Common Causes of Hair Loss and Their Treatment Options

Diya Doshi

Abstract

Research on hair loss is a constantly developing topic, with many studies still being conducted to gain a better, more thorough understanding of different conditions and hair diseases. 35 million men and 21 million women suffer from hair loss worldwide, with a hair loss market worth 52.37 billion USD in just 2022 itself. There are many types of hair loss, though the most common of which are androgenetic alopecia (AGA), telogen effluvium, and alopecia areata (AA). There is no clear path to reducing the effects of hair loss. Rather, many different medications and treatments may be suggested to yield favorable results. Clinicians and patients should take the time to discuss each option and its cost, benefits, and adverse effects. This paper will discuss the efficacy and adverse effects of different treatments for each of these three causes of hair loss.

Introduction

Hair loss research and treatment options are a developing field, with studies continuously being conducted to grasp a fuller understanding of the various conditions and hair diseases. Millions of men and women experience hair loss globally, totalling to 35 million men and 21 million women. With such a large population suffering from hair loss, the market has risen to 52.37 billion USD in 2022.

There are two classifications of hair loss: non-cicatricial and cicatricial alopecia. Non-cicatricial alopecia is more commonly seen than its counterpart, which is characterized by irreparable hair loss and scarring. Non-cicatricial alopecia may have many causes including stress, drugs, a poor diet, vitamin deficiencies, the immune system, and genetic changes. Of the types of non-cicatricial alopecia, this paper will be focusing on the most common types: androgenetic alopecia (AGA), telogen effluvium, and alopecia areata (AA). To get a proper diagnosis of the patient's condition, the clinician should begin by understanding their history and any medical conditions before conducting a physical exam. Performing a trichoscopy is crucial to help diagnose, though scalp biopsies may be performed in severe or uncertain circumstances.

Topical and oral treatments may be used to enhance hair growth and minimize hair loss. Medications like finasteride and minoxidil are especially common, though the patient should consult with a provider before beginning treatment, discussing the pros and cons of both types. Topical minoxidil, for example, requires patients to use it twice a day for a long period of time. The time commitment for such medications presents an obstacle for patients who do not have the time to dedicate to a treatment. Oral finasteride has seen large success rates, though patients reported sexual adverse effects. If such medications are not viable options, patients can turn towards other procedures like laser therapy or PRP. However, such surgical procedures can average out to be around $5000-$10000, so they may not be for everyone.

To better understand how hair loss works, one must understand hair on the cellular level. Hair is made of the hair shaft, which makes up the outside portion of the skin, and the follicle, which is underneath the top of the skin. The follicle, where hair grows, is made of the outer and inner root sheaths. The hair bulb produces hair and surrounds the dermal papilla, which has the key role of determining the size and color of the hair shaft through different growth factors and proteins. The hair cycle is cyclical, coming in phases of growth of the hair shaft followed by

phases of rest and regression. There are three phases in the hair cycle: anagen (growth), catagen (transition), and telogen (rest) (Hoover et al.).

Hair loss is a result of when the hair cycle is altered. For example, telogen effluvium can be caused by a disruption in the follicular cycle with a shift from the growth to rest phase, resulting in hair loss due to a change in the hair growth cycle (Alessandrini et al.). Androgenetic alopecia may be caused by a change in androgen (hormone) metabolism and by getting older, which leads to the shortening of the anagen phase, thus reducing the size of the hair follicle (Kaiser et al.). It is said that patients of alopecia areata develop antibodies that impact the structure of their hair follicles while in the anagen phase (Alessandrini et al.).

There are many different treatment options for hair loss, all with varying degrees of efficacy. Not all treatment options in this review are weighed equally as some have been heavily researched while others are new. The goal of this review is to summarize possible treatment options for the three most common causes of hair loss. Patients should consult their physicians before making final decisions on their treatment. Table 1 summarizes the most common treatment options for each type of hair loss discussed in this review, and their respective side effects.

Table 1. Information about the most common treatment options for each type of hair loss mentioned in this review.

Treatment	Administration	Side Effects	Conditions it Treats
Minoxidil	Topical Oral	Scaling, pruritus, initial increase in hair shedding, unpleasant odor Hypertrichosis, hair shedding, scalp pain, dizziness	AGA, TE, AA
Finasteride	Topical Oral	Skin irritation, pruritus Birth defects, depression, sexual dysfunction	AGA
Spironolactone	Oral	Hypotension, hyperkalemia, headache, menstrual disorder, pruritus	AGA
PRP	Intralesional	Infection, scalp sensitivity, scalp scaling	AGA, AA
Laser Light Therapy	Regional	Dry skin, irritation, scalp sensitivity, itching, tenderness	AGA
Microneedling	Regional	Temporary bleeding, erythema, pruritus, headache	AGA, AA
Corticosteroids	Topical Systemic	Skin thinning, folliculitis Chronic inflammatory diseases,	TE, AA

		immunosuppression, asthma	
Immunotherapy	Topical	Dermatitis, urticaria, eczema, blistering, contact leukoderma	AA
JAK Inhibitors	Systemic	Increased risk of infection	AA
Statins	Systemic	Myopathy, headache	AA
Anthralin	Topical	Pruritus, erythema, scaling, staining of the treated skin, and folliculitis	AA
Sulfasalazine	Oral	Gastrointestinal distress, rash, headache	AA

