

Therapeutic Options to Refractory Alopecia Areata

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ABSTRACT

Alopecia areata is a relapsing chronic condition that causes hair loss without leaving scars. Alopecia areata's clinical history varies; the condition may resolve spontaneously, persist, recur, or advance. Alopecia areata sufferers are treated in numerous ways, including: Information about the progression and prognosis of alopecia areata Consideration of medical treatment continuation; Treatment selection (for individuals who desire to continue treatment); Provision of psychological support resources; and Discussion of aesthetic possibilities.

ARTICLE DETAILS

Published On:
10 January 2023

Available on:
<https://ijmscr.org/>

INTRODUCTION

Alopecia areata is a recurrent, chronic inflammatory condition of the hair follicles that causes hair loss without scarring. The severity of the condition ranges from minor patches of alopecia in any location with hair to full hair loss on the scalp, brows, eyelashes, and body.¹

Alopecia areata management include treating the patient's psychosocial needs and providing treatment to those who desire it. Alopecia areata has been treated with a range of topical, intralesional, and systemic medicines, as well as devices, but response to therapy varies greatly, and well-designed clinical trials are scarce. The treatment of refractory illness will be described more below.²

REFRACTORY DISEASE

Oral Janus kinase inhibitors (JAK), dupilumab, immunosuppressants, oral sulfasalazine, or topical anthralin may be effective for individuals who have failed or are unable to receive early therapy. The ideal treatment for illness resistant to first therapy has not been determined, and other techniques may be appropriate. Treatment selection requires taking into account effectiveness and safety data, as well as patient preference and treatment availability.³

In alopecia areata, Janus kinase (JAK) inhibitors stimulate hair growth. JAK inhibitors may have a favorable effect on alopecia areata by inhibiting T cell activation.⁴

More research is needed, however, before judgments concerning long-term effectiveness and safety can be reached. The FDA has issued boxed warnings for oral JAK inhibitors due to the risk of severe infections, death,

malignancy, substantial adverse cardiovascular events, and thrombosis.⁵

Hair regrowth has been observed in people with alopecia areata who were treated with oral tofacitinib (a selective JAK inhibitor that principally inhibits Janus kinase 1 [JAK1] and Janus kinase 3 [JAK3]). Patients are often given 5 mg twice day.⁶

Oral Ruxolitinib: An open-label pilot research, case series, and case reports describing the use of oral ruxolitinib [57,72-75] add to the evidence that JAK inhibitors may be useful in the treatment of alopecia areata. In an open-label trial, 9 of 12 patients (75%) with moderate to severe alopecia areata who were given ruxolitinib 20 mg twice daily for three to six months saw at least 50% hair growth at the conclusion of therapy.⁷

Data from the phase 2 study show that experimental oral JAK inhibitors such as ritlecitinib, brepocitinib, and CTP-543 are effective.⁸

The effectiveness of topical JAK inhibitors in alopecia areata is unknown. A 24-week experiment in which 39 people with alopecia areata (hair loss ranging from 25% to 100%) were randomly allocated to ruxolitinib 1.5% cream twice daily or vehicle revealed no significant difference between the two groups in the proportion of patients who obtained a 50% improvement in SALT scores. In a small randomized study (n = 31), topical delgocitinib, an experimental JAK inhibitor, was no more efficacious than the vehicle. Furthermore, some topical JAK inhibitor studies were ended early due to causes such as ineffectiveness, futility, or sponsor choice.⁹

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Other research indicates a possible advantage. A 28-week phase 1 trial in which 16 adults with alopecia universalis applied 2% facitinib ointment, 1% ruxolitinib ointment, 0.05% clobetasol dipropionate ointment, or vehicle to one of four randomized areas of the scalp and eyebrows twice daily found new hair growth in the treated area in 6, 5, 10, and 0 patients, respectively. Furthermore, in a 24-week open research, hair regrew in three of ten persons with alopecia areata or alopecia totalis who used 2% tofacitinib ointment. In a case series of 11 children with alopecia areata, alopecia totalis, or alopecia universalis who were refractory to oral and topical corticosteroids, treatment with 2% tofacitinib ointment was associated with an improvement in SALT score in eight children, including three children who had enough hair growth to cover the scalp or hide residual areas of hair loss.¹⁰

During therapy with dupilumab, patients experienced improvement, onset, reactivation, and worsening of alopecia areata. More research is needed to assess the efficacy of dupilumab in the treatment of alopecia areata.¹¹

A baseline serum immunoglobulin E (IgE) level of at least 200 international units/mL, a personal or family history of atopy, and a shorter time since previous hair regrowth were all linked with a higher chance of response.¹¹

Dupilumab has also been shown to be beneficial in case reports and case series. Four of six children with active disease at the time of dupilumab beginning and at least four months of clinical follow-up improved in disease severity in a group of 16 children with both alopecia areata and atopic dermatitis treated with dupilumab (300 mg every two weeks). The children who improved had ophiasis pattern (two), alopecia universalis (one), or patchy alopecia areata (one); the two who did not react had alopecia universalis.¹²

Immunosuppressants like as methotrexate, azathioprine, and cyclosporine are occasionally used to treat refractory alopecia areata. These medicines have little efficacy data, and therapy with these medications necessitates frequent laboratory monitoring owing to possible toxicity.¹³

Methotrexate may be useful, according to a systematic review and meta-analysis of mostly retrospective observational studies, especially when administered in adults or in combination with systemic glucocorticoids. Patients were often given dosages ranging from 7.5 to 25 mg per week. 63% of patients had an excellent or full response (at least 50% hair regrowth). The first signs of hair growth with methotrexate may appear after approximately 3 months, and it may take 6 to 12 months of medication to fully recover. However, recurrence appears to be prevalent when methotrexate levels steadily decline.¹⁴

