RECENT PERSPECTIVE IN MEDICATION FOR ALOPECIA ARAETA

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Abstract- **Alopecia areata (AA) is a common autoimmune disease that causes unexpected, recurrent patchy hair loss. Its chronic pathogenesis remains mostly unknown. The ability of hair follicles to regenerate is preserved indefinitely as the follicles are not completely damaged. A patchy AA is the most prevalent kind. The most common related diseases are autoimmune thyroiditis and atopy. Histopathology is characterized by peribulbar and intrabulbar lymphocytic inflammatory infiltrates that resemble a "swarm of bees." The main objective of treatment is to reduce the activity of the illness. The recommended medications for topical, intralesional, or systemic therapy are corticosteroids. The current AA therapies have low efficacy rates ranging from 23% to 75%. There are many therapeutic alternatives available, however, there is a high recurrence rate and certain adverse effects connected with the present treatment choices, thus the quest for novel techniques is still ongoing. In difficult situations, wigs may serve as an alternate type of camouflage.**

Keywords: **New Treatment, Alopecia areata, Scar-free, Hair loss; Autoimmune Diseases, Nonscarring alopecia, Camouflage.**

I. INTRODUCTION

Alopecia areata (AA) is a frequent non-scarring alopecia affecting the body or scalp that is defined by hair loss in the absence of clinically discernible inflammation. (1) Alopecia areata is a long-term, immune-mediated disorder that affects nails, the retinal pigment epithelium, and hair follicles. This autoimmune disorder causes hair loss when the immune system mistakenly attacks hair follicles. Alopecia areata is commonly characterized by discrete, silky, non-scarring patches of hair loss on the scalp or in any place where hair grows (3). One of the most commonly seen types of hair loss in dermatology is alopecia areata, which accounts for 25% of all cases. (2,4) Cornelius Celsus wrote the first description of it, and Sauvages first used the word AA in 1760. In the UK and USA, it makes up 2-3% of new dermatological cases; in China, it makes up 3.8%, and in India, it makes up 0.7%. The estimated frequency in the general population was 0.1-0.2%, with a 1.7% lifetime risk. Although studies have indicated a male majority, both genders are equally impacted. All ages are susceptible to it. The oldest was in his late eighties, while the youngest was four months old. In the AA group, 60% of patients received their first patch before age 20, with 20% of cases involving minors.The age group between 30 and 59 years old has the highest frequency. Families have been affected in 8.7–20% of instances. Although alopecia areata is a chronic illness with recurrent periods of hair loss, many affected individuals have spontaneous hair regrowth within a year. To control the amount and length of hair loss, a variety of therapeutic alternatives are available, such as immunotherapy, topical treatments, Janus kinase (JAK) inhibitors, and corticosteroids.(4) This overview of alopecia areata aims to provide medical professionals with a thorough understanding of the condition. It covers the pathophysiology, clinical manifestations, and treatment approaches, as well as important topics like patient expectations, communication, and emotional support. (2,5)

II. EPIDEMIOLOGY

Alopecia areata, a condition characterized by hair loss, presents a lifetime risk of 2% in the general population, equating to approximately 1 in 1000 individuals. Research indicates a higher prevalence among individuals of Asian, Black, or Hispanic descent, although no clear evidence suggests a gender preference (3,4). This condition affects both adults and children, with an elevated occurrence associated with advancing age. On average, males tend to experience onset at around 32 years, while females typically face the condition around the age of 36 (6).

III. CLINICAL FEATURES

Although alopecia areata can affect any hair-bearing surface, including eyebrows, eyelashes, beards, underarm hair, and pubic hair, it typically appears as isolated patches of hair loss on the scalp. entire body may be affected in more severe instances (AU). The areas affected usually have a smooth surface, normal skin tone, and no secondary abnormalities such as scaling or follicular changes. Periodically, erythematous (reddened) regions might appear. The presence of "exclamatory mark hairs," which are short hairs with distal thickening and broadening and proximal

tapering close to the scalp, is one characteristic that sets them apart. The main diagnostic method is clinical, though dermoscopy can be useful in unclear situations (7).

Fig.1. Alopecia areata localized patch on scalp (9)

IV. TYPES OF ALOPECIA AREATA AND THEIR CAUSES

There are several different types of alopecia, as the condition can have various underlying causes. Alopecia areata, anagen effluvium, telogen effluvium, traction alopecia, androgenic alopecia, trichotillomania, and chemotherapy-induced alopecia (CIA) are common types of hair loss. There are two categories of alopecia: scarring alopecia and non-scarring alopecia. Scarring alopecia is caused by inflammation and swelling due to follicular injury. On the other hand, non-scarring alopecia is more common and can be caused by a variety of factors such as hormones, medication, diet, and certain medical conditions. (10)

4.1. Alopecia areata (patchy hair loss)- Hair loss in coin-sized patches on the scalp or other body parts. Alopecia totalis or total hair loss on the scalp, and alopecia universalis, or total hair loss on the body, including the scalp, eyebrows, eyelashes, and other parts, can also result from this kind of alopecia.

4.2. Androgenic Alopecia- This is male pattern balding, another name for this type of hereditary hair loss. Male pattern baldness and female pattern baldness are two frequent types of baldness that affect both sexes. Men are more affected than women because they generate higher levels of testosterone, the male sex hormone that causes it. Women with thinning hair on the scalp experience hair loss, unlike men who experience hairline recession.

