered scars. Consulting with a qualified surgeon is essential for understanding potential side effects and ensuring proper aftercare. [37,38,39]

3.2 Platelet-Rich Plasma (PRP) Therapy

Platelet-Rich Plasma (PRP) therapy is an innovative treatment approach that harnesses the body's own healing mechanisms to promote hair growth, particularly for individuals suffering from various forms of alopecia. This therapy involves the extraction of a small amount of the patient's blood, which is then processed to concentrate the platelets, growth factors, and other healing components. The resulting PRP solution is rich in proteins and growth factors, which play a vital role in tissue regeneration and repair. This makes PRP therapy a promising non-surgical option for treating hair loss and enhancing overall scalp health. The process begins with a simple blood draw from the patient, typically from the arm. The collected blood is then placed in a centrifuge, which spins the blood at high speeds to separate its components. After centrifugation, the blood separates into three layers: red blood cells at the bottom, a middle layer containing

the concentrated platelets and plasma, and the top layer consisting of serum. The platelet-rich plasma is carefully extracted and prepared for injection into the scalp.[39]

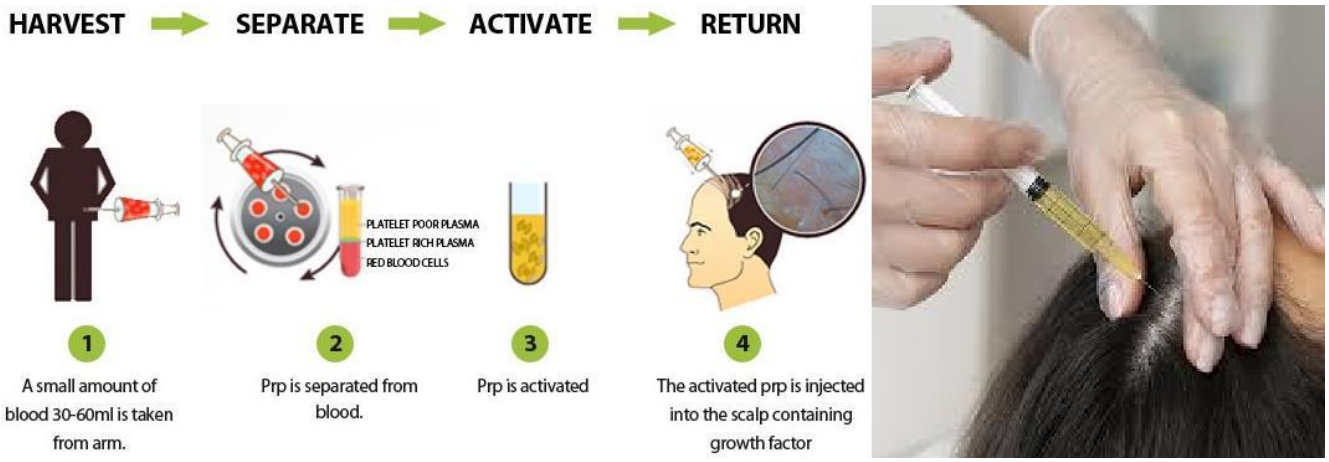

Fig: Platelet-Rich Plasma Therapy[39]

