

New Treatment Strategies in Management of Alopecia Areata: Review Article

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ABSTRACT

Background: Alopecia areata is a common and unpleasant illness that manifests as abrupt, circular patches of complete hair loss that heal scar-free. For most individuals with patchy alopecia areata, intralesional or topical corticosteroids are regarded the first therapeutic option due to their relative safety and convenience; nevertheless, there is limited evidence for their efficacy.

Objective: Review of the literature on New Treatment Strategies in Management of Alopecia Areata.

Methods: We looked for data on New Treatment Strategies and Alopecia Areata, treatment in medical journals and databases like PubMed, Google Scholar, and Science Direct. However, only the most recent or extensive study was taken into account between November 2002 and December 2021. References from related works were also evaluated by the writers. There are not enough resources to translate documents into languages other than English, hence those documents have been ignored. It was generally agreed that documents such as unpublished manuscripts, oral presentations, conference abstracts, and dissertations did not qualify as legitimate scientific study.

Conclusion: When a ligand attaches to their specific cytokine receptor, janus kinases (JAKs) can phosphorylate signal transducers and activators of transcription (STATs). Hair regrowth is facilitated by oral formulations because they are simple to ingest. Tofacitinib comes in 5-mg and 11-mg doses and can be taken once or twice day. Treatment options for alopecia areata of the scalp are limited, but the 308-nm excimer laser has proven to be helpful in restoring hair growth in affected areas.

Keywords: New Treatment, Alopecia Areata, Scar-free, Hair loss.

INTRODUCTION

The rapid onset of smooth, scar-free patches of scalp is the hallmark of alopecia areata, a widespread and unpleasant condition of unknown cause. Both the amount of bald patches and the disease's progression are highly unpredictable; sometimes it will go into remission, and other times it will spread to the rest of the scalp and/or body hair ⁽¹⁾.

The hair loss condition known as alopecia areata (AA) typically presents itself suddenly and can be either localised or widespread. Dystrophic anagen or telogen follicles and a mononuclear cellular infiltrate in and around hair follicles are the hallmarks on histology, however scarring is uncommon. In Latin, alopecia means baldness, and alopecia areata describes the often-scattered thinning of hair that occurs with alopecia ⁽¹⁾.

Varying degrees of diffuse scalp (alopecia totalis) or body involvement (patchy baldness) can be seen in patients with this condition (alopecia universalis). Most people with AA go through cycles of

remission and relapse. However, it can be long-lasting in many patients, especially when the hair loss is severe ⁽¹⁾. As of yet, we know very little about the precise pathophysiology of AA. Hair follicles in the anagen stage of the hair growth cycle prematurely enter the involutive catagen and resting telogen stages due to the autoimmune illness alopecia areata. This causes accelerated hair loss and stunted hair growth (figure 1). Alopecia areata differs from cicatricial alopecia in that its inflammatory process does not result in permanent hair follicle damage ⁽²⁾.

Alopecia areata can be diagnosed based on the pattern and severity of hair loss, the presence of telltale exclamation marks, and the presence of nail dystrophy ⁽³⁾. Inspection is the standard method of diagnosis. A diagnosis of AA is usually made based on the presence of discrete bald spots or alopecic areas with intact follicular ostia. When diagnosing AA, it is important to get a thorough patient and family history, paying special attention to the timing and severity of hair loss and any other symptoms that may have developed ⁽⁴⁾.