4.3. Traction alopecia- The hairline surrounding the temple area recedes or falls out, which is indicative of this condition. Traction alopecia can result from wearing your hair in tight hairstyles or braids for extended periods. If the traction is ignored, the hairline may sustain irreversible damage.

4.4. Chemotherapy-induced alopecia- Chemotherapy-induced alopecia, sometimes referred to as chemotherapy-induced hair loss, is a typical adverse effect of several cancer therapies. Chemotherapy medications that are cytotoxic target cells that divide quickly, such as hair follicle cells. Hair loss on the scalp, eyebrows, eyelashes, and other body hair may result from this.

4.5. Anagen effluvium- One kind of hair loss that happens during the anagen (growth) phase of the hair development cycle is called anagen effluvium. Anagen effluvium is usually accompanied by an abrupt and extensive loss of actively developing hairs, in contrast to ordinary pattern baldness. Anagen effluvium is often caused by radiation therapy, exposure to chemicals, or cancer chemotherapy treatments.

4.6. Telogen effluvium- Non-scarring hair loss caused by prematurely pushing hair follicles into the inactive telogen stage is known as telogen effluvium. (11) The disease is prevalent in the elderly, in individuals who are physically and mentally disturbed, and in those who have thyroid or other hormonal imbalances (12, 13). The amount of effluvium depends more on the severity and length of exposure to the causal agent than the agent itself. There are three types of telogen effluvium: critical (lasting less than six months), chronic (lasting more than six months), and chronic repetitive.

4.7. Trichotillomania (hair pulling)- Trichotillomania is a psychiatric disorder characterized by an inability to stop removing hair, which ultimately results in hair loss. Hair pulls are most frequently made from the scalp, eyebrows, and eyelashes (10).

Fig.2. Various Types of Alopecia Areata

V. SIGNS AND SYMPTOMS

1. Hair loss in patches.
2. A smooth, round, or oval area of baldness on the scalp.
3. Loss of beard hair.
4. Nail Changes.
5. Itching, tingling, or a burning feeling where hair loss is about to begin or has already started.
6. Irritated eyes from losing eyebrows or eyelashes.

VI. ETIOPATHOGENESIS(7)

The three unique stages of the hair cycle are anagen, catagen, and telogen. The keratinization of the proximal end of the hair shaft occurs during the catagen phase, whereas the anagen phase denotes rapid hair development. The hair follicle then sheds and the remaining proximal end goes through apoptosis. Telogen is the term used to describe the period that passes between the old follicle regressing and the start of the subsequent anagen phase. There are six stages of hair growth during the anagen phase, and stage VI denotes the completion of a fully developed anagen follicle. This normal process is interfered with by autoimmune disorders like alopecia areata. Alopecia areata causes the hair follicles to stop growing in stages III or IV, causing the telogen or catagen phase to begin earlier than usual.This causes sudden hair loss and insufficient regeneration of hair.(6)

Alopecia Areata (AA) is considered to be a condition that affects the resting (telogen) phase of the hair growth cycle. It is a disease that affects hair cycling.

The following etiological variables are thought to contribute to the development of alopecia areata:

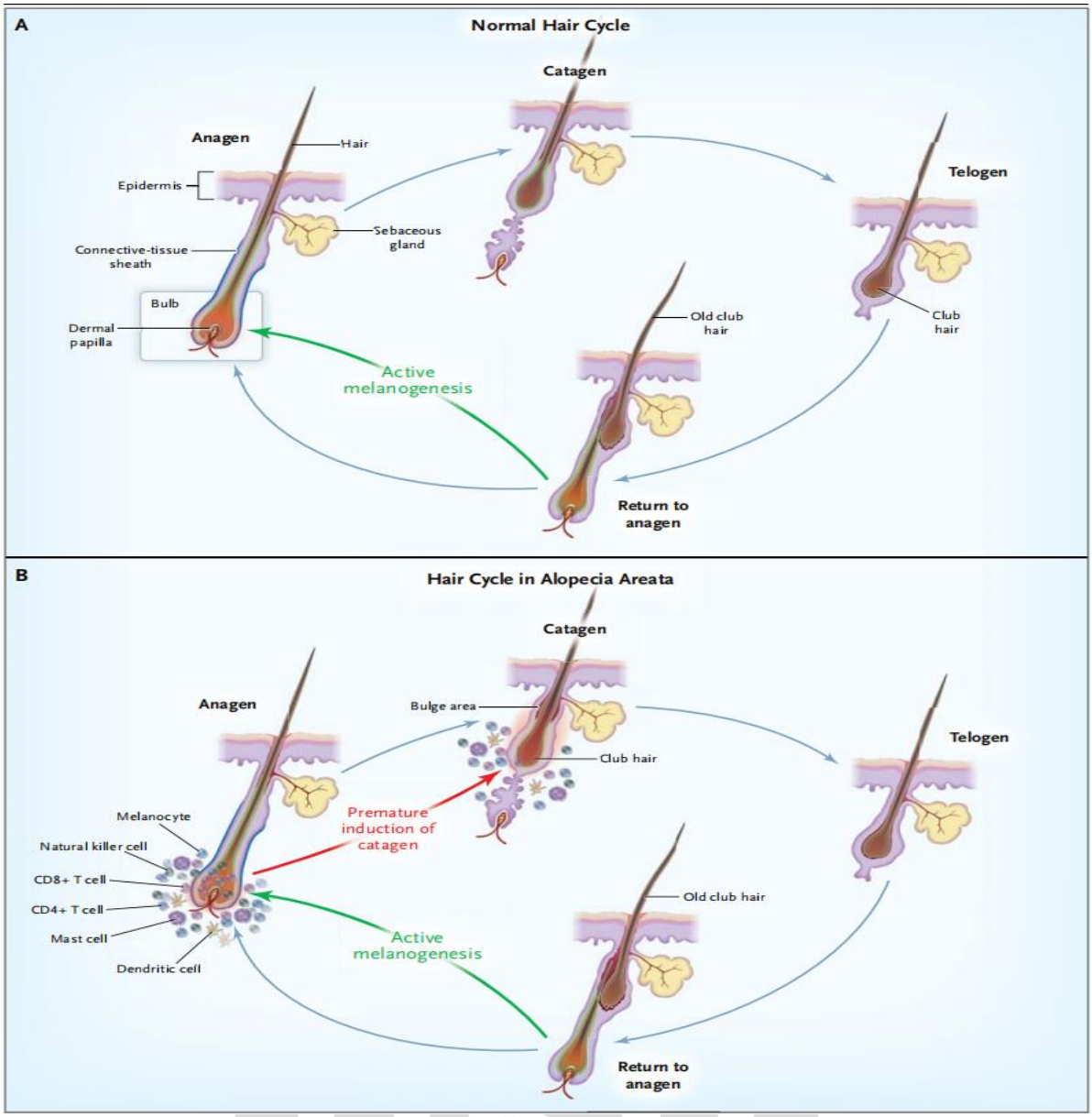

Fig. 3: Alopecia Areata's Disordered Hair Cycle and Normal Cycle.(2)

6.1.Genetic factors

The genesis of AA is significantly influenced by genetic factors. A family history of AA is present in a large percentage of patients (10% to 42% of cases). (14,15) Patients with the early start of AA have a much greater probability of a family history. According to reports, the familial incidence of AA is 7.1% in patients whose first patch was placed after the age of 30, and 37% in patients whose first patch was placed before the age of 30.5. Additionally, cases of AA have been reported in twins, with the concordance rate reaching up to 55% in identical twins. (16, 17)

6.2. Atopy

Alopecia areata has been linked to atopic conditions in several uncontrolled investigations; individuals with atopic diathesis experience a more severe and earlier development of the illness. Further, these individuals are said to have a poor prognosis (18).

6.3. HLA (Histocompatibility complex gene) Associations

Major histocompatibility complex (MHC) genes on chromosome 6 have been closely linked to alopecia areata, particularly the class II alleles (HLA-DQB10301 and HLA-DRB11104). There are further reported susceptibility loci on chromosomes 10, 16, and 18. Certain genetic markers for AA have recently been found through genome-wide association studies (GWAS), which may raise the risk for AA. Following a comprehensive genome study, Petukhova et al. discovered 139 single nucleotide polymorphisms (SNPs) for AA, which were grouped in 8 different genomic areas. (19) Important genes for T-cells (IL2/IL21, IL2RA, CTLA4, IKZF4, HLA) and hair follicles (NK-activating

ligands-ULBP3, ULBP6, STX17, PRDX5) have been discovered in AA by GWAS research (20). Each of them points to a genetic susceptibility for the development of AA.

6.4 Autoimmunity

Rothman was the first person to suggest a connection between autoimmune diseases and alopecia areata. When compared to control persons, alopecia areata patients show a higher incidence of circulating organ-specific and non-specific autoantibodies. In the peripheral blood of AA patients, there is an increase in hair follicle-specific antibodies, particularly to keratin 16 and trichohyali. (21) The hair follicle is thought to be an immune-privileged location. (22) TGF-β, IGF-1, and α-MSH are highly expressed in healthy hair follicle epithelium than major histocompatibility complex (MHC) class I and II molecules. AA is an autoimmune illness that targets hair follicles and is triggered by genetics and environmental factors.(24)

Cell-mediated Immunity

Cell-mediated immunity studies in AA have shown contradictory results. It has been found that the total number of T lymphocytes in circulation is either normal (42) or decreased (41). Friedmann43 proposed that the degree of circulating T cell decrease in AA is correlated with the severity of the illness. He further proposed that alterations in suppressor T-cell counts and helper T-cell function may be indicators of shifting disease activity. Hair loss is connected with an increased ratio of helper to suppressor cells, with a minor increase in helper T cells (CD4) and a drop in several suppressor T cells (CD8). The immune-mediated pathophysiology in AA is further supported by the effective treatment of AA with immunomodulatory drugs such as systemic steroids and oral cyclosporine.

6.5 Stress

Stress is seen as one of the causes, however, controlled trials have failed to establish this. Although isolated examples have shown emotional trauma from a linked death or accident as a triggering cause, no controlled investigations have been conducted to support this theory (25).

6.6. Diet

One research found that 24–71% of females with AA had iron deficiency (26). People who consume a diet high in soy have been reported to exhibit AA less frequently. While some studies have reported inconsistent results, others have revealed lower zinc levels in the blood of AA patients (27, 28).