Cause #1: Androgenetic alopecia (AGA)

Androgenetic alopecia is the most common cause of non-cicatricial alopecia. It is caused by dihydrotestosterone (DHT), a testosterone metabolite, that leads to constant hair thinning (Alessandrini *et al.*). High levels of DHT are found in patients with AGA, meaning more terminal hairs are reverted back into vellus hairs. The root cause of AGA is a change in androgen metabolism that occurs during the aging process, and this leads to the reduction in hair follicle size and shortening of this anagen phase. Because of genetic factors and age-related causes that result in a defective androgen mechanism, vellus hairs, which are fine and short hairs commonly known as “peach fuzz,” cannot become longer, thicker, and darker terminal hairs. Rather, hair follicles turn back into vellus hairs (Gokce et al.). AGA decreases the number of terminal hairs and fibrous streamers, replacing them with small vellus hairs in the temporal, vertex, and mid-frontal areas of the scalp (Kaiser et al.; Alessandrini et al.).

Furthermore, while the anagen phase is reduced, the telogen phase is increased, resulting in the shrinkage of the hair follicle. The lag phase, the time between the loss of a telogen hair and the emergence of its replacement anagen hair, increases with each consecutive hair cycle, leading to a decrease in the percentage of hair follicles in anagen phase (only 60-80%), compared to the normal 90% of scalp hair. The shortening of the anagen phase causes the hair to look smaller (Van Neste et al.). The hair follicles are also shortened until they can not penetrate the epidermis, the surface layer of the skin, due to an increased activation of androgen receptors (Kaiser et al.).

In males, AGA affects the fronto-temporal region and vertex region, while in women it primarily affects the frontal region, behind the hairline (Alessandrini et al.). For women, the hairline is typically not impacted. It is the crown and bitemporal scalp areas (Kaiser et al.).

Treatment Options

Topical Minoxidil

Minoxidil is one of only two drugs approved by the FDA for hair loss (Abdullah). It works by acting on ATP-gated smooth muscle potassium (K^+) channels that lead to reduced blood pressure. This increases blood supply and nutrients to the hair follicles, thus increasing hair growth (Kaiser et al.). By increasing blood circulation, minoxidil is able to facilitate quicker hair

growth and thicker hair, lengthen the anagen phase, and stimulate kenogen follicles to begin a new hair cycle (Katzer et al.). This treatment helps reduce the excess inflammation that contributes to AGA by reducing the amount of pro-inflammatory cytokines. Topical minoxidil is a good option for when less than 20% of the scalp is affected by AGA (Katzer et al.). When the 5% solution was applied two times daily for men, results showed that it was more efficacious than its 2% counterpart, but the opposite was seen for women. However, a meta-analysis showed that topical minoxidil had far better results than the placebo at all concentrations (*Minoxidil and Its Use in Hair Disorders: A Review - PMC*). Studies demonstrate that after 16 weeks of constant application, less than 40% of patients experienced results. The earliest period that minoxidil may display its effects is at 6 to 8 weeks, while the maximum effect may be seen by 12 to 16 weeks. Topical minoxidil has demonstrated success in treating hair loss, though the long-term commitment may be difficult for some patients because of the need to apply the formula twice daily. For some, the process may be irritating and can cause scaling and pruritus, which is severe itching of the skin, as well as a temporary increase of hair shedding when beginning the treatment. Although minoxidil is considered a safe treatment, patients may also experience hypertrichosis, which is excessive hair growth anywhere on the body, and headaches (Kaiser et al.). The treatment may also result in an undesirable hair texture, and has an unpleasant odor that deters patients from continuing treatment (Ramírez-Marín and Tosti).

Oral Minoxidil

Oral minoxidil has recently been suggested as an alternative therapy for AGA. Due to the commitment required for topical minoxidil, oral minoxidil is seen as a more convenient treatment as it requires one pill daily. Oral minoxidil is processed into its active form in the liver, allowing increased bioavailability, leading to improvements for patients who had no success using topical minoxidil (Kaiser et al.). Although there are no clinical trials on the efficacy of oral minoxidil for AGA, an epidemiological study in Spain revealed that oral minoxidil was prescribed to patients with male pattern hair loss by 50.6% of dermatologists, and to pre- and post-menopausal women by 67.9% and 63% of dermatologists, respectively (Ramírez-Marín and Tosti). The benefits of oral minoxidil include its convenience, as it is easier to take a pill than apply topically, improving patient compliance. Additional benefits include hair that does not turn gray, as well as lack of product residue and cost effectiveness. Oral minoxidil should be used for patients who have difficulty with compliance or negative side effects with topical minoxidil. In a study conducted on men for 6 months, it was shown that 5 mg daily works faster than other therapies, and low doses were shown to yield the best results (Kaiser et al.). Adverse effects are common in individuals taking 5 mg of oral minoxidil. Hypertrichosis occurred in more than half of patients, though it was dose dependent for younger patients. Hair shedding also occurred in approximately ⅓ of patients , and it was typical for younger men (Kaiser et al.).