One of the key benefits of PRP therapy is its natural approach. Since the treatment uses the patient's own blood, there is a minimal risk of allergic reactions or complications associated with foreign substances. The growth factors present in PRP, such as platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and transforming growth factor-beta (TGF-β), stimulate hair follicles, enhance blood circulation in the scalp, and encourage the production of new hair strands. PRP therapy is particularly effective for individuals with androgenetic alopecia, which affects both men and women and is characterized by gradual hair thinning. In cases of androgenetic alopecia, the hair follicles become miniaturized due to hormonal influences, primarily dihydrotestosterone (DHT). PRP therapy helps to counteract this miniaturization by revitalizing the hair follicles and prolonging the growth phase of the hair cycle (anagen phase). Many patients experience an improvement in hair density and quality after undergoing PRP treatments, making it a highly sought-after option for restoring hair. In addition to androgenetic alopecia, PRP therapy has shown promise for treating other forms of alopecia, including alopecia areata, which is an autoimmune condition that results in patchy hair loss. By injecting PRP into the affected areas, the therapy may help stimulate hair regrowth and restore the normal hair cycle. Studies have indicated that patients with alopecia areata may benefit from the anti-inflammatory properties of PRP, as the growth factors can reduce inflammation in the scalp and promote healing. The treatment protocol typically involves a series of sessions, often spaced four to six weeks apart, to achieve optimal results. Many patients report noticeable improvements in hair thickness and fullness within three to six months after starting treatment. While results may vary among individuals, the long-term benefits of PRP therapy can be significant, especially when combined with other hair restoration techniques or medications. PRP therapy is generally well-tolerated, with minimal downtime or side effects. Patients may experience mild discomfort or swelling at the injection sites, but these effects are usually short-lived. It is important for individuals considering PRP therapy to consult with a qualified medical professional who can assess their specific hair loss condition and recommend an appropriate treatment plan tailored to their needs. One of the notable aspects of PRP therapy is its role in encouraging a healthy scalp environment. By enhancing blood flow to the hair follicles, PRP helps deliver essential nutrients and oxygen, which are crucial for hair health. A healthy scalp is fundamental for effective hair growth, and PRP therapy contributes to creating the ideal conditions for hair follicles to thrive. Moreover, PRP therapy is a promising adjunct treatment that can be used alongside other hair restoration methods, such as hair transplants or topical medications like minoxidil. This multifaceted approach can lead to improved outcomes and more comprehensive solutions for individuals experiencing hair loss. [40,41]

3.2.1 Side Effects:

Common side effects include mild pain or discomfort at the injection site, which may also lead to temporary swelling, redness, and bruising. Some patients may experience headaches following the procedure, particularly if they are sensitive to injections. Although rare, there is a potential risk of infection at the injection site, as with any procedure that involves needles. Additionally, individuals with certain blood disorders or conditions that affect platelet function should avoid PRP therapy, as it may not be suitable for them. Other potential side effects, though infrequent, can include allergic reactions to the anaesthetic used during the procedure or the development of scar tissue at the injection site. Overall, while side effects are typically mild and temporary, patients should consult with their healthcare provider to discuss any concerns and ensure that PRP therapy is appropriate for their individual circumstances. [41,42]

3.3 Corticosteroid therapy

Corticosteroid therapy is a widely used treatment option for various types of alopecia, particularly alopecia areata, an autoimmune condition characterized by sudden, patchy hair loss. Corticosteroids are synthetic drugs that mimic the effects of hormones produced naturally by the adrenal glands, specifically cortisol. These medications work by reducing inflammation and suppressing the immune system, which is especially beneficial in conditions where the body mistakenly attacks its own hair follicles, leading to hair loss. In alopecia areata, the immune system mistakenly attacks hair follicles, causing inflammation and hair loss. Corticosteroids reduce this immune response, helping hair follicles recover and promoting regrowth.

Treatment options topical, intralesional, or systemic are chosen based on the severity and extent of hair loss. Topical corticosteroids, applied as creams or ointments to affected areas, are commonly used for mild cases. While effective in reducing inflammation around follicles, they may take longer to show results and are best for smaller, localized patches of hair loss.[43] Intralesional corticosteroid injections are often used for extensive or resistant alopecia areata, injecting diluted corticosteroids directly into hair loss patches to target follicles and achieve quicker results. Improvement is typically seen within four to six weeks, with repeat injections possibly needed every four to six weeks based on response. For severe or widespread cases, systemic corticosteroids may be prescribed to suppress the immune response across the entire body. Systemic treatment, often reserved for alopecia totalis or universalis, carries a higher risk of side effects and requires close monitoring by healthcare providers.[44] Corticosteroid therapy is effective for many patients with alopecia areata, with 60-80% responding positively. Hair regrowth generally begins within a few months once inflammation is controlled, though relapse is possible after stopping treatment. Corticosteroids work by altering the immune response, reducing inflammation around hair follicles, and allowing follicles to recover. However, long-term use can lead to side effects, so treatment duration is usually limited. Besides alopecia areata, corticosteroids may also aid other inflammatory hair loss conditions, like lichen planopilaris. Combining corticosteroids with other treatments, such as minoxidil or light therapy, can enhance outcomes. [45]