6.7. Vaccination

Larger investigations have not confirmed any such connection, despite the involvement of the hepatitis B vaccine (29).

6.8. Infectious etiology

An infectious etiology was first suggested by AA epidemics that were reported from schools and hospitals. There was a suggested viral etiology. Although studies have not been able to prove it, cytomegalovirus infection has been implicated. (30)

VII. MEDICATION FOR ALOPECIA ARAETA

There are multiple treatments for alopecia, however, there have been several complaints of side effects and ineffectiveness. There are reports of both synthetic and natural treatments, although the FDA has only approved two medications for hair regrowth: oral finasteride and topical minoxidil. Due to the variety of alopecia forms, medications for alopecia are not always recommended; instead, they are tailored to a particular kind.

Key facts: 1.Depending on the severity of the condition, spontaneous remission rates for alopecia areata can range from 8% to 68%, therefore for a portion of patients, no therapy may be necessary. 2. The most crucial variables to take into account when choosing treatment strategies are the patient's age and the degree of hair loss. 3. Patients need to be informed about camouflage techniques and hairpieces.

7.1 CURRENT TREATMENT FOR ALOPECIA AREATA

7.1.1 Intralesional Corticosteroids

Key facts: 1. Intralesional corticosteroids can be administered as an additional therapy in cases with serious conditions and are considered to be the first-line treatment for limited disease. 2.Patients should be watched for adverse symptoms such as skin shrinkage, which may necessitate dosage adjustments or therapy termination.

Intralesional corticosteroids, most frequently triamcinolone acetonide (TAC), are the gold standard for treating cosmetically sensitive regions like the eyebrows and patchy AA to a limited extent. Intralesional betamethasone is usually utilized as an alternate when TA is not easily available. According to Tan et al, out of 127 patients with minimal AA, 82.1% had <50% scalp involvement and were treated with TAC injections. (31) Patients who responded better to treatment were often younger (33 vs 53 years old) and had had AA for a shorter period of time (2.5 vs 16.7 years).One surprising finding was that in the responder group, 5 of 6 patients had a positive pull test, whereas 4 of 6 had exclamation point hairs on inspection. There was just one nonresponder with significant hair evidence, and all of the others had negative pull tests. Patients who exhibit clinical indications of active inflammation may be better candidates for intralesional TAC since the pull test and exclamation point hairs are potential markers of inflammation.(32) Recent research has shown that in patients with patchy AA, 2.5 mg/mL of TAC provides the same

effect as either 5 or 10 mg/mL. Thus, the authors suggest using low-dose TAC to the scalp at a greater volume (2.5 mg/mL, total volume 8 mL) and to the eyebrows at a volume of less than 0.5 mL per eyebrow. (33)

