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Review Article

Drug Armamentarium for alopecia areata

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ABSTRACT

Alopecia areata (AA) is a nonscarring, autoimmune hair loss on the scalp, and/or body. The AA occurs in people of all ages and affects 1–2%. Patients with the disease can face significant emotional and psychological stress as a result, there is no cure for the condition. Many therapeutic modalities have been used to treat alopecia areata, with variable efficacy and safety profiles. Unfortunately, none of these agents is curative or preventive. The treatment plan is designed according to the patient's age and extent of disease. Global Alopecia Treatment Market is valued at USD 2.54 billion in 2018 and expected to reach USD3.98 billion by 2025 with the CAGR of 5.80% over the forecast period.

1. Introduction

1.1. Defining terminologies

Alopecia (Hair loss) is a very common problem in recent scenario. Alopecia, which is associated with progressive thinning of the scalp hair, follows a defined pattern. Alopecia is due to a structural or functional defect in the follicle or to a change in the hair itself.

There are different types of alopecia, classified based on how the hair falls out.

Alopecia areata is when hair loss occurs in patches. With this type, hair loss cycles over time. One area may lose hair and then grow back while another area begins losing hair. It is one of the most common form of hair loss seen by dermatologists and accounts for 25% of all the alopecia cases.

Alopecia areata is characterized by patchy scalp baldness. This disease usually begins in children and young adults, but it can start at any age. People of all races and sexes get alopecia areata. Most common reasons of alopecia areata are pregnancy, hormone pills, thyroids disorder, and sexually transmitted disease like syphilis, gonorrhea, anemia and arthritis**.**

Alopecia totalis (AT) is when all of the hair on the scalp falls out.

Alopecia universalis (AU) is when all of the hair on the entire body falls out.

In general population, the **prevalence** was estimated at 0.1-0.2% with a lifetime risk of 1.7%. Paediatric studies report a higher prevalence in children ranging from 10-50%, especially for those with a family history of alopecia areata. This is usually observed in patients with thyroid and vitiligo disease. Patient do not have other symptoms, but experience a burning or itching sensation. These conditions are not contagious.

2. Stages of Hair Growth Cycle

Hair growth is cyclic, with phases of growth (anagen), involution (catagen), and rest (telogen) [Figures 3 and 4]. Every scalp hair has a phase of growth (anagen) or growing phase, which lasts two to six years determines length of hair, a phase of involution (catagen) or transition phase, which lasts two to three weeks. The hair follicle shrinks and detaches from the dermal papilla and a resting phase (telogen), which lasts two to three months where 10-15 % hairs are in this phase, this is followed by shedding.

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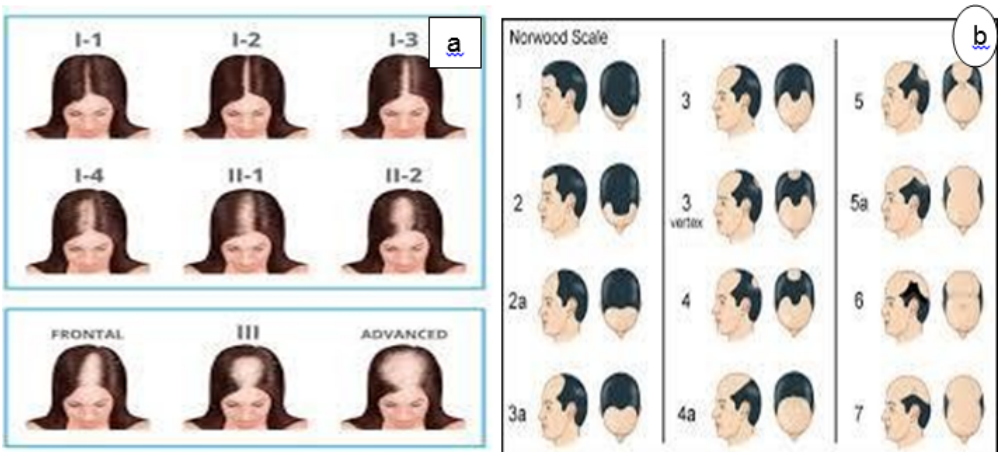