3.3.1 Side Effect

Corticosteroid therapy is often used to treat hair loss disorders like alopecia areata, effectively reducing inflammation and promoting hair regrowth. However, it can lead to various side effects, particularly with long-term use or high doses. Common local side effects include skin thinning (atrophy), skin discoloration, and stretch marks. When administered orally or via injection, systemic side effects may occur, including weight gain, mood swings, increased appetite, and sleep disturbances. Prolonged use can disrupt hormone balance, leading to adrenal suppression, and may elevate blood sugar levels, posing risks for individuals with diabetes. While corticosteroids can be beneficial, patients should consult their healthcare provider to discuss potential side effects and manage treatment duration safely. [43,45]

3.4 Immunotherapy

Immunotherapy is an innovative treatment approach that harnesses the body's immune system to combat various diseases, including autoimmune conditions like alopecia areata. Alopecia areata is characterized by sudden hair loss due to an inappropriate immune response that targets hair follicles. In this condition, the immune system mistakenly identifies hair follicle cells as foreign invaders, leading to inflammation and hair loss. Immunotherapy aims to reprogram or modulate the immune response to prevent this attack and promote hair regrowth. One common form of immunotherapy used in treating alopecia areata is the application of topical sensitizers, such as diphencyprone (DPCP). In this method, a small amount of the sensitizer is applied to the scalp, inducing a localized allergic reaction. This reaction serves as a distraction for the immune system, redirecting its focus away from attacking the hair follicles.[46] The initial inflammatory response can lead to the activation of immune cells that may promote hair regrowth by enhancing the healing process of the hair follicles. This method has shown promising results in stimulating hair regrowth in many patients, especially those with less extensive hair loss. Another form of immunotherapy is systemic immunosuppressants, which work by broadly suppressing the immune system. While these medications can be effective in managing severe cases of alopecia areata, they are generally not first-line treatment due to the potential for significant side effects.

[47] Systemic treatments like methotrexate and cyclosporine, used for extensive alopecia, help manage the autoimmune response to encourage hair regrowth, though they require careful monitoring due to immunosuppressive risks. Intralesional corticosteroid injections offer localized immunotherapy, reducing inflammation in specific bald patches and promoting hair regrowth within weeks. For severe cases like alopecia totalis or universalis, more aggressive, combined immunotherapy treatments are often necessary. Emerging treatments, such as Janus kinase (JAK) inhibitors like tofacitinib, have shown promise in clinical trials by blocking immune pathways involved in hair loss. These therapies may also benefit mental health,

helping alleviate anxiety and depression related to hair loss. Since immunotherapy responses vary, personalized treatment plans and regular healthcare monitoring are essential to manage risks and optimize outcomes. [48]

3.4.1 Side Effects

It can lead to side effects, including localized inflammation, redness, and itching at the injection site, which are typically mild and temporary. Allergic reactions to the immunotherapy agents may occur, resulting in hives or rashes. Systemic side effects can include flu-like symptoms, fatigue, and fever, particularly when treatments alter the immune response. There is also a risk of developing other autoimmune conditions due to changes in immune function. As the long-term effects of immunotherapy are still being studied, patients should discuss potential risks and benefits with their healthcare provider for informed decision-making. [47,48]

3.5 Low-Level Laser Therapy (LLLT)

Low-Level Laser Therapy (LLLT), also known as low-level light therapy or cold laser therapy, is a non-invasive treatment that uses specific wavelengths of light to stimulate cellular activity in the body. This therapy has gained popularity in recent years for its potential to promote hair regrowth in individuals experiencing various types of alopecia, particularly androgenetic alopecia and alopecia areata. The principle behind LLLT is based on the concept that certain wavelengths of light can penetrate the skin and be absorbed by the cells, stimulating metabolic processes and encouraging healing.