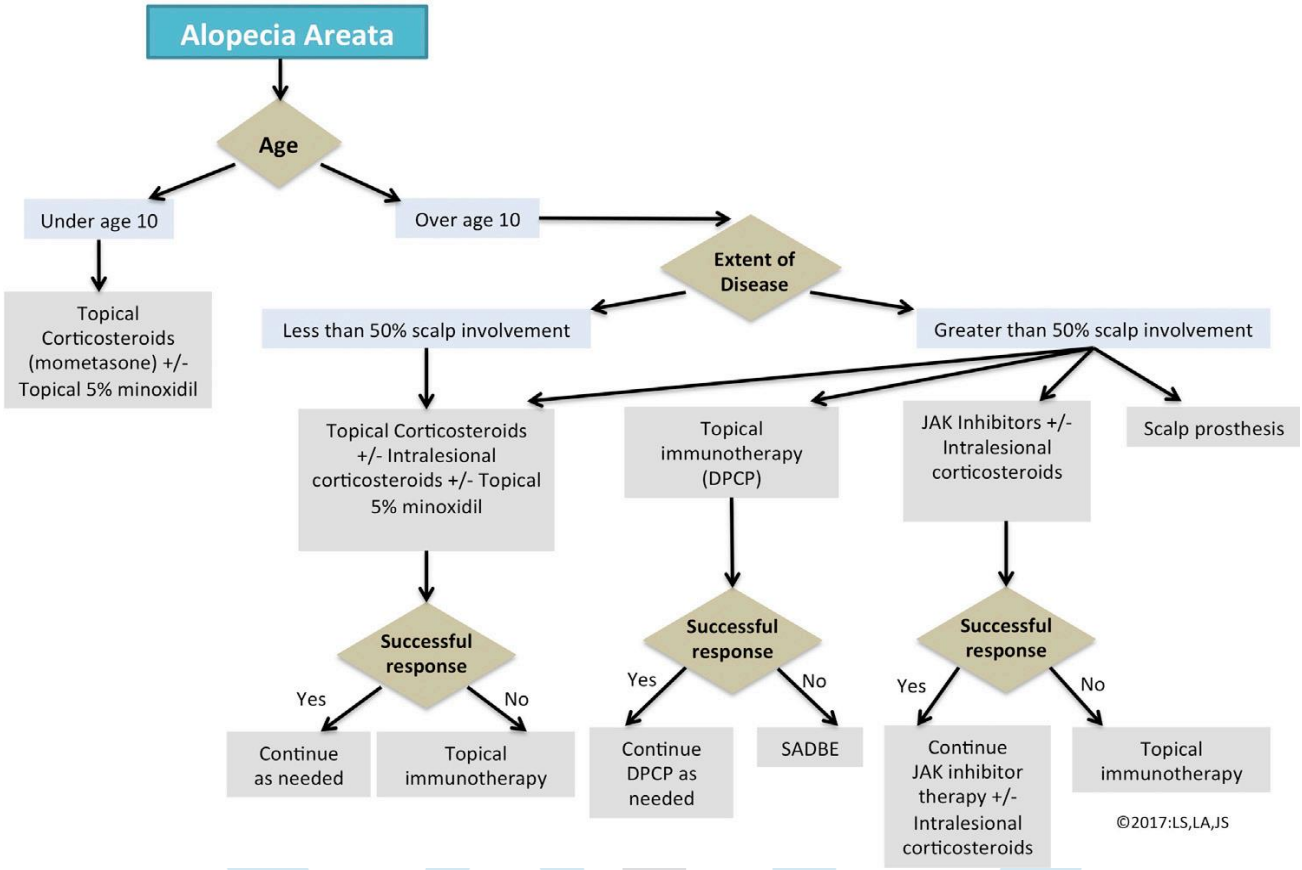

Fig. 4. Treatment algorithm for alopecia areata. Diphenylcyclopropenone (DPCP); Janus kinase (JAK); squaric acid dibutyl ester (SADBE).

7.1.2. Topical Corticosteroids

Key facts: 1. Topical corticosteroids can be used either alone or in combination with other therapies, such as intralesional corticosteroids. 2. Topical corticosteroids may be the preferred course of therapy for pediatric patients as compared to injections.

Topically administered corticosteroids are likely to benefit AA patients, particularly those with modest illness, although the effects may be inferior than intralesional treatment. Split scalp investigations have shown evidence that the medication's local effects, rather than its systemic effects, are what cause regrowth. (34) Complete regrowth was greater in the corticosteroid-treated group (57.7% vs. 39.3%) in 54 patients with patchy AA who applied either 0.25% desoximetasone or placebo twice daily for 12 weeks; however, the difference between the groups was not statistically significant. Only 14 patients were available for follow-up, although 13 of the 19 patients who chose intralesional TAC therapy for their incomplete regrowth recovered completely in a span of one to three months. In this investigation, the intralesional TAC response rate was substantially higher than that of the desoximetasone cream (P=.03). Typically, we advise using 0.05% superpotent steroid clobetasol propionate foam. However, the less effective mometasone is more frequently administered in children under the age of ten. Topical steroid cream works more effectively when occlusion is present. Topical corticosteroids can cause striae, telangiectasia, moderate itching, burning, acneiform eruptions (which are more prevalent in ointment formulations than in foam), and skin atrophy. (35)

7.1.3. Topical Immunotherapy

Key facts: 1. Diphenylcyclopropenone has an approximately 60% to 70% success rate and is an alternative for the treatment of individuals with significant illness (>50% scalp involvement). 2.Squaric acid dibutyl ester can be used to treat patients who do not react to diphenylcyclopropenone.

Contact immunotherapy can promote hair growth by causing allergic contact dermatitis on parts of the scalp that are thinning. Diphenylcyclopropenone (DPCP) and squaric acid dibutyl ester (SADBE), two topical sensitizers, are used to achieve this. Following this treatment, hair regrowth can result from the inflammatory infiltration surrounding hair follicles being redirected toward the dermatitis that was created. It is generally acknowledged that contact immunotherapy is effective in treating adults and children with diffuse or patchy long-standing AA, even if it is ineffective in cases of AA that are acute and fast progressing (47).

7.1.4. Anthralin

For many years, alopecia areata patients have been treated with anthralin 0.5–2% cream; but still, there is doubt over this treatment's success. It has been demonstrated to suppress TNF-a and IFN-g in the skin of mice with alopecia areata, while its exact mode of action is uncertain. From 25% in AT to 75% in spotty AA, response rates range widely. Using the cream once a day for up to two hours, or until low-grade dermatitis develops, the afflicted areas are treated before being cleaned. Regional lymphadenopathy and discoloration of the skin, fair hair, and clothing are among the side effects.

7.1.5. Minoxidil

Key facts: In alopecia areata, 5% minoxidil foam or solution can be administered as adjuvant treatment. The only topical treatment approved by the FDA for alopecia is minoxidil, better known by its brand name Rogaine.

Minoxidil is a derivative of pyrimidine that was first used orally to treat hypertension. (36) Minoxidil, which is well-known for promoting hair growth, was coincidentally found to have this effect as a side effect while treating hypertension. (37) Minoxidil prescriptions are often supplied in strengths of 2% for female usage and 5% for male use. The medicine is known to stimulate potassium channels, which cause cell membranes to become hyperpolarized, but its exact method of promoting hair regeneration is yet unknown.More blood, oxygen, and nutritional food may enter the follicles more easily as a result of hyperpolarization, which also opens potassium channels, angiogenesis, and vasodilation. (38,39) Therefore, it is likely that adequate blood flow and nutritional support play a major role in minoxidil-induced hair regeneration. Minoxidil helps follicles in the telogen phase return to the anagen phase. Further observations following topical Minoxidil therapy indicate a prolonged active growth phase.