Fig. 1: a-b Hair loss in pattern in women and men

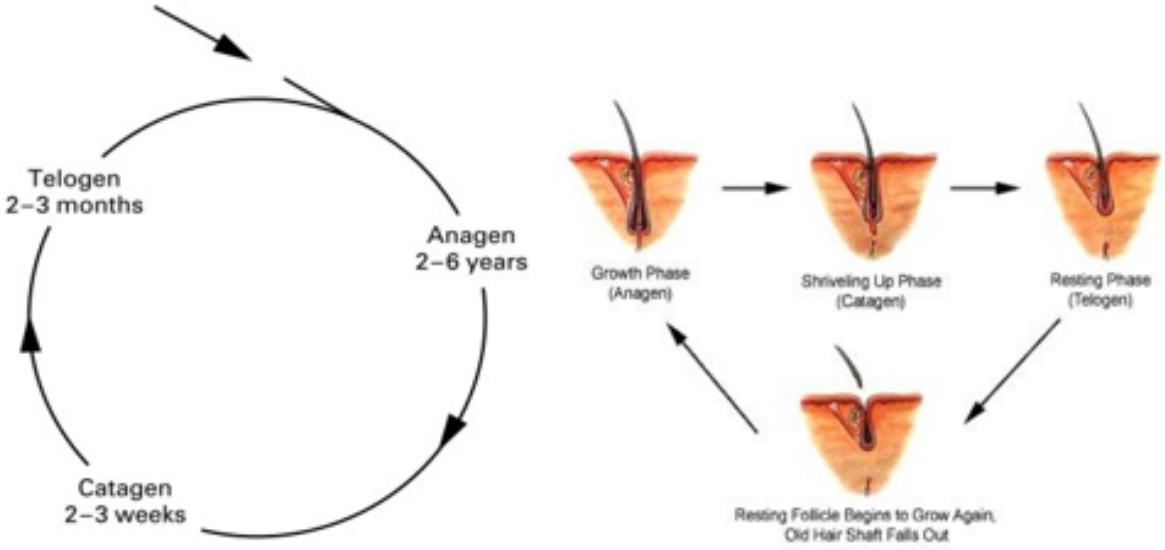

Fig. 2:

Approximately 50 to 150 hairs can fall out daily, this is considered to be normal hair shedding. [1]

2.1. Etiopathogenesis

The exact pathophysiology of alopecia areata remains unknown. The most widely accepted hypothesis is that alopecia areata is a T-cell–mediated autoimmune condition.

Evidence suggests that AA is caused by an autoimmune reaction to the hair follicles due to both genetic and environmental factors. [Figure 5]

2.1.1. Immunological or autoimmunity

Observational studies show a high correlation (10%–42%) between AA and family history.

1. Hair follicles are immune-privileged sites where Cytotoxic CD8+ , CD4+ , natural killer cells and plasmacytoid dendritic cells infiltrate around the hair follicles during the growth (anagen) phase. CD8+ T cells and NKG2D+ cells are around the peribulbar area of the affected hair follicles. JAK-STAT signaling pathway was first discovered as a pathway for IFN signaling. Subsequently, a large number of cytokines, particularly γc cytokines, have been found to activate the JAK-STAT pathway. Overexpression of JAK3 and, to a lesser extent, JAK1 and JAK2 was observed in skin biopsy specimens of patients with AA.
2. Increased cytokine activity, particularly IFN-γ, results in disruption of the hair follicle immune privilege and premature termination of the anagen phase, followed

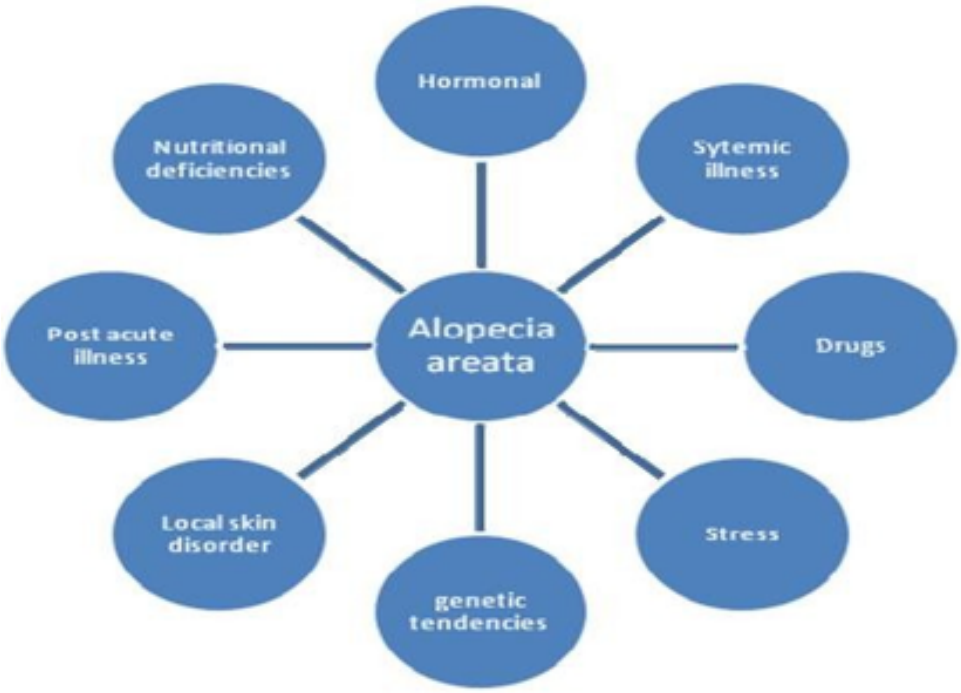

Fig. 3:

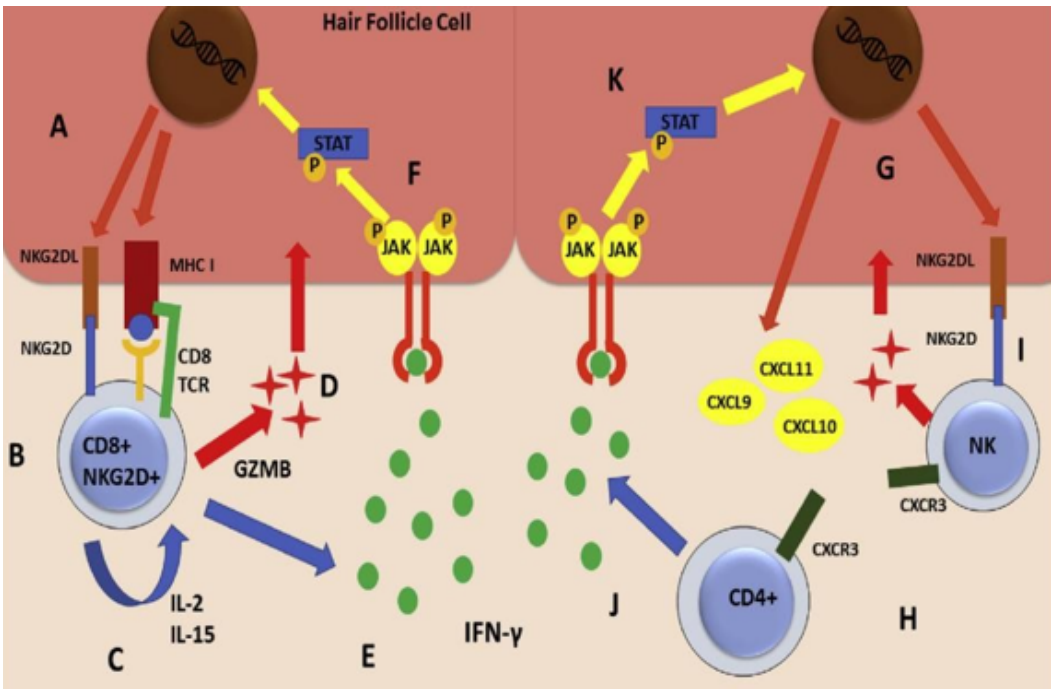

Fig. 4: Janus Kinase pathway

by hair follicle atrophy and dystrophy in persistent disease

3. TNF-α inhibition causes different types of hair loss including severe alopecia areata and scarring alopecia.

2.2. Genetic factors

Ooccurrence of AA in identical twins with concordance of 55%. Higher incidence of alopecia areata in individuals with Down's syndrome. Some HLA class II genes are shown to be associated with alopecia areata: DQ3, DQ7, DR11, DR4, DR5, and DPW4.

2.3. Environmental stressors

That may be implicated in AA include infections, vaccinations, hormone fluctuations, and diet, although their exact impact is unknown. AA patients have lower levels of hydroxy vitamin D than healthy subjects.

2.4. Dietary factors

Excessive intakes of nutritional supplements may actually cause hair loss and are not recommended in the absence of a proven deficiency.

2.5. Infection

Hepatitis B vaccination has been implicated, but larger studies have failed to confirm any such association. influenza that causes excess production of interferons IFN-γ. Gram-negative bacteria from the periodontal pocket to the bloodstream, are common causes.

Long term chronic endurance of **stress** is a common factor compared to recent trauma while precipitation of alopecia areata by a fresh traumatic event has been reported across studies

2.6. Drugs

Cimetidine, Tricyclic antidepressants, Levodopa, Bromocriptine, Antithyroid drugs, Retinoids, Valproic acid, NSAID scan lead to hair shedding.[2–4]

3. Treatment Guidelines for Alopecia areata

Algorithm for management of Alopecia areata (Journal of the American Academy of Dermatology 2018) Table 1.[5] Alopecia areata has two peaks of onset – one in childhood and one in adulthood. In half of patients with alopecia areata, individual episodes of hair loss last less than one year, and hair grows back without treatment. These patients may experience recurrent episodes of hair loss that spontaneously regrow or respond quickly to treatments. There is no known effective method of prevention, although the elimination of emotional stressis felt to be helpful Most of modalities usually remain noneffective in severe AA and high relapse rates limit their usage.

3.1. No Treatment

Leaving alopecia areata untreated is a legitimate option for many patients. Spontaneous remission occurs in up to 80% of patients with limited patchy hair loss of short duration (< 1 year). Such patients may be managed by reassurance alone, with advice that regrowth cannot be expected within 3 months of the development of any individual patch.

4. Pharmacotherapy

4.1. Minioxidil

Is a potassium channel opener, causing hyperpolarization of cell membranes, by dilating blood vessels and opening potassium channels, it allows more oxygen, blood, and nutrients to the follicles. Minoxidil might activate the prostaglandine-endoperoxidase-synthetase enzyme type 1 which stimulates the hair growth.

Table 1: Topical uses of minoxidil

FDA approved indication
Androgenetic alopecia
Female pattern hair loss
Off-label use
Alopecia areata
Beard enhancement
Central centrifugal cicatricial alopecia
Chemotherapy-induced alopecia
Eyebrow enhancement
Frontal fibrosing alalopecia
Monilethrix
Loose anagen hair syndrome
Telogen effuvium

The current 2% formulation is most likely to elicit cosmetically acceptable regrowth in those with patchy alopecia areata. Many studies have suggested that topical minoxidil offered some benefits to AA patients as it slightly increased hair growth without altering disease progression or inducing remission.(Minoxidil directly affects follicles by stimulating proliferation at the base of the bulb).