Fig: Low-Level Laser Therapy (LLLT)[48,49]

In the context of hair restoration, LLLT works by increasing blood circulation to the scalp, which in turn enhances oxygen and nutrient delivery to hair follicles. This improved circulation can invigorate dormant hair follicles, promoting hair growth and potentially reversing the effects of hair loss. Laser light is thought to stimulate mitochondria in the cells, leading to increased ATP (adenosine triphosphate) production. ATP is crucial for cellular energy and function, making it vital for hair follicle health. Clinical studies have shown promising results for LLLT in treating alopecia. Many participants have reported noticeable improvements in hair density and thickness after a series of LLLT sessions. Unlike traditional hair restoration methods, such as surgical transplants, LLLT is painless, requires no recovery time, and can be administered in a salon or clinical setting. Many devices for LLLT treatment are also available for home use, allowing patients to manage their hair health conveniently.[49] The effectiveness of low-level laser therapy (LLLT) for hair loss varies among individuals, influenced by factors such as the severity of hair loss, the underlying cause of alopecia, and adherence to treatment protocols. Optimal results typically require multiple sessions, with recommendations of two to three treatments per week, each lasting 20 to 30 minutes. LLLT can safely complement other hair loss treatments, such as minoxidil or finasteride, potentially enhancing their effectiveness by improving blood flow to the scalp. While many patients report better outcomes when combining LLLT with topical treatments, individual responses can vary significantly; some may see minimal improvement, while others experience significant regrowth. Factors like genetics and

hormonal influences can affect treatment success, so it's important for patients to have realistic expectations. LLLT is considered a low-risk, non-invasive therapy with few side effects, making it a suitable option for those hesitant to pursue more aggressive treatments.[50]

3.5.1 Side Effect

Generally considered safe, LLLT can have some side effects, although they are typically mild and temporary. The most common side effects include scalp irritation, such as redness, itching, or discomfort at the treatment site. Some individuals may experience a slight warming sensation during the procedure, which is usually well-tolerated. In rare cases, patients may develop headaches or eye strain if proper protective eyewear is not used during treatment sessions. There is also a low risk of photosensitivity reactions in individuals with certain skin conditions or sensitivities to light. Overall, while LLLT is a promising option for hair restoration, patients should discuss any potential side effects with their healthcare provider to ensure they are well-informed and to assess the suitability of this therapy for their specific needs.[50]

3.6 Stem cell therapy

Stem cell therapy in hair transplantation is an innovative and emerging treatment that leverages the regenerative properties of stem cells to promote hair growth and potentially reverse hair loss. Unlike traditional hair transplant methods, which involve relocating hair follicles from one part of the scalp to another, stem cell therapy aims to stimulate the body's own ability to regrow hair by harnessing stem cells. These cells, often referred to as progenitor cells, have the unique ability to develop into various types of cells, including hair follicle cells, making them a promising solution for hair regeneration.[51] The procedure generally begins with the extraction of stem cells from the patient's own tissue, typically from areas rich in stem cells, such as adipose tissue (fat) or bone marrow. After collecting, the stem cells are processed in a lab to isolate and concentrate on them. In some methods, the stem cells are cultured to increase their numbers before being reintroduced into the scalp. The processed stem cell solution is then injected into areas of thinning or balding on the scalp, where they work by regenerating damaged hair follicles, stimulating the growth of new hair, and enhancing the overall density and quality of the existing hair.[52] One of the significant advantages of stem cell therapy for hair loss is that it is minimally invasive, involving only small injections rather than surgical incisions. It also holds the potential for a long-lasting solution, as stem cells can regenerate damaged hair follicles, leading to new hair growth. Additionally, since the stem cells are derived from the patient's own body, the risk of rejection or allergic reactions is extremely low. Clinical studies and research into this area are still ongoing, but early results are promising, with some patients experiencing notable improvements in hair density and thickness within a few months of treatment. However, stem cell therapy for hair loss is still considered experimental and is not yet as widely available or standardized as more established treatments like Follicular Unit Extraction (FUE) or Follicular Unit Transplantation (FUT). Additionally, because the treatment is relatively new, it can be expensive, and long-term effectiveness is still under investigation. Nonetheless, as research continues to advance, stem cell therapy represents a cutting-edge approach in the field of hair restoration, offering hope for individuals with various forms of hair loss, including androgenetic alopecia and scarring alopecia.[53]