Topical Finasteride

Finasteride reduces DHT production in the hair follicles by blocking the conversion of testosterone to DHT by more than 60% in the scalp and serum (Katzer et al.; Kaiser et al.). Topical finasteride may be safer than its oral form as it has fewer systemic effects. (Kaiser et al.). The 0.25% solution used twice daily lowered scalp DHT levels. In a Phase III randomized and controlled clinical trial by Piraccini et al, 323 patients using 0.25% topical finasteride spray daily saw an increase in hair count after 24 weeks. No drastic difference was found in the average hair count between topical and oral finasteride (Kaiser et al.). When 0.25% topical

finasteride solution was compared to 1 mg/day of oral finasteride, both yielded similar results in DHT inhibition after a week. However, topical application lowered finasteride in the plasma more than oral use (Katzer et al.). Some adverse effects include skin irritation and pruritus, with no patients experiencing sexual dysfunction. Evidence shows that pharmacokinetics lessens systemic absorption, though more studies are needed to research the best formula and dose (Kaiser et al.).

Oral Finasteride

Oral finasteride is one of only two medications approved by the FDA to treat hair loss. Its anti-androgen properties and role as a 5α-reductase type II inhibitor make it a potential treatment for men with AGA (Kaiser et al.). The scalp converts testosterone to DHT, which is responsible for the shrinkage of the hair follicles, as it plays a large role in the pathogenesis of male pattern hair loss. By inhibiting 5α-reductase, finasteride can decrease DHT levels in the scalp (Van Neste et al.). When used daily, 1 mg of oral finasteride has been shown to reduce AGA (Kaiser et al.). A study found that 1 mg daily boosts the conversion of hair into the anagen phase, resulting in notable improvements in hair growth and quality. When continued for 2 years, there was a significant improvement in the quality of hair, and hair density remained stable (Van Neste et al.). Oral finasteride was best in treating the vertex region of the scalp, but was not as effective in the frontal region. Optimal improvement was seen after 1 year of treatment, with minimal improvement after 4 years. Off-label use of this medication has shown clinical efficacy in women. Some adverse effects present in both men and women include birth defects, depression, sexual dysfunction, gynecomastia (the enlargement of breast tissue in men/boys), and muscle atrophy. There is a dearth of information regarding the long-term safety profile of finasteride. Sexual side effects are the most common side effect, present in 1%-40% of patients (Kaiser et al.). Overall, oral finasteride treatment is well-tolerated in men (Van Neste et al.).

Oral Spironolactone

Oral spironolactone, which is converted into canrenone in the liver, works by blocking the effects of the hormone aldosterone. It can bind and hinder androgen receptors, helping treat acne and abnormal facial hair growth in female patients (Kaiser et al.). This medication is used off-label for AGA in females. It lowers the levels of circulating androgens by abrogating adrenal androgen production and thus the effect of androgens in the hair follicle (Kaiser et al.). James et al found that about 50% of women using this as monotherapy for female pattern hair loss saw an improvement. The medication must be used for more than 12 months at a dosage of 100 to 200 mg in order to see clinical improvement for female AGA. In addition, Famenini et al found that 74% of females using spironolactone long-term experienced clinical improvement (Kaiser et al.). In a subset of 5 different studies, 81% of the 195 females reported improvement in hair growth when receiving a dose between 25-200 mg daily. Another study showed that oral spironolactone was just as effective in restoring hair count or preventing further hair loss when compared to daily usage of cyproterone acetate (Wang et al.). Adverse effects that are common include hypotension, which is low blood pressure, hyperkalemia, which is when there are high levels of potassium in the blood, and sometimes urticaria, which is an intense skin rash (Kaiser et al.). Other effects include headache, menstrual disorder, rash, nausea, and scalp pruritus (Wang et al.).

Platelet Rich Plasma Treatment (PRP)

Platelet Rich Plasma (PRP) is the isolated plasma and platelets from the blood (Kaiser et al.). It is obtained by the centrifugation of patient blood (Katzer et al.). PRP contains chemokines, growth factors, cell signaling molecules, and cytokines, all of which are important in controlling and regulating cellular processes. The alpha granules made and kept in the platelets are the most important molecules found in PRP to treat AGA since these granules have many different types of growth factors that promote angiogenesis, a process in which new blood vessels are formed, and are crucial in beginning the process of stem cell differentiation. PRP releases large amounts of platelet-derived growth factors (PDGF) which are important in minimizing follicular apoptosis and in boosting follicular cell growth (Kaiser et al.). Overall, PRP increases both hair density and thickness(Katzer et al.). Gkini et al led an experiment with 20 patients in which significant results were shown at 6 months and 1 year. Growth peaked at 3 months and continued for 1 year. Furthermore, a meta-analysis by Gupta et al found that all the studies he evaluated using PRP saw a significant increase in hair growth and density. He recommended that PRP treatment should be continued for 3 months in 1 month intervals, then followed by maintenance sessions (Kaiser et al.). Although PRP is a minimally invasive treatment, there is a risk of infection, scalp sensitivity, and mild scalp scaling. PRP may not be suitable for everyone. For example, it is not for patients with a history of malignancy, platelet disorders, anemia, bleeding disorders, and pregnant women (Kaiser et al.).