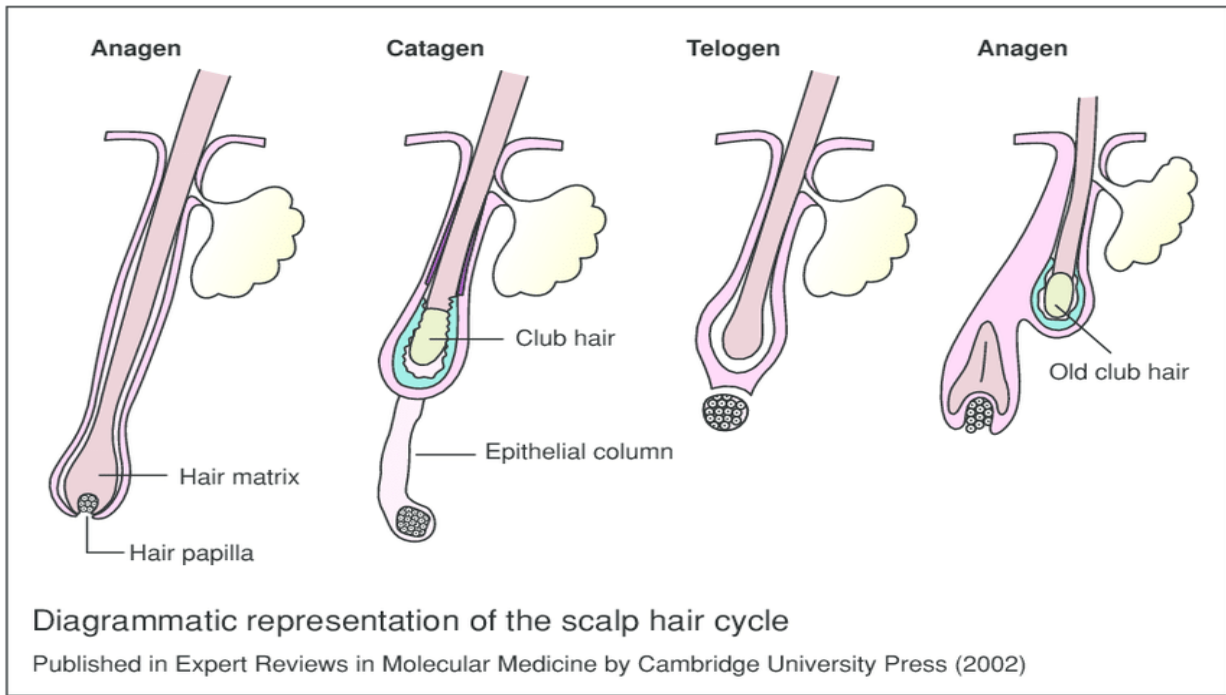


Figure (1): The typical life span of a human hair ⁽⁵⁾.