3.6.1 Side Effect

Stem cell therapy for hair loss can lead to mild and temporary side effects, including localized swelling, redness, and tenderness at the injection site. Some patients may also experience itching or discomfort during the healing process. Although the risk of infection is generally low when performed in a sterile environment, it remains a possibility. There may also be allergic reactions to any additives or growth factors used in the treatment. As this field is still evolving, the long-term effects of stem cell therapy are not fully understood, necessitating further research. Patients should consult with a qualified healthcare provider to discuss potential risks and determine their suitability for the procedure. [52,53]

4. CONCLUSION

Alopecia is a condition that affects many people, and while there are several treatments available, they come with both benefits and challenges. Traditional treatments like minoxidil, finasteride, and corticosteroids can help reduce hair loss or promote regrowth, but they often have side effects, such as scalp irritation, hormonal changes, and other systemic impacts. These side effects can limit the suitability of these treatments for certain individuals or affect their long-term use. As a result, many patients experience frustration when trying to balance the effectiveness of a treatment with the discomfort or risks it may bring. Emerging therapies like platelet-rich plasma (PRP) therapy and stem cell treatments offer new hope for more effective and personalized solutions. PRP and stem cell therapies focus on regenerating hair follicles and stimulating growth, while JAK inhibitors target autoimmune conditions like alopecia areata. However, these newer treatments are still in the experimental phase, and while they show potential, there is still much to learn about their long-term safety and effectiveness. More research is needed to fully understand both the benefits and side effects of existing and emerging treatments. A one-size-fits-all approach is unlikely to be the solution, as different forms of alopecia require different treatments, and patients vary in how they respond to these therapies.

5. FUTURE SCOPE

Alopecia, or hair loss, affects millions worldwide, with current treatments like minoxidil, finasteride, and corticosteroids offering temporary relief for some. Researchers are exploring long-term solutions, including stem cell therapy, which regenerates damaged hair follicles for potentially permanent results. Early studies in stem cell treatment are promising, and ongoing research aims to refine the technique. Gene therapy is another innovative approach, targeting the genetic causes of hair loss by modifying specific genes to prevent or reverse it. Though still in its infancy, gene therapy could enable personalized treatments based on individual genetic profiles. These advancements signal a hopeful future for more effective and lasting alopecia treatments. JAK inhibitors, originally used for arthritis, show promise in treating autoimmune hair loss like alopecia areata by blocking inflammatory pathways and promoting hair regrowth. Advanced techniques like follicular unit extraction (FUE) and experimental hair cloning aim to offer natural-looking and permanent solutions. Non-medical options, including artificial hair implants and improved wigs, provide realistic alternatives for those unsuitable for medical treatments. Platelet-rich plasma (PRP) therapy, which uses growth factors from a person's blood to stimulate hair growth, is gaining traction with ongoing research enhancing its effectiveness. Together, these advancements represent a diverse and evolving landscape of hair restoration options. Future developments should focus on creating safer, more effective, and personalized treatments that minimize side effects while maximizing benefits. With ongoing advancements in medical science, there is hope that better solutions for alopecia will continue to evolve, providing more targeted treatments that offer improved quality of life for patients dealing with hair loss.

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