7.1.6. Finasteride (Propecia)

Finasteride (synthetic 4-azasteroid molecule) is an FDA-approved medication for alopecia. Finasteride was unintentionally found to be a hair growth enhancer, much like minoxidil. Finasteride was used to treat men's enlarged prostates before being utilized in trichology. (40) It appears that only male patients who are experiencing hair loss are administered the medication. Inhibiting 5 alpha-reductase, an enzyme that catalyzes the conversion of testosterone into dihydrotestosterone (DHT), is how finasteride works. Finasteride prevents testosterone from being converted to DHT by competitively inhibiting the 5 alpha reductase enzymes on androgen receptors.Finasteride treatment of androgenic alopecia can be effectively managed when the medication is taken early, ideally before the hair follicles die. Finasteride is not recommended for use by female patients, especially those who are pregnant, due to its teratogenic impact. In contrast, minoxidil is safe for use by both genders of patients. Finasteride treatment for androgenic alopecia frequently results in reversible hair loss since the medication does not address the underlying genetic source of the problem, increasing the likelihood that hair loss may return. (41)

7.1.7. Corticosteroids (Oral)

Key facts: Oral corticosteroids used for short periods (6 weeks) are frequently effective in stimulating hair regrowth; but, long-term usage is not recommended due to the adverse effect profile, and recurrence is quite likely.

Although systemic corticosteroids are not as effective in treating ophiasis and alopecia universalis (AU) types, they are frequently used in the treatment of autoimmune illnesses and have shown significant improvements in most clinical forms of Alopecia areata. (42) Thirty-two patients (mean age of 0.8 mg/kg) who had received at least a 6-week course of prednisone at a rate of >25% and 25%, respectively, of regrowth were seen in this research. Remarkably, alopecia totalis (AT) or AU affected 50% of these individuals. This study demonstrates that a brief course of steroids is frequently adequate to treat AA, while other studies have reported similar outcomes in individuals treated for three to five months at a dosage of 20 to 30 mg/day.The response to pulse steroids, however, can not last long, and many patients experience relapses 4–9 weeks after stopping the medication. (43) Long-term steroid usage is often not recommended due to its adverse effects. The pituitary-adrenal axis is suppressed, bone development or integrity is affected, ocular abnormalities occur, and diabetes or hypertension worsens. (44)

7.1.8 Azathioprine

Azathioprine suppresses helper T-cell cytokine production and cytotoxic T-cell proliferation by inhibiting purine synthesis enzymes, hence decreasing the immunological response. Reduced T-cell colonization around hair follicles allows for appropriate growth phase development. Azathioprine tapering treatment may be useful for individuals using oral corticosteroids as an alternative to systemic steroids, which have a significant risk of serious side effects. Azathioprine is a highly effective adjuvant therapy alongside corticosteroids in the treatment of severe, drug-resistant AA (45).

7.1.9 Methotrexate

Key facts: Methotrexate may be useful for people who have failed normal treatment.

Methotrexate may be helpful for patients with severe alopecia areata. The response rate is higher and more thorough when methotrexate and corticosteroids are combined. Methotrexate appears to be a promising option for treating severe AA, with a median weekly dosage of 20 mg (46).

7.1.10. Cyclosporine

Cyclosporine can decrease the function of helper T cells, which may have a pathogenic impact on alopecia areata. In a clinical study for alopecia areata, the six participants' scalp hair regrows between the second and fourth weeks of oral cyclosporine 6 mg/kg/day for 12 weeks. Clinical response was associated with changes in immune cell infiltration surrounding follicles (46).

7.2 HERBAL TREATMENT FOR ALOPECIA AREATA:

Currently, no herbal therapy for alopecia has been permitted, although multiple studies have demonstrated that certain phytochemicals can stimulate hair growth in vitro and in vivo.

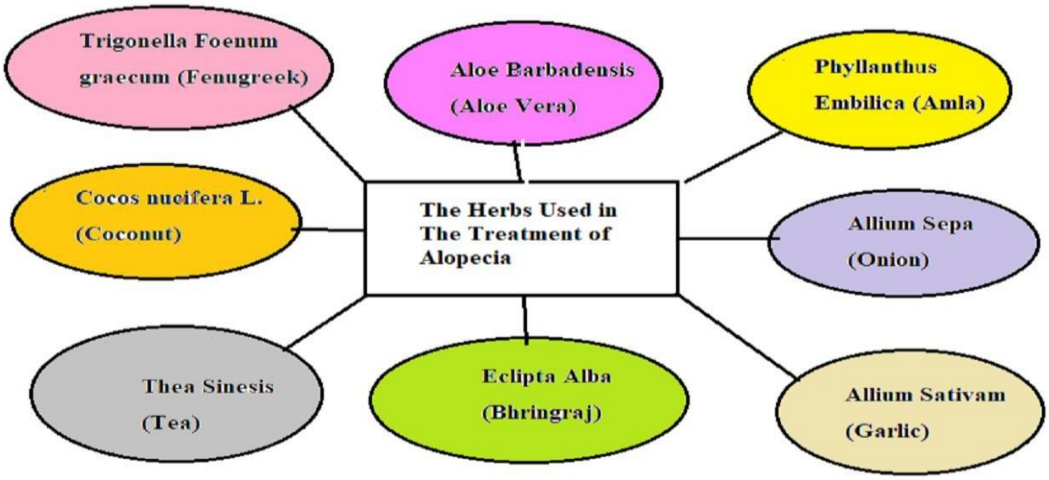

Fig.5. Herbs Used for Alopecia Treatment

7.2.1 Aloe Vera (Aloe Barbadensis)

▪ Chemical components: Aloe-Emodin, Aloenin, and Barbaloin.