Clinical response usually happens within 2 months of treatment and usually reaches a peak by 4 months. Minoxidil prolongs the duration of anagen and activates -catenin pathway. It is possible that this drug increases the duration of anagen hair cycle via - catenin pathway. Topical minoxidil is the only topical drug approved by the US Food and Drug Administration (FDA) for the treatment of androgenetic alopecia.[6]

5. Topical Steroids

Topical steroids are popular for treating alopecia, largely because they can easily be applied directly to the

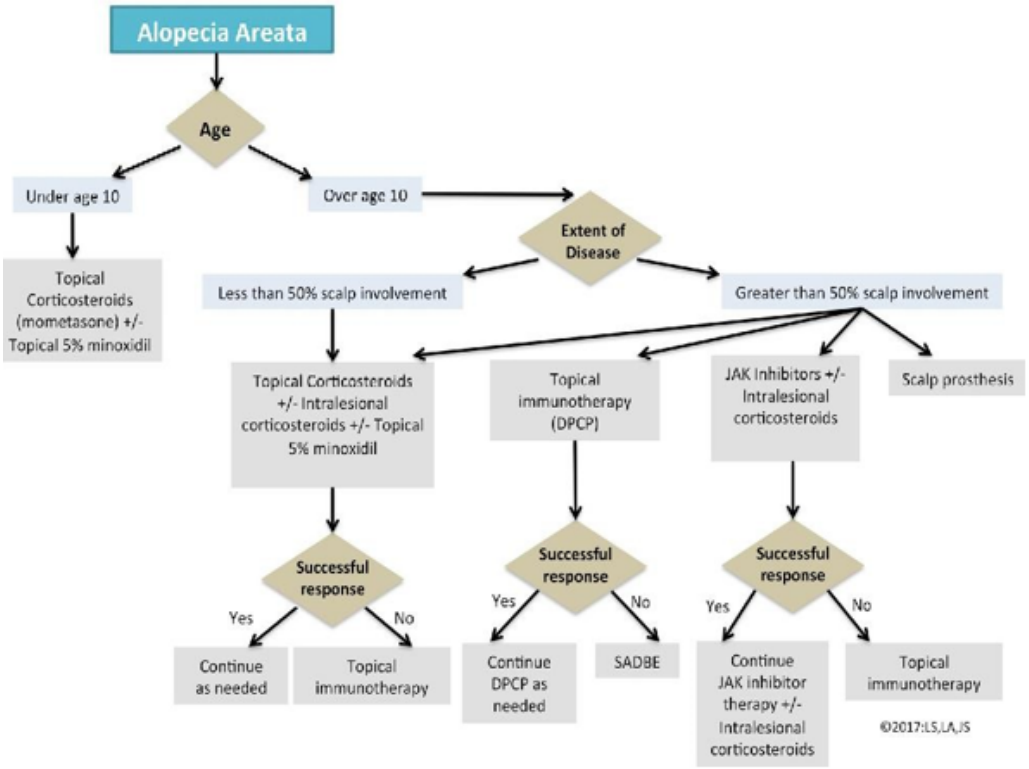

Fig. 5:

affected areas. These include fluocinolone acetonide cream, fluocinolone scalp gel, betamethasone valerate lotion, clobetasol propionate ointment, dexamethasone in a penetration- enhancing vehicle and halcinonide cream.

61% percent of patients using 0.1% betamethasone valerate foam achieved more than 75% hair regrowth in comparison with 27% in the 0.05% betamethasone dipropionate lotion group. Topical corticosteroids are far less effective in alopecia totalis and alopecia universalis.

Topical steroids: are a good option in children because of their painless application and wide safety margin. Folliculitis is a common side effect of corticosteroid treatment, appearing after a few weeks of treatment. Telangiectasia and local atrophy have also been reported.[7]

6. Intralesional Steroids (ILCs)

6.1. Action

Corticosteroids suppress the T-cell-mediated immune attack on the hair follicle. Preparations used include triamcinolone acetonide, triamcinolone hexacetonide, and hydrocortisone acetate.

Triamcinolone acetonide is the preferred intralesional product because it is less atrophogenic than triamcinolone hexacetonide.

6.2. Utility

ILCs preferably triamcinolone acetonide is the first-line therapy for adult patients with less than 50% scalp involvement. Patients with extensive AA, rapidly progressive disease, and greater than two years' duration of the current episode, respond poorly.[Figure 6]

Fig. 6:

6.3. Strength

Triamcinolone acetonide is the first-line therapy for adult patients with less than 50% of scalp involvement. Concentrations of 2.5 to 10 mg/mL may be used, but 5 mg/mL (maximum volume of 3 mL per session) is the

preferred concentration for scalp. For the eyebrows and face, 2.5 mg/mL can be used (0.5 mL to each eyebrow).

These injections are repeated about every four to six weeks and are usually given by a dermatologist. Triamcinolone injection is marketed as in 2 strengths: 10 mg per ml and 40 mg per ml.

Steroids may also be administered by a needleless device (e.g. Dermajet^{TM}). The device should be sterilized.

The common adverse effects noted during ILCs therapy are, pain, atrophy of skin and hair follicles, telangiectasia, hypo / depigmentation and cushingoid features, due to systemic absorbtion.[8] The suggested dosages of prednisolone are 1 mg/kg/day for adults and 0.1–1 mg/kg/day for children. The dosages necessary to maintain hair regrowth in AA are between 30 and 150 mg daily. Treatment course can range from 1 to 6 months.