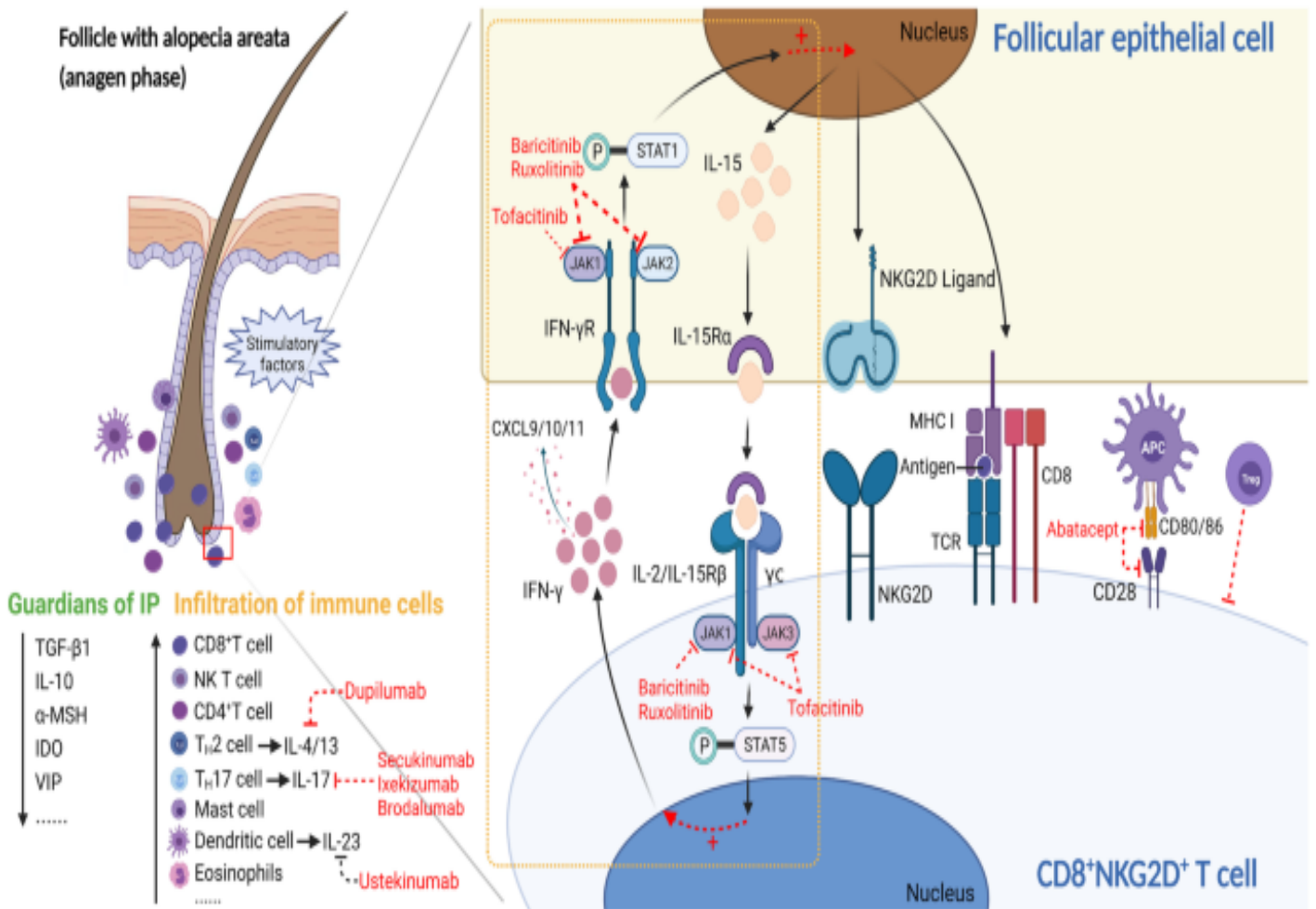


Figure (2): Areata Alopecia and Its Immunopathogenic Origins ⁽¹⁾.

Management:

The pathophysiology of alopecia areata has been linked to several cytokines. Using immunohistochemistry and gene expression analysis, we compared biopsies collected from lesional and non-lesional (NL) scalp of AA patients before and after treatment ⁽⁶⁾.

A primary goal of treatment is to promote hair regeneration while slowing the course of illness ⁽⁷⁾. The severity of hair loss and the patient's age are the two most influential aspects in selecting the most effective treatment ⁽⁸⁾.

Traditional Therapies

Patients with patchy alopecia areata often turn first to the relatively safe and widely available corticosteroids, intralesional or topical, despite minimal evidence for their usefulness. Patients with advanced illness may benefit from using topical immunotherapy as an initial treatment option (having greater than 50 percent scalp hair loss) ⁽⁹⁾.

➤ *Contact Immunotherapy:*

By inducing an allergic contact dermatitis on thinning areas, contact immunotherapy can stimulate hair regrowth. This is accomplished through the application of topical sensitizers such diphenylcyclopropenone (DPCP) and squaric acid dibutylester (SADBE). Hair regrowth after this therapy may be due to the diversion of inflammatory infiltration around hair follicles to the produced dermatitis. Although contact immunotherapy has not been shown to be successful in acute, rapidly advancing cases of AA, its efficacy in treating adults and children with diffuse or patchy long-standing AA has been widely accepted ⁽⁸⁻¹⁰⁾.

➤ *Topical corticosteroids:*

For small patches, the most common treatment for adults and children with AA is topical corticosteroids (TCs) ⁽¹¹⁾.

When used topically, corticosteroids help reduce inflammation around hair follicles, allowing them to resume their regular development cycle. There was a considerable increase in hair regeneration with the use of both desoximetasone cream and clobetasol propionate foam compared to the use of placebo. Only topical treatments were compared, and topical steroids outperformed anthralin and tretinoin. While clobetasol propionate cream outperformed hydrocortisone cream, betamethasone valerate foam performed better than lotion. Occlusion improves the efficacy of topical steroid creams ⁽¹²⁾.

➤ *Intralesional corticosteroids:*

An intralesional steroid injection is the gold standard treatment for alopecia areata that appears in patches. The most typical dosage ranges for intradermal injections of triamcinolone acetonide (TA) is between 2.5 and 10 mg/ml. When TA is not readily available, intralesional betamethasone is typically used as an alternative ⁽¹³⁾.

Pitting atrophy is the most significant drawback of ICs. A few months later, however, it disappears ⁽¹⁴⁾.

➤ *Minoxidil:*

Minoxidil, a vasodilator intended to treat hypertension, has been widely used to cure hair loss, especially alopecia areata (AA), due to its ability to stimulate hair growth. Although topical minoxidil has been shown to be successful in treating AA in localised areas, it may not be sufficient as a monotherapy to restore full hair growth in cases of widespread AA ⁽¹⁵⁾.

Therefore, in addition to topical minoxidil, other medicines, including corticosteroids, are often used to treat AA. With low-dose (0.25-5 mg) oral minoxidil twice daily, 18-82.4 percent of patients (including those with severe and resistant AA) saying clinical improvement ⁽¹⁶⁾.

➤ *Systemic corticosteroids:*

In the acute, progressive stage of androgenetic alopecia, systemic corticosteroids (SCs) are frequently used to treat the loss of large amounts of hair ⁽¹⁷⁾.

For individuals with mild to severe alopecia areata, a 6-week tapering course of oral prednisolone resulted in >25% hair regrowth, according to a small, largely controlled research ⁽¹⁸⁾.

The clinical efficacy and adverse effect profile of pulse corticosteroid therapy were shown to be superior to those of oral daily steroid administration (OD). Pulse corticosteroid therapy combined with OD was found to be effective for treating AT/AU, with 80.6 percent of patients showing improvement and 71.1% showing total hair regrowth in the trial. About a third of patients, especially those receiving combo therapy, had side effects. Because of this, it is suggested that prolonged usage of corticosteroids be avoided wherever feasible ⁽¹⁸⁾.