▪ Mechanism of action: The vitamins A, C, and E included in aloe vera help to strengthen and recover hair strands. This group of vitamins promotes optimal cell growth, aids in cell renewal, and enhances hair luster. Aloe vera gel also has vitamin B12 and folic acid. By using these two ingredients, hair loss can be avoided.

▪ Use: The primary ingredient in aloe vera, aloin, stimulates hair growth in those with alopecia. (48)

7.2.2 Amla (Phyllanthus Emblica)

▪ Chemical Components: Gallic Acid, Ellagic Acid, and Ascorbic Acid (Vitamin C).

▪ Mechanism of Action: The antifungal qualities of amla assist to protect the scalp from fungal infections and dandruff. Amla is an effective inhibitor of 5-alpha reductase. Additionally included in aloe vera gel are folic acid and vitamin B12. The medication finasteride, which is used to treat hair loss in both sexes, also functions by blocking 5-alpha-reductase. ▪ Use: Amla is used to cure baldness in both men and women. Amla neutralizes the blood, reduces dandruff, and enhances scalp health. (49)

7.2.3 Onion (Allium Cepa)

▪ Chemical Components: Alliin, diallyl sulfide, allyl propyl disulfide, protein (albumin), and allicin.

▪ Mechanism of Action: Zinc prevents hair loss caused by dandruff by assisting in the generation of vital scalp oil. Iron helps the body's red blood cells carry oxygen throughout the body. It is necessary for appropriate hair development and for keeping healthy hair.

▪ Use: The sulfur in onions encourages thick, strong hair, which stops hair loss and stimulates hair growth. Hair growth and the development of healthy skin cells are aided by collagen. (48)

7.2.4 Garlic (Allium Sativam)

▪ Chemical components: Allicin, amino acids, and essential oil (0.06–0.1%) include diallyl and propyl disulfides.

▪ Mechanism of Action: Garlic's antimicrobial qualities prevent scalp injury and inhibit hair growth. It's well known that raw garlic is high in vitamin C and benefits hair health. Moreover, it increases the synthesis of collagen, which encourages the development of hair.

▪ Use: Vitamin B-6, vitamin C, manganese, and selenium are among the many vitamins and minerals found in raw garlic that support healthy hair. (50)

7.2.5 Bhringraj (Eclipta Alba)

▪ Chemical components: daucosterol and wedelolactone.

▪ Mechanism of Action: During the telogen (resting) phase, the methanol extract from Eclipta alba encourages anagen in hair follicles, which increases hair growth.

▪ Uses: It provides nourishment to the scalp and hair follicles, encouraging hair follicles to produce new hair. The vitamin E-rich herb known as the bogus daisy plant strengthens and nourishes the hair strands. moisturizes the skin, giving it a glossy, healthy appearance. (48)

7.2.6 Tea (Thea Sinesis)

▪ Chemical Components: theaflavin, caffeine, and catechin.

▪ Mechanism of Action: Caffeine, which is found in tea, stimulates hair follicles and increases scalp blood flow.

▪ Use: The compound called epigallocatechin gallate (EGCG) found in tea inhibits hormones that trigger hair loss and stimulates hair follicles to encourage hair growth. (51)

7.2.7 Fenugreek (Trigonella Foenum graecum)

▪ Chemical Components: The principal constituents of fenugreek seeds are nitrogen compounds, which are further classified as volatile and non-volatile, as well as carbohydrates, proteins, lipids, alkaloids, flavonoids, fibers, saponins, and steroidal saponins.

▪ Mechanism of Action: The body's DHT (dihydrotestosterone) molecule can interact with several plant components found in fenugreek. Hair loss eventually results from DHT's attachment to hair follicles. The ability of DHT to attach to hair follicles can be reduced by fenugreek.

▪ Uses: Fenugreek contains proteins and amino acids that heal damaged hair shafts from dryness, heat styling, chemicals, UV damage, and color treatments. Promotes cuticle integration into the hair shaft, which results in thicker hair growth. (48)

7.2.8 Coconut (Cocos nucifera L.)

▪ Chemical Components: Coconut is composed of triglycerides of saturated fatty acids that are taken from the hard, dry endocarp. This oil contains around 95% saturated fatty acids with 8 carbon atoms. There is 2% caprylic acid present. 3-5 percent lauric acid, 50–80% capric acid, and 1% myristic acid.

▪ Mechanism of action: Coconut oil contains lauric acid, which binds hair proteins and protects the hair's roots and strands from harm. The antioxidants in coconut oil promote healthy hair growth. It's well known that coconut oil penetrates the hair shaft to protect it from environmental toxins and excessive heat. Coconut oil's antifungal and antibacterial properties help protect against bacterial problems that might inhibit the growth of hair.

▪ Use: Moisturizing hair reduces damage.

7.2.9 Almond (Prunus amygdalus)

▪ Chemical components: About 20% of almonds are proteins, mucilages, and emulsions, while 40–55% are fatty oils. Amygdalin, a crystalline, colorless cyanogenic glycoside, is found in bitter almonds in levels between 2.4% and 4.1%.