7. Oral Steroids

Oral corticosteroid pulse therapy may be a safe and effective treatment for alopecia areata (Grade B)

Patients received methylprednisolone (Low dose steroids)16 mg orally for 2 consecutive days every week. After 3 months, among patients, 40% recovered well, and 55.6% recovered fairly. After 6 months, 82.2% recovered well, 17.8% recovered fairly. No adverse events were detected. Or the dose of 30 mg oral prednisolone for 3 consecutive days in a week for 6 months is tried.(minidose). There are also lesser serious side effects like development of hypertension, diabetes and suppression of the HPA axis.[9]

7.1. Topical immunomodulators

Topical immunotherapy relies on inciting an allergic contact dermatitis (ACD) by applying potent contact allergens to the affected skin. It is believed that contact sensitizers act through immunomodulation of the skin,

8. Diphenylcyclopropenone (DPCP)

DPCP is a sensitizing agent which is used in the treatment of alopecia areata. The agent is topically applied weekly and left in place for 6–24 h. Approximately 50% of patients treated with DPCP respond with regrowth of hair after 6 months of treatment. This acts by decreasing the CD4/CD8 ratio and decreasing levels of interferon-gamma at the site of application. DPCP treatments are expected to cause a contact dermatitis, with redness and itching. More severe reactions, including swelling, burning, urticaria, and blistering, can occur. DPCP treatments provide response rates in alopecia areata as high as JAK inhibitors, at a lower cost and with a less severe side-effect profile.

8.1. Dose of DPCP

The very first dose is usually a 2 % solution which is applied to a small coin-shaped area on the scalp. It should be covered to protect from light. The scalp can be washed at the end of the day. When the patient returns for the second treatment in two weeks, a very low dose of DPCP is applied (0.0005%).[10]

8.2. Photochemotherapy

Combining oral or topical methoxsalen and UV-A irradiation of the scalp or of the whole body. Patients with multiple plaques of alopecia areata, alopecia totalis, and alopecia universalis, who were treated with oral methoxsalen and total body irradiation, had complete or more than 90% hair regrowth.[11,12]

8.3. Anthralin

Anthralin is a synthetic tar-like substance which has been shown to be helpful in some patients with the hair loss condition alopecia areata. In an open study, a cosmetic response was seen in 25% of patients with severe alopecia areata treated using 0.5%–1.0% anthralin cream. Anthralin needs to be applied in a high enough concentration (0.5%–1%) and sufficiently frequently daily to produce a mild irritant reaction in order to be effective. Use of anthralin in the promotion of hair regrowth in AA, which may provide an attractive option for patients preferring topical over systemic therapy. Burning, irritation and enlarged lymph nodes are observed following its use.[13]

8.4. Bexarotene

Bexarotene gel 1% is a member of a subclass of retinoids that selectively activate retinoid X receptors (RXRs). In a randomized bilateral half-head study, hair regrowth of at least 50% on treated sites was noticed in only 26% of patients treated bexarotene gel. Mild irritation is a common side effect.[14]

8.5. Capsaicin

It causes depletion of neuronal substance P and activates vanilloid receptor-1, thereby increasing the release of calcitonin gene-related peptide (CGRP) from sensory neurons, and CGRP has been shown to increase IGF-I production which might promote hair growth as its potent stimulant for increasing the activity of blood flow around dermal papillae. In a nonblinded randomized study, patients with alopecia areata showed cosmetically acceptable hair regrowth after 12 weeks of applying capsaicin ointment. Concentration of capsaicin is 0.01% w/w. or 0.075% concentration. More recently, a study showed that topical capsaicin and clobetasol 0.05% are comparable.[15,16]

8.6. Cyclosporine

Cyclosporine acts to interfere with early events involved in T-cell activation, specifically by preventing transcription of the interleukin (IL) 2 gene after antigen exposure. Cyclosporine prevents the generation of an antigen-specific population of T cells capable of coordinating an immune response. Oral cyclosporine, 6 mg/kg/day for 12 weeks provides effective results.$

8.7. Bimatoprost

A prostaglandin F2a analog analog which was discovered to promote eyelash growth. It has been approved by the FDA for this indication. Its mechanism of action is to promote the entry of hair follicles into the anagenphase.and a decrease in telogen and late catagen follicles, suggesting that bimatoprost extends the duration of anagen phase. Bimatoprost 0.03% may influence the growth cycle of eyelashes by stimulating follicles to enter anagen earlier and remain there longer. Eyelash hair follicles, in particular, are known to be proportionally higher in the telogen phase, which supports the effectiveness of bimatoprost for hypotrichosis of the eyelashes [17]

8.8. Methotrexate

Methotrexate is safe and relatively inexpensive and should be considered for alopecia areata that does not respond to local therapies. There are two types of action of MTX, the antiproliferative action (mediated by folate-dependent pathway) and anti-inflammatory action (due to increase in aminoimidazole carboxamide ribonucleoside [AICAR] levels). MTX at a mean dose of 20 mg/week appears to be a safe and promising option for the treatment of severe forms of AA. A mean cumulative dose of 180 mg was required for onset of response, and total cumulative doses of 1000-1500 mg were associated with the best responses. 77.8% % of patients experienced a more than 50% regrowth rate, with the best responses observed in those with < 5 years of disease progression (81%). [18]