Low-Level Laser Therapy (LLLT):

Laser light therapy is a new and effective treatment option for AGA. Due to the cost effectiveness and non-invasive nature of laser light therapy, it is a popular treatment option for patients with AGA (Kaiser et al.). It exposes tissues to luminous energy (Katzer et al.). LLLT helps reverse hair loss by promoting telogen hair follicles to reenter the anagen phase, increasing the length of the anagen phase, and preventing anagen hairs from turning into catagen hairs too early (Kaiser et al.). It stimulates cellular activity in tissues, and its range of wavelengths promote tissue repair and regeneration (Pillai and Mysore). LLLT is the only FDA approved device to treat AGA (Katzer et al.). The Laser HairMax comb was approved by the FDA in 2007 for men and in 2011 for women. A laser cap, providing full scalp coverage and even distribution, was also approved by the FDA (Pillai and Mysore). Out of the 32 patients using LLLT for three sessions weekly, 28 patients displayed signs of moderate to significant improvement in 3 to 24 months. A review by Afifi et al discovered that 9 out of 11 studies demonstrated significant improvement in hair count and density. Furthermore, LLLT increased hair growth in both short and long term follow ups for men and women (Kaiser et al.). Another study researched 28 males and 7 females with AGA who used the HairMax LaserComb every other day for 5-10 minutes. Significant improvement was seen in all patients after 6 months. The strength of the hair also increased (Katzer et al.). Overall, the treatment sessions for LLLT usually lasts for 15-20 minutes and occurs 3 times a week for 6 months (Pillai and Mysore). In a study using the HairMax Laser Comb, side effects were uncommon, though some experienced dry skin, irritation, scalp sensitivity, and itching (Katzer et al.). LLLT generally has minimal adverse effects, though some include temporary hair loss, pruritus, tenderness, and acne (Kaiser et al.). It is a safe and effective treatment used to treat AGA as more than half of the studies displayed an improvement in hair regrowth, hair density, and tensile strength (Pillai and Mysore).

Microneedling

The microneedling device works by instilling controlled and repetitive tissue micro-injuries that make transdermal microchannels in the stratum corneum, the outer layer of the skin. It promotes growth factors, activates bulge stem cells, and increases gene expression for genes correlated with hair growth (Kaiser et al.). Rollers and electric pens are the most common devices used to perform this procedure, though the needles used may vary in length and number (Katzer et al.). In a study conducted with 29 females and 14 males over 6 months, participants were told to use topical minoxidil for 24 hours after microneedling. All patients saw reduced hair loss. It is recommended to patients who want to see quick improvements to use microneedling (Kaiser et al.). Another study consisted of two groups, the first group was given the microneedling treatment weekly with 5% minoxidil lotion twice a day, and the second group was only given the 5% minoxidil lotion twice a day. The mean change in hair count after 12 weeks of treatment was greater for the microneedling group compared to the minoxidil group. Furthermore, 82% of patients in the microneedling group saw more than 50% improvement compared to only 4.5% in the minoxidil group. The microneedling group saw noticeable hair growth earlier at 6 weeks, while in the minoxidil group it was seen at 10 weeks (Dhurat et al.). Microneedling is a good option for those wanting quick results. However, it can be painful during the treatment itself. Adverse effects include temporary pinpoint bleeding, erythema, larger lateral cervical lymph nodes, pruritis, seborrheic dermatitis, and headaches. There may also be a risk of infection, though there is an overall low risk of adverse effects (Kaiser et al.).

Cause #2: Telogen effluvium (TE)

Telogen effluvium is characterized by non-scarring and diffuse shedding of the hair (*Telogen Effluvium: A Review of the Literature - PMC*). Patients experience hair loss every 3 months after a triggering event, and it lasts for 6 months. Hair loss is less than 50% of the scalp hair, and is more common in adult females (Alessandrini *et al.*). Patients can easily extract clumps of telogen hair from the vertex and margins of the scalp, and diffuse loss is seen over the whole scalp (Malkud).

TE may be due to 5 different mechanisms. The first is the disruption of the follicular cycle with an early shift from the anagen to telogen phase, increasing hair shedding in the next 2 to 3 months. The second is a delayed anagen release, which results in increased hair loss during the telogen phase. The third is short anagen syndrome, which is due to the shortening of the anagen phase, leading to continuous TE. The fourth is an immediate telogen release, which leads to large amounts of club hair, hair that has reached the end of the growth stage, loss. The last is a delayed telogen release that results in a stalled transition to the anagen phase (*Telogen Effluvium: A Review of the Literature - PMC*).