▪ Mechanism of Action: Since almond oil contains biotin, rubbing it into your hair is a fantastic way to provide it with the necessary vitamins to prevent thinning and promote hair growth.

▪ Uses: Applying almond oil to the scalp and epidermis enhances blood circulation to the hair roots, stimulating hair development and fortifying hair. It helps to renew and manufacture enough keratin to make hair thicker or thinner. (48)

7.2.10 Tulsi (Oscimum Sanctum)

▪ Chemical Constituents: contains 20% eugenol methyl ether, carvacrol, and around 70% eugenol. It also has caryophylline in it. Alkaloids, glycosides, saponins, tannins, significant levels of vitamin C, and trace amounts of maleic, citric, and tartaric
acids have also been linked to the plant.

▪ Mechanism of Action: Tulsi has beneficial effects on the hair, rejuvenating the hair follicles and strengthening the hair roots to control hair loss. This herbal treatment increases blood flow to the scalp and keeps it cool.

▪ Uses: Tulsi has been used to prevent hair loss and thinning and improve hair thickness. The anti-inflammatory ingredients in Tulsi are thought to irritate the scalp.(48)

7.3 NEW TREATMENT APPROACHES:

7.3.1. Janus kinase (JAK) inhibitors and signal transducer and activator of transcription (STAT) inhibitors:

For example, after a ligand-to-associated cytokine receptor contact, a JAK can phosphorylate a STAT, activating transcription. STATs go from the cytoplasm to the nucleus as soon as they are phosphorylated, where they bind to specific DNA sequences to control gene transcription. Of the individuals receiving oral JAK inhibitors, 67–75% showed signs of hair growth. Oral formulations can promote hair regeneration since they are easy to take. Tofacitinib can be taken once or twice a day in dosages of 5 mg and 11 mg. The unwanted side effect most commonly associated with JAKi is increased susceptibility to infections like as colds, flu, and herpes virus.

7.3.2. Platelet-Rich Plasma Therapy:
Platelet-rich plasma (PRP) is a preparation of autologous plasma that has a high concentration of platelets and is abundant in cytokines and growth factors. It is crucial for encouraging tissue healing as a result. PRP's anti-inflammatory method of enhancing TGF expression and decreasing MCP-1 expression may further explain why it is effective in treating AA.

7.3.3. Excimer Laser:
There are limited treatment options for scalp alopecia areata, however the 308-nm excimer laser has been shown to help restore hair growth in damaged regions. Excimer lasers can treat alopecia areata by decreasing cutaneous immune responses and stimulating anagen hair growth. The moveable arm allows you to get straight to the lesions you wish to treat while without damaging the surrounding hairs.

7.3.4. Superficial Cryotherapy:
Many neoplastic and inflammatory illnesses can be treated with superficial cryotherapy, which uses liquid nitrogen. Liquid nitrogen superficial cryotherapy is a valid therapeutic option with excellent treatment outcomes and few side effects for mild to severe AA.

7.3.5. Phosphodiesterase 4 Inhibitor:
Advanced immune system small-molecule modulators known as phosphodiesterase (PDE) 4 inhibitors reduce inflammation by blocking the synthesis of cyclic adenosine monophosphate (cAMP) inside cells.

7.3.6. Prostaglandin Analogues:
Prostaglandin analogs, including latanoprost and bimatoprost, are commonly used as antiglaucoma drugs. The use of these drugs has been associated with eyelash hypertrichosis. Bimatoprost and latanoprost are examples of prostaglandin F2-(PGF2) equivalents. Probably by extending the anagen phase of hair follicles, they cure alopecia and promote hair growth, particularly in the eyelid and eyebrow regions (47).

VIII. CONCLUSION

This review has covered many kinds of alopecia, with a focus on their effects on the hair follicle and growth cycle. Alopecia causes, including genetic susceptibility, drug side effects, food, stress, autoimmune disorders, and extended illness, have been examined along with how they affect hair development. Alopecia is an autoimmune condition that is more common in cities and rare in rural regions. Many environmental issues arise in cities as a result of lifestyle changes. Excessive use of allopathic medications, such as anticancer treatments, can cause alopecia. Chemotherapy treatments can cause severe hair loss, and in certain situations, a family history of the disorder may also be responsible. Therefore, a large number of doctors advise against using synthetic or allopathic medications, and almost 80% of doctors advocate for the use of herbal therapy. Male hair loss is most commonly caused by hormonal imbalances such as DHT. Alopecia is an illness that is primarily treatable in mild forms but difficult to treat in severe forms. So, herbal medications such as aloe vera, amla, onion, garlic, bhringraj, tea, fenugreek, coconut, almonds, and tulsi are the finest and safest alternative treatments for alopecia. These natural medications are more effective in treating alopecia, or hair loss. Baldness is successfully treated with the extraction oil from these herbal crude medications. Janus kinases (JAKs) can phosphorylate signal transducers and activators of transcription (STATs) when a ligand binds to their particular cytokine receptor. Because they're easy to swallow, oral formulations can promote hair growth. Tofacitinib is available in 5-mg and 11-mg dosages, which can be taken once or twice a day. There are limited treatment options for scalp alopecia areata, however, the 308-nm excimer laser has been shown to help restore hair growth in affected areas.

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