8.9. Sulphasalazine

Sulfasalazine and/or its metabolites inhibit the release of cytokines produced by various cell types, especially T-lymphocytes which are responsible for IL-2. induction and monocytes/ macrophages, responsible for IL-1, IL-6, IL-12 and tumor necrosis factor (TNF)-α induction . Possibly through regulations of these cytokines, as well as T-cell proliferation, natural killer cell activity and activation of B cells, sulfasalazine halts AA progression. In this regard, sulfasalazine may have an important role as there are reports on successful and safe use of sulfasalazine in inducing hair regrowth in AT and AU in both adults and children. .Among those who completed a course of sulfasalazine, 80% with limited AA had excellent benefit [19]

8.10. Azathioprine

Azathioprine and its analogues interfere with DNA synthesis by inhibition of enzymes of purine synthesis, thereby affecting proliferation of cytotoxic T-cells. Reduction in colonization of T-cells around follicles, normal follicular growth phase resumes and clinical response is seen in the form of hair growth. Patients were kept on minimal dose of azathioprine (1 mg/kg). Severity of Alopecia Tool (SALT) score for alopecia areata (AA). Treatment with azathioprine as a systemic monotherapy clinically produces relevant improvement in moderate-to-severe alopecia areata improving salt score. minimal dose of azathioprine (1 mg/kg). [20]

9. Biological Drugs

9.1. Janus Kinase inhibitors

9.1.1. Mode of action

Cytokines- IL-2, IL-4, IL-7, IL-9, IL-15 and IL-21, play key roles in controlling cell growth and the immune response. Many cytokines function by binding to and activating type Iand type IIcytokine receptors. These receptors in turn rely on the Janus kinase(JAK 1, 2) family of enzymes for signal transduction. Hence drugs that inhibit the activity of these Janus kinases block cytokine signalling. Janus kinases phosphorylate activated cytokine receptors, which is blocked by Tofacitinib, Fluxolitinib and Baracitinib It has been proved that JAK-STAT signaling pathway enhances release of interleukin (IL)-4, IL-5 and IL-13, which play an important role in stimulating TH2 differentiation. Ruxolitinib and Baracitinib mainly inhibit Janus kinase 1 and 2. Tofacitinib inhibits Janus kinase 1 and 3. [Figures 7 and 8]

9.1.2. Use in Alopecia areata

Topical JAK inhibitors represent a promising therapeutic option for at least a subset of patients with AA. If confirmed to be effective in clinical trials, topical administration might be preferable for certain populations, including children and patients with more limited disease. Oral tofacitinib (5 mg BID or Oral tofacitinib (15 mg daily) , Oral ruxolitinib (15mg, 20 mg BID, Topical 0.6% ruxolitinib (BID) and oral baricitinib 7 mg in the morning and 4 mg in the evening have been evaluated successfully. (75%) treated with ruxolitinib showed significant scalp hair regrowth and improvement of AA with ruxolitinib. Ruxolitinib cream used twice daily for 12 weeks in a case of refractory Alopecia universalis resulted in full eyebrow regrowth and also 10% of scalp hair regrowth, They can reduce baldness in either sex. [21,22]

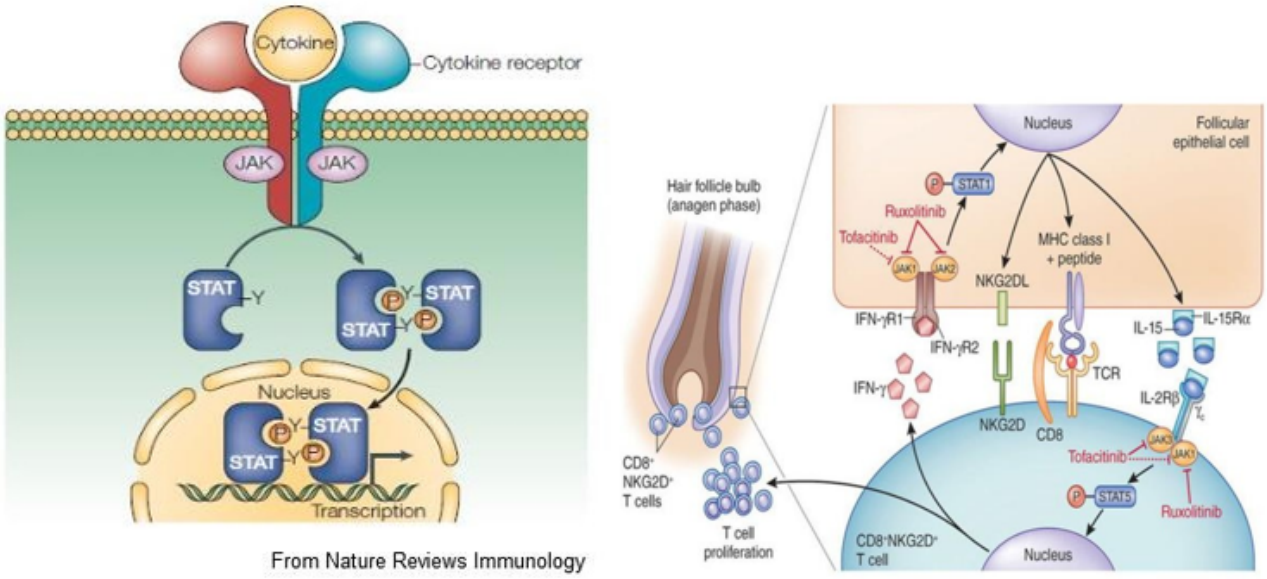

Fig. 7:

9.2. Other biological modifiers

Tralokinumab is a human monoclonal antibody that inhibits interleukin 13, which is an important cytokine for developing hair loss in alopecia areata.