Acute TE is due to harmful events, such as diseases, drugs, and weight loss, that allow the entry of many follicles into the telogen phase (Alessandrini *et al.*). Acute and chronic stress are known as primary causes of TE (Gokce *et al.*). Acute TE lasts for less than 6 months, and hair loss occurs for 2 to 3 months after the trigger (*Telogen Effluvium: A Review of the Literature - PMC*). Few drugs have been scientifically proven to decrease hair loss. Chronic TE is when hair loss occurs for more than 6 months. It mostly impacts middle-aged women and is characterized by an increased percentage of hair follicles in the catagen or telogen phase (Alessandrini *et al.*). TE is seen as reversible, though it does impact the psychosocial state of the patient. It is hard to diagnose and treat as there are many factors that can lead to this disease (Gokce *et al.*).

Treatment Options

Minoxidil & Finasteride, & Inhibition

Topical or oral minoxidil may help prolong the anagen phase (Alessandrini *et al.*). In addition, minoxidil and finasteride cannot effectively block the catagen (transition) phase or induce the anagen (growth) phase. Catagen-inducing drugs (retinoids, antithyroid drugs, beta-blockers, etc) should not be used, and catagen-inducing endocrine disorders should be assessed and treated (*Telogen Effluvium: A Review of the Literature - PMC*). Substitution therapy for catagen-promoting deficiencies, like iron and zinc, can also be started. Additionally, there are also therapeutic options in treating TE. These include the inhibition of catagen to prolong anagen, the induction of anagen in telogen hair follicles, and the inhibition of exogen (shedding) to minimize hair shaft shedding (Grover and Khurana).

Healthy Diet & Correcting Deficiencies

When underlying conditions are at the root of the hair loss, it is important to directly fix them as well. This includes conditions like endocrine disorders, nutritional deficiencies, and other causes such as psoriasis and seborrheic dermatitis, a condition that results in scaly patches and red skin primarily on the scalp. Treatment for these may include a proper diet and healthy body weight (Alessandrini et al.; *Telogen Effluvium: A Review of the Literature - PMC*).

Patient Education

Patients should be well-informed regarding their condition. Disease and triggers correlate with each other, so the timing of the hair loss should be discussed. Losing hair can cause great psychological stress for the patient, so patient education is crucial (*Telogen Effluvium: A Review of the Literature - PMC*). Patients should also be notified that hair loss may take 3 to 6 months to stop, and regrowth may take 3 to 6 months after the trigger is found and corrected. Significant improvement in hair growth may be seen in 12 to 18 months (Malkud).

Topical & Systemic Corticosteroids

Topical corticosteroids, also known as steroids, are a type of anti-inflammatory medication used by dermatologists for treatment. If a side effect of the application of this medication is decreasing trichodynia, it means the therapy is working. Corticosteroids can also be given routinely to patients with chronic TE (*Telogen Effluvium: A Review of the Literature - PMC*).

CNPDA

A new cosmetic treatment has been developed by Davis et al (Grover and Khurana). This treatment is a combination of caffeine, niacinamide, panthenol, dimethicone, and an acrylate polymer (*Telogen Effluvium: A Review of the Literature - PMC*). It works by increasing the diameter of existing terminal scalp hair fibers, which may result in an increase of 10% in the cross-sectional area (Grover and Khurana).

Cause #3: Alopecia areata (AA)

Alopecia areata is a T-cell mediated autoimmune condition, meaning one's own immune system attacks their hair follicles in the anagen phase, resulting in the collapse of the anagen

hair bulb (Gokce et al.). It is characterized by non-scarring hair loss in round patches around the scalp, and initially presents itself as one or more patches of alopecia, most likely on the scalp and beard (*Alopecia Areata: Review of Epidemiology, Clinical Features, Pathogenesis, and New Treatment Options - PMC*; Alessandrini et al.). Acute AA patients may display exclamation hairs, which are damaged hairs that are thicker at its end and thinner on the end closer to the scalp. The first step in hair recovery is the emergence of thin white hair, then healthy pigmented hair (*Alopecia Areata: A Comprehensive Review of Pathogenesis and Management | SpringerLink*).

AA may occur at any age, though the median is 33 years old. It equally affects both men and women, and is equally prevalent across races (Malhotra and Madke). Studies suggest that 34-50% of patients can recover in a year, while 14-25% of patients' conditions will worsen, making it difficult to completely recover (*Alopecia Areata: Review of Epidemiology, Clinical Features, Pathogenesis, and New Treatment Options - PMC*). AA is caused by environmental factors such as infections, stress, and diet, immunologic factors such as thyroid disease and type 1 diabetes, as well as genetic factors (Alessandrini et al.).

When AA progresses to complete baldness, it is called alopecia totalis (AT). Another type of AA is called ophiasis, which is when hair loss occurs in the shape of a wave along the circumference of the head (*Alopecia Areata: A Comprehensive Review of Pathogenesis and Management | SpringerLink*). AA is unpredictable and there may be relapses in patients (Alessandrini et al.). 30-50% of patients with patchy AA will experience spontaneous remission, the phase in which signs of a disease or condition disappear, in the first 6-12 months of disease onset, and 66% of patients show complete hair regrowth in 5 years. Overall, the chance of going into relapse is about 85%, and about 100% for patients observed over 20 years (*Alopecia Areata: A Comprehensive Review of Pathogenesis and Management | SpringerLink*). Treatment depends on the extension, activity of disease, and age of the individual (Alessandrini et al.). Treatment should also focus on regrowth and maintaining the regrowth (Malhotra and Madke).