➤ *Azathioprine:*

Azathioprine inhibits the production of cytokines by helper T-cells and the proliferation of cytotoxic T-cells by blocking enzymes involved in purine synthesis, therefore reducing the immune response. Reduced T-cell colonization near hair follicles permits proper progression through the growth phase ⁽¹⁹⁾.

As an alternative to systemic steroids, which have a high risk of major adverse effects, azathioprine tapering therapy may be helpful for patients on oral corticosteroids. The use of azathioprine as an adjuvant therapy alongside corticosteroids is highly successful in treating severe, drug-resistant AA ⁽²⁰⁾.

➤ *Methotrexate:*

Patients with severe alopecia areata may benefit from methotrexate. In compared to methotrexate alone, the response rate when combined with corticosteroids is both greater and more comprehensive. Methotrexate, at a median weekly dose of 20 mg, shows promise as a viable choice for the management of severe AA ⁽²¹⁾.

➤ *Cyclosporine:*

Helper T cells, which may play a pathogenic role in alopecia areata, can have their activity suppressed by

cyclosporine. The scalp hair of all six patients in a clinical trial of oral cyclosporine 6 mg/kg/day for 12 weeks for alopecia areata grew back between the second and fourth weeks of medication. Alterations in immune cell infiltration around follicles were linked with clinical response ⁽²¹⁾.

New Treatment Strategies:

➤ **Janus kinase (JAK) inhibitors/ Signal transducer and activator of transcription (STAT) inhibitors:**

For instance, a JAK can phosphorylate a STAT to trigger transcription after a ligand-to-associated cytokine receptor interaction. As soon as they are phosphorylated, STATs travel from the cytoplasm to the nucleus, where they bind to particular DNA sequences and regulate gene transcription ^(22, 23).

Hair regrowth was observed in 67–75% of patients taking oral versions of JAK inhibitors. Hair regrowth is facilitated by oral formulations because they are simple to ingest. Tofacitinib comes in 5-mg and 11-mg doses and can be taken once or twice day ⁽²⁴⁾.

Increased susceptibility to infections like as colds, the flu, and herpes zoster is the most common unwanted side effect of JAKi ⁽²¹⁾.

➤ **Platelet-Rich Plasma Therapy:**

Platelet-rich plasma (PRP) is an autologous plasma preparation with a high platelet content and a rich source of growth factors and cytokines. Therefore, it plays an essential role in promoting tissue repair. The ability of PRP to lower MCP-1 expression while increasing TGF-expression, an anti-inflammatory mechanism, may further contribute to its efficacy in treating AA ⁽²⁵⁾.

➤ **Excimer Laser:**

Treatment options for alopecia areata of the scalp are limited, but the 308-nm excimer laser has proven to be helpful in restoring hair growth in affected areas. Therapy for alopecia areata can be achieved using excimer lasers by suppressing cutaneous immune responses and inducing anagen phase of hair growth. The movable arm makes it easy to go right to the lesions you want to treat, without putting the surrounding hairs at risk ⁽²⁶⁾.

➤ **Superficial Cryotherapy:**

Treatment of many neoplastic and inflammatory disorders can be achieved with the help of superficial cryotherapy using liquid nitrogen. In mild to moderate AA, the use of liquid nitrogen for superficial cryotherapy is a legitimate therapeutic alternative with great treatment results and few adverse effects ⁽²⁷⁾.

➤ **Phosphodiesterase 4 Inhibitors:**

Innate immune system small-molecule modulators called phosphodiesterase (PDE) 4 inhibitors dampen inflammation by preventing the production of cyclic

adenosine monophosphate (cAMP) inside of cells (cAMP) ⁽²⁸⁾.

➤ **Prostaglandin Analogues:**

Common antiglaucoma medications include prostaglandin analogues like latanoprost and bimatoprost. Hypertrichosis of the eyelashes has been linked to the usage of these medications. Prostaglandin F₂- (PGF₂) equivalents include latanoprost and bimatoprost. They treat alopecia and stimulate hair growth, especially in the eyelid and eyebrow areas, most likely by prolonging the anagen phase of hair follicles ⁽²⁹⁾.

CONCLUSION

When a ligand attaches to their specific cytokine receptor, janus kinases (JAKs) can phosphorylate signal transducers and activators of transcription (STATs). Hair regrowth is facilitated by oral formulations because they are simple to ingest. Tofacitinib comes in 5-mg and 11-mg doses and can be taken once or twice day. Treatment options for alopecia areata of the scalp are limited, but the 308-nm excimer laser has proven to be helpful in restoring hair growth in affected areas.

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