Abatacept is effective therapy in moderate to severe alopecia areata by blocking re-activation of a special type of immune cell a memory T-Cell (CD8+NKG2D+) thereby blocking the inflammatory response underlying recalcitrant alopecia areata

Ustekinumab, an mAb targeting the IL-12/IL-23 p40 subunit, was reported to be somewhat effective in cases of extensive AA.

Platelet-rich plasma (PRP) is autologous concentration of platelets contained in small volume of plasma which accelerates the rejuvenation of skin and hair follicles (HFs) due to presence of various growth factors and cellular adhesion molecules. Platelet Rich Plasma has been shown to increase hair growth in androgenetic alopecia, presumably by stimulating stem cells in the bulge region to regenerate hair follicles and induce anagen transition

The effects of parathyroid hormone-related peptide (PTHrP) agonists causes initiation of the anagen phase, likely by upregulating beta-catenin and LEF-1. PTHrP also accelerates the transition of the hair follicle from the anagen to the catagen phase, the overall effect being to accelerate the hair cycle.

Stem cells play a critical role in hair follicle regeneration and in the hair cycle. Stem cells are located in the bulge region of the hair follicle An autologous transplant is viewed as the standard, its use is limited because of a lack of data and the diminished viability of cells .Adipose-derived stem cells are a promising alternative because of their limited immunogenicity. They are easy to obtain, are multipotent, and can differentiate into different cell lines. They also have significant potential for angiogenesis.[23]

9.2.1. Herbal drugs

Herbal cosmetics have attracted and growing demand on the grounds that of their good effect and comparatively lesser side effect. In alopecia treatment market a lot of products are available which are formulated from herbal extracts as their basic ingredients.

The plants with the most evidence-based effect against alopecia are Curcuma aeruginosa (pink and blue ginger), Serenoa repens (palmetto), Cucurbita pepo (pumpkin), Trifolium pratense (red clover), and Panax ginseng (Chinese red ginseng). The assumed mechanism of action is predominately inhibition of 5α-reductase, with enhanced nutritional support and scalp blood circulation playing a role as well.[24]

9.2.2. Natural products

Oral L-cystine (70 mg) in combination with retinol was evaluated for the treatment of diffuse alopecia, with increases seen in both hair density and anagen rate. Supplementation with L-cystine (20 mg), medicinal yeast, pantothenic acid, thiamine, keratin, and para-aminobenzoic acid resulted in significant improvement and normalization of the mean anagen hair rate after 6 months.

In a trial of 40 AA patients, topical 5% garlic gel in combination with betamethasone was evaluated in comparison to placebo. After 3 months, good to moderate responses were observed in 95% of those treated compared

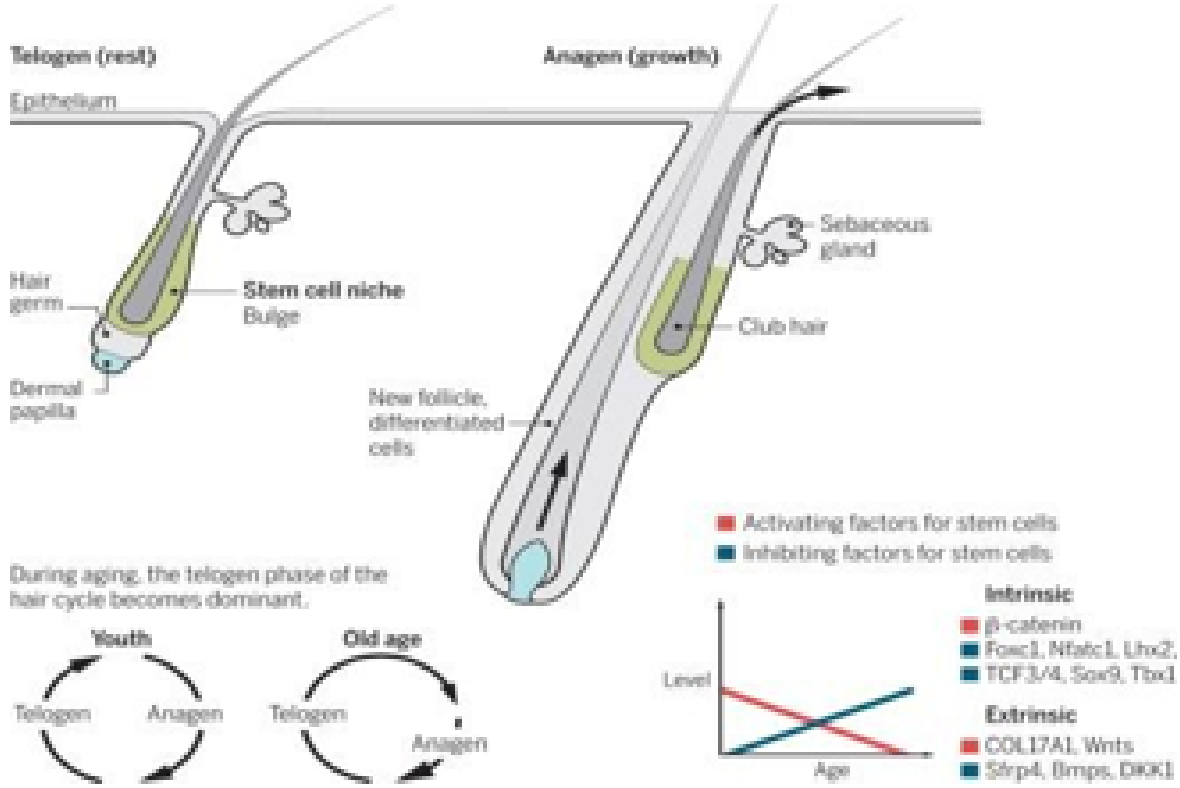

Fig. 8:

to 5% with placebo. No adverse effects were reported.