Treatment Options

Topical, Intralesional, & Systemic Corticosteroids

Topical corticosteroids are most commonly used to treat AA due to its safety and painless application (Malhotra and Madke). They work by containing inflammation and quickening the recovery of damaged hair follicles (*Alopecia Areata: Review of Epidemiology, Clinical Features, Pathogenesis, and New Treatment Options - PMC*). Treatment should be used for at least 3 months to see hair growth occur (Malhotra and Madke). In one study, 57% of patients displayed complete hair regrowth during treatment (*Alopecia Areata: Review of Epidemiology, Clinical Features, Pathogenesis, and New Treatment Options - PMC*).

Intralesional corticosteroids are a first-line treatment for AA conditions involving less than 50% of the scalp. Common treatments are hydrocortisone acetate at 25 mg/ml and triamcinolone at 5-10 mg/ml. Intralesional triamcinolone acetonide at 5-10 mg/ml is locally injected every 4 to 6 weeks in multiple 0.1 ml injections 1 cm apart, in or beneath the dermis. Injections should not be administered at the same site repeatedly, and should not be used in high concentrations as it may lead to skin atrophy. Severe cases of AA may not react well to this treatment (Malhotra and Madke). Overall, this therapy has better results than topical corticosteroids, with one study showing 63% of patients displaying complete hair regrowth. A side effect is increased risk of skin atrophy at the treatment site (*Alopecia Areata: Review of Epidemiology, Clinical Features, Pathogenesis, and New Treatment Options - PMC*).

Systemic corticosteroids are used for refractory cases, cases that do not respond to treatment, and for acute and widespread AA (Alopecia Areata: Review of Epidemiology, Clinical Features, Pathogenesis, and New Treatment Options - PMC; *Alopecia Areata: A Comprehensive Review of Pathogenesis and Management | SpringerLink*). It is recommended to take 0.5-1 mg/kg a day for adults, for 1 to 6 months to see results, and should not be used for longer to minimize side effects (Alopecia Areata: Review of Epidemiology, Clinical Features, Pathogenesis, and New Treatment Options - PMC). To prevent side effects, it is recommended to use pulsed administration (*Alopecia Areata: A Comprehensive Review of Pathogenesis and Management | SpringerLink*). Oral minipulse therapy displayed signs of hair regrowth by 71.43% in a study in which a dose of 5 mg a day was administered for 2 consecutive days for 4 months (Malhotra and Madke). Furthermore, relapse rates are high, between 33-75% (*Alopecia Areata: Review of Epidemiology, Clinical Features, Pathogenesis, and New Treatment Options - PMC*).

Immunotherapy

Diphenylcyclopropenone (DCPC) is an immunotherapeutic agent used to treat AA. DPCP is an experimental drug that creates an immune reaction, thus inhibiting perifollicular immune response to restore hair growth. Immunotherapy works by creating antigenic competition, thus preventing CD4+ T-cells from hurting the hair follicles. Side effects include urticaria, dermatitis, blistering, and depigmentation (*Alopecia Areata: Review of Epidemiology, Clinical Features, Pathogenesis, and New Treatment Options - PMC*). Today, DPCP is the primary choice for topical immunotherapy treatment for AA. In a study of 68 patients with severe AA who were treated with topical DPCP for at least 5 months, researchers Pericin and Trüeb found that 30.9% went into complete remission, and 39.7% went into partial remission. Long periods of therapy are needed and may increase the response for patients. Furthermore, DPCP has a high relapse rate, so maintenance therapy is recommended. Overall, DPCP is well received by most patients (*Alopecia Areata: A Comprehensive Review of Pathogenesis and Management | SpringerLink*).

JAK Inhibitors

Multiple Janus Kinase (JAK) inhibitors, all oral medications, have been successful in treating AA, including tofacitinib, ruxolitinib, baricitinib, CTP-543, PF-06651600, and PF-06700841 (Malhotra and Madke). They work by preventing the production of IFN-γ, a proinflammatory immune molecule which is needed for the immune response of AA (*Alopecia Areata: Review of Epidemiology, Clinical Features, Pathogenesis, and New Treatment Options - PMC*). A study led by Khan et al demonstrated that 72.4% of patients responded partially or completely to JAK oral inhibitors. It took an average of 2.2 months for initial hair growth, with complete hair growth taking around 6.7 months. Some side effects include nausea, headaches, infection, anemia, and high cholesterol. There may also be relapse after stopping treatment (Malhotra and Madke).

PRP

PRP changes the hair growth cycle through induction and maintenance of the anagen phase. It is injected locally into the alopecia areas. PRP injections may not be as beneficial to those with chronic and severe AA as treatment is needed everywhere on the scalp and is thus painful. PRP treatment for acute AA is typically well received (Malhotra and Madke). In randomized studies, PRP improved hair growth compared to triamcinolone scalp injections, which is another steroid used to treat AA, and to placebo; there were no adverse effects.

However, in another study of patients with severe AA, PRP had inconsistent effects. Another trial found that PRP and topical minoxidil increased hair regrowth compared to placebo. PRP also displayed an earlier response than the minoxidil (*Alopecia Areata: Review of Epidemiology, Clinical Features, Pathogenesis, and New Treatment Options - PMC*).

Statins

Statins are drugs that decrease bad cholesterol (LDL) and overall inflammation as reflected by the lowered levels in C-reactive protein (Malhotra and Madke). Its anti-inflammatory and immunomodulatory effects may help them improve hair regrowth. One trial found that out of the 19 patients with 40-70% hair loss who completed the treatment, 14 patients actually responded. However, in another study of patients with greater than or equal to 70% of hair loss who were treated with simvastatin, none showed signs of hair regrowth (*Alopecia Areata: Review of Epidemiology, Clinical Features, Pathogenesis, and New Treatment Options - PMC*).

Microneedling

Microneedling is a new procedure that works by puncturing the skin with small needles. To treat AA, topical corticosteroids are injected using the microneedling technique. Ito et al successfully used a microneedling device to administer intralesional corticosteroid in patients with AA, and Deepak et al also successfully treated 3 patients with resistant AA with scalp roller therapy, a type of microneedling device (*Alopecia Areata: Review of Epidemiology, Clinical Features, Pathogenesis, and New Treatment Options - PMC*).

Anthralin (dithranol)

Anthralin inhibits DNA replication, slowing cell division and stopping cells from rapidly multiplying. This helps in autoimmune reactions such as those underlying AA. Anthralin effectively treats AA when combined with DPCP blocking due to its immunosuppressant and anti-inflammatory properties. It should be used in concentrations of 0.5-1% for 20 to 30 minutes after shampooing the scalp, every other day and daily as time progresses. Some adverse effects include pruritus, erythema, scaling, staining of the treated skin, and folliculitis. A study conducted by Wong et al showed that 25% of patients completely responded to treatment, while an additional 39.5% had a good response (Malhotra and Madke).

Topical Minoxidil

This is usually used in less severe cases. Minoxidil increases the activity of ATP synthase, which in turn increases the amount of ATP produced. The ATP can be broken down into adenosine, which makes more growth factors such as VEGF, lengthening the anagen phase and reverting vellus hairs to terminal hairs. This means that minoxidil is important in aiding hair growth. No more than 25 drops of 5% solution should be used twice a day. Results can be seen in 3 months, but continuous application is needed to see noticeable results (Malhotra and Madke).

Sulfasalazine

Sulfasalazine is an inflammatory drug used in various autoimmune conditions. Its immunomodulatory and immunosuppressive actions have made it a good therapy option in treating AA. It results in the inhibition of T-cell growth and natural killer cell activity, and it also

inhibits the creation of antibodies. Treatment begins at a low dose, around 500 mg two times a day, and is slowly increased to 1 g three times a day (Malhotra and Madke).

Supplements and Hair Oils

Maintaining a balanced and regular diet is important in dealing with hair loss. Quick weight loss, low-calorie diets, unbalanced diets, obesity, and too many vitamin and mineral supplements can result in hair loss. Micronutrients are the key parts of the hair cycle, and thus are important in alopecia. Micronutrients aid in cell renewal, a process seen in dividing hair follicles. Proteins and minerals are also needed to maintain healthy hair. Plant rich diets like the mediterranean diet (rich in antioxidants, anti-inflammatory, estrogenic components) have chemicals that boost hair growth by reducing the generation of reactive oxygen species in the dermal papilla cells, allowing growth hormones to be released (Gokce et al.).

Vitamin B: Vitamin B can be taken in through a good diet, and examples of this vitamin include pantothenic acid, riboflavin, thiamine, niacin, B6, B12, and folate. Hair loss is linked to patients deficient in riboflavin (B2), biotin (B7), B12, and folate. B12 and folic acid may have a role in the growth of hair follicles, though research on vitamin B12 on hair loss is insufficient. There is not enough evidence to show that biotin supplements aid in hair loss (Gokce et al.). It is said that the consumption of biotin in the diet is good for healthy hair, though not many studies show the impact of biotin in patients who are already healthy (Abdullah).

Iron: Iron is important in quickly growing cells, like those in the hair follicle matrix. Some studies show that a few genes in the hair follicle are regulated by iron. The amount of serum ferritin, also called iron-binding protein, is a correlate of iron stores in the body and is used in hair loss research as an indicator. Women with hair loss most likely have an iron deficiency. Furthermore, more research is needed to further expand on iron supplement guidelines and cures for patients with hair loss due to an iron deficiency (Gokce et al.).

Vitamin C: Vitamin C could be important for those who experience hair loss due to iron deficiencies, as Vitamin C helps in the absorption and use of iron. Citrus juices and other oral supplements are recommended for patients with an iron deficiency. There is, however, no evidence of a correlation between vitamin C and hair loss (Gokce et al.).

Vitamin D: Vitamin D regulates keratinocyte development and differentiation by attaching to the vitamin D receptor (VDR). The VDR is present in higher amounts during the anagen phase, and is present in lower amounts when there is less anagen initiation. This is used to demonstrate how VDR is expressed in hair follicle keratinocytes, which are skin cells involved in the process of hair growth and development, demonstrating how Vitamin D is related to hair development. However, this does not show that it is enough to maintain the typical hair cycle. People with VDR mutations and vitamin D resistance have severe alopecia on the body and scalp (Gokce et al.).