After treatment with melatonin, patients with diffuse alopecia had a significant increase in anagen hair at the occiput versus the frontal hairline.

Topical 1% procyanidin B2, derived from apple juice, resulted in a significant increase in total and terminal hair counts at 4 months and 6 months in 29 patients with AGA compared to placebo.

Biotin deficiency (< 100 ng/L) and suboptimal biotin levels (100–400 ng/L) were reported in 38% and 49% of healthy women complaining of hair loss.

10. Mesotherapy

Mesotherapy employs multiple injections of pharmaceutical and homeopathic medications, plant extracts, vitamins, and other ingredients into the target tissue. In treatment of alopecia, mesotherapy can be of help by causing hair regrowth by delivering medications into the middle layer under the skin. Mesotherapy uses a dual-action process, which employs both chemical stimulation and mechanical stimulation to the affected area. Mesotherapy for skin rejuvenation does not result in statistically significant histological changes or clinical improvement.

Hypnotherapy, Psychotherapy, Yoga, Aromatherapy, Massage with olive oil (oil consists of monounsaturated fatty acids which help in strengthening the roots and the tips of the hair.) are alternative models which are proposed to stimulate hair growth.[25]

10.1. Micronutients [Table 3]

The role of micronutrients for the hair follicle function and the mechanisms by which deficiency could lead to hair loss are not completely understood.

Most studies of zinc have identified lower serum levels in patients with AA compared to controls. Serum levels also appear to be inversely associated with severity of disease.controls.

Patients of AA had lower selenium levels compared to controls, Selenium is essential for the production of the thyroid hormones that help to regulate hair growth.

Several studies showed significantly higher prevalence of vitamin D insufficiency in patients with AA than the control group. Topical calcipotriol has been reported to be used successfully in treating AA, vitamin D3 significantly

Table 2:

Nuritient	Laboratory	Normal level	Hair loss association	Recommended supplementation
Iron	Serum Ferritin	>40 ng/l	CTE ATE AA AGA	150-200 mg/day of element iron. Ferritin tests at 3 months interval and continue oral iron therapy for 3-6 months after the iron deficiency is corrected
Zinc	Serum Zinc (ZC)	>10.7 mmol/L	TE	50mg Zc gluconate daily for 12 weeks or 5 mg/kg/day Zn Sulphate for 3 months
Vitamin D	Serum 25(OH) D2	>30 ng/mL	CTE	50,000 IU once a week for 1-3 months. Maintenance dose of 800-2000 IU to avoid recurrences
		Insufficiency: <30 ng/mL	FPHL	
		Deficiency	AA	
Biotin	Urinary excretion of biotin/organic acids and Carboxylase activity in peripheral blood lymphocytes	Deficiency: Biotin urinary excretion low 20ug/L or 25 ug/24 hours	No evidence of hair loss association	No evidence for biotin supplementation for hair loss treatment
Vitamin C	Serum vitamin C	>11mmol/L or 0.6-2.0 mg/dL	Crork screw hairs	300-1000 mg daily of oral vitamin C for 1 month
Vitamin A	Serum Retinol concentration	Deficiency below 20 mcg/dL	Deficiency: TE and Hair breakage Overlode: TE	

TE: telogen effluvium, CTE: chronic telogen effluvium, ATE: acute telogen effluvium, AA: alopecia areata, AGA: androgenetic alopecia, FPHL: female pattern hair

inhibits the production of IFN-γ and decreases the secretion of IFN-γ by human $CD4^+$ T cells. 1,25(OH)2D inhibits the proliferation of human CD8 and CD4 T cells . High dose of 10,000 IU orally daily for 3 months has produced significant effects.

Correcting serum iron levels would lead to better treatment responses, as shown previously in ndrogen-dependent alopecia.

Studies suggest associations between AA and low red cell folate levels. Folic acid helps keep red blood cells healthy. Folic acid is the synthetic form of folate, a type of B vitamin.[26,27]

11. Conclusion

No uniformly dependable treatment is known. Some treatments can induce hair growth, though none is able to alter the overall course of the disease. Any treatments that carry serious risks should be avoided, as alopecia areata itself has no adverse effect on physical health. High-quality randomized- controlled trials with large sample sizes are lacking .for most drugs, According to the guidelines of the British Association of Dermatologists, contact immunotherapy and corticosteroids are the most effective and best documented, but even these treatments often fail to induce hair growth. Therefore, the need exists for more efficient treatments which are based on molecular mechanism of the disease process. Biologicals are suitable options most of them are now evaluated in well designed clinical studies.

12. Conflict of Interest

None.

13. Source of Funding

None.

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