Zinc: A zinc deficiency can lead to telogen effluvium, thin white and brittle hair, and other dermatological issues. A contributing factor to alopecia areata called superoxide dismutase is a type of zinc-dependent enzyme. Furthermore, zinc is linked to the Hedgehog signaling pathway, which correlates with the development of the hair follicle's shape and structure. In a study of 312 people with hair loss and 32 controls, those with telogen effluvium and alopecia areata had low zinc, indicating a correlation between zinc and hair loss (Gokce et al.).

Green Tea: Green tea has many antioxidant compounds like polyphenols and flavonoids. Its anti-inflammatory effects and ability to reduce stress have the potential to improve hair

growth. Green tea also has a compound called epigallo-catechin gallate (EGCG), which blocks 5α-reductase, thus boosting hair growth (Abdullah).

Coconut Oil: Coconut oil has emollients, creating a coating over the hair shaft and sealing the cuticle to retain moisture in the hair. It is also a lubricant, so it detangles hair, smoothens and flattens the cuticle surface, and improves the health and look of hair strands. It is also effective in preventing protein loss as it can penetrate inside the hair shaft (Abdullah).

Castor Oil: Castor oil is very moisturizing due to the presence of ricinoleic acid and its derivatives. Ricin and ricinoleic acid protect the scalp and the hair shaft from fungal and microbial infection. The fatty acids in castor oil also have excellent penetrability, so they are able to nourish the hair follicle (Abdullah).

Argan Oil: Argan oil is good at regulating sebum secretion due to its high oleic acid content, and it is also moisturizing as it has good water retention. Topical application has been shown to increase elasticity when comparing results from after 2 months to the start of the study (Abdullah).

Fenugreek Oil: Disogenin, which is found in fenugreek, is shown to have oestrogenic activity, and it can block dihydrotestosterone. A study found that mixing 1 ml of fenugreek extract with 3 ml of water (1:4) decreased Malassezia furfur, a naturally-occurring yeast that may cause inflammation and damage to the hair follicles. Lastly, fenugreek oil has lecithin, a natural emollient that strengthens and moisturizes the hair (Abdullah).

Sesame Oil: Sesame oil has lignans, which are polyphenolic compounds, that provide anti-inflammatory effects. It can also increase penetration, preventing dryness by moisturizing the hair follicle. In addition, sesame oil increases scalp circulation. This leads to increased hair growth and less graying (Abdullah).

Rosemary Oil: Rosemary's spasmolytic activity is shown to increase microcapillary perfusion, which may allow it to increase blood supply to the hair follicle. Furthermore, rosemary oil has antioxidant activity, which is crucial in patients with alopecia (who have low levels of antioxidants). In a study of 100 men with AGA, there was no significant difference in the change of hair count for the rosemary and minoxidil groups at the 3 month checkpoint. At the 6 month point, however, there was a significant increase for both groups. There was no significant difference in hair count between both groups at either point of the study. A patient treatment satisfaction questionnaire showed that rosemary oil treatment was favored over the 2% topical minoxidil (Panahi et al.).

Pumpkin Seed Oil: Pumpkin seed oil (PSO) has phytosterols that inhibit 5α-reductase and has anti-androgenic effects in rats (Cho et al.). It is also made of anti-inflammatory substances that have antioxidant and 5α-reductase inhibition properties (Katzer et al.). After 24 weeks, self-rated improvement scores were significantly higher for those treated with PSO than in the control group. 44.1% of the PSO group slightly or moderately improved compared to only 7.7% in the control group. Overall, the study shows that PSO has a positive anabolic effect on hair growth (Cho et al.).

Peppermint Oil: After week 2 of a study on mice, peppermint oil bolstered hair growth quicker than saline and jojoba oil. At week 3, peppermint oil promoted more hair growth than saline, jojoba oil, and even minoxidil. At week 4, peppermint oil showed to yield hair growth of 92%, while minoxidil only yielded 55%. Topical application of peppermint oil and minoxidil produced thick and long hair growth while also elongating the hair follicles (Oh et al.).

Conclusion

Hair loss remains a crucial field of research that is currently under development as new studies continue to be published. Novel treatments are still being discovered and tested, such as CNPDA for telogen effluvium. Although this review covers the most common types of hair loss, there are many others including anagen effluvium, loose anagen hair syndrome, stress induced alopecia, and endocrine imbalances. Physicians and patients should consult with one another regarding the most cost effective and efficacious treatment for them, considering factors such as patient history and financial status. Combinations of treatments may also be used, such as laser light therapy and topical minoxidil for androgenetic alopecia, which could improve patient compliance when used together. Note that this review does not cover all treatment options for each type of hair loss, simply the most common and well-researched ones. The treatment options mentioned in this review have differing degrees of evidence and data to factually support the efficacy of the treatment option. An important point to take into consideration is that some treatments mentioned are relatively new, while others, like minoxidil and finasteride, have already been approved by the FDA.

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