Small, uncontrolled trials show that azathioprine stimulates hair growth in some people with moderate to severe alopecia areata. Six individuals had their hair regrown under therapy with azathioprine (2.5 mg/kg per day adjusted for thiopurine methyltransferase [TPMT] levels) in a prospective trial of 14 adult patients with alopecia universalis, with all attaining

regrowth in 75 percent or more of the scalp. Responses occurred four to six months after treatment beginning, and four of the six responders continued to improve after therapy was discontinued. Adverse symptoms (diarrhoea, increased liver enzymes, pancreatitis, or bone marrow suppression) occurred in 5 of the 14 individuals, prompting four patients to discontinue treatment.¹⁵

Cyclosporine can stimulate hair growth in alopecia areata sufferers. Cyclosporine treatment, on the other hand, is accompanied with the likelihood of substantial side effects that limit long-term therapy. As a result, we generally avoid using cyclosporine to treat alopecia areata.¹⁶

Cyclosporine efficacy data are few. A 12-week experiment in which 36 individuals with moderate to severe alopecia areata (including 21 adults with alopecia totalis or alopecia universalis) were randomly assigned to cyclosporine (4 mg/kg per day) or placebo discovered a non-statistically significant trend in favor of cyclosporine's effectiveness. At week 12, 31% of patients treated with cyclosporine vs 6% of patients treated with placebo improved their SALT score by at least 50%. Further research with bigger sample sizes or longer treatment durations may be valuable in verifying cyclosporine's efficacy.¹⁷

Data from case studies and uncontrolled research support the use of cyclosporine with or without systemic glucocorticoids. Doses of cyclosporine more than 4 mg/kg have also been utilized. Alopecia areata has also been described as a side effect of cyclosporine medication.¹⁷

Sulfasalazine is an immunosuppressive and immunomodulatory medication. Uncontrolled research and a retrospective assessment of medical records revealed that around one-quarter of individuals with alopecia areata received therapeutic treatment. Relapse rates of up to 45 percent have been documented, however. Sulfasalazine side effects may include gastrointestinal discomfort, headache, fever, rash, and, less often, haematological problems and hepatotoxicity.¹⁸

Starting treatment at a low dosage may help to alleviate gastrointestinal issues. Patients can be given 0.5 g twice daily for one month, then 1 g twice daily for one month, and 1.5 g twice daily for at least three months. Complete blood cell counts and liver function tests should be regularly monitored during the first three months of treatment and then every three to six months after that.¹⁹

Anthralin is a skin irritant. Case studies with insufficient controls provide evidence of effectiveness for alopecia areata. Anthralin appears to be less effective than intralesional corticosteroids and topical immunotherapy. Children may also have difficulties tolerating anthralin discomfort.²⁰

Brown hair, skin, and clothes will be stained by anthralin. Patients should promptly wash their hands with cold or warm water after application.²¹

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CONCLUSION

Alopecia areata hair loss is typically stressful for sufferers. The doctor's awareness of the psychological effect of hair loss is a crucial aspect of the therapeutic interaction. Psychosocial support options, such as a clinical or behavioral health psychologist or psychiatrist and the National Foundation for Alopecia Areata, may also be beneficial.

Cosmetic procedures can help some individuals. Wigs, hairpieces, scalp shaving, and other therapies for scalp hair loss are available. Temporary tattoos can aid with brow loss. False eyelashes can be beneficial for lash alopecia.

REFERENCES

- I. Gao, Y., Huo, S., Sun, M., Zhang, C., Wang, J., Gao, J., ... & Lv, Y. (2022). Evaluation of several immune and inflammatory indicators and their association with alopecia areata. *Journal of Cosmetic Dermatology*, 21(7), 2995-3001.
- II. Davey, L., Clarke, V., & Jenkinson, E. (2019). Living with alopecia areata: an online qualitative survey study. *British Journal of Dermatology*, 180(6), 1377-1389.
- III. Moretz, D. (2021). OHSU Drug Effectiveness Review Project Summary Report—Atopic Dermatitis.
- IV. Gilhar, A., Keren, A., & Paus, R. (2019). JAK inhibitors and alopecia areata. *The Lancet*, 393(10169), 318-319.
- V. Winthrop, K. L., & Cohen, S. B. (2022). Oral surveillance and JAK inhibitor safety: The theory of relativity. *Nature Reviews Rheumatology*, 18(5), 301-304.
- VI. Crowley, E. L., Fine, S. C., Katipunan, K. K., & Gooderham, M. J. (2019). The use of Janus kinase inhibitors in alopecia areata: a review of the literature. *Journal of cutaneous medicine and surgery*, 23(3), 289-297.
- VII. Mackay-Wiggan, J., Jabbari, A., Nguyen, N., Cerise, J. E., Clark, C., Ulerio, G., ... & Clynes, R. (2016). Oral ruxolitinib induces hair regrowth in patients with moderate-to-severe alopecia areata. *JCI insight*, 1(15).
- VIII. Luo, Y., Alexander, M., Gadina, M., O'Shea, J. J., Meylan, F., & Schwartz, D. M. (2021). JAK-STAT signaling in human disease: From genetic syndromes to clinical inhibition. *Journal of Allergy and Clinical Immunology*, 148(4), 911-925.
- IX. Olsen, E. A., Kornacki, D., Sun, K., & Hordinsky, M. K. (2020). Ruxolitinib cream for the treatment of patients with alopecia areata: A 2-part, double-blind, randomized, vehicle-controlled phase 2 study. *Journal of the American Academy of Dermatology*, 82(2), 412-419.
- X. AREATA, A. 7th World Congress for Hair Research.
- XI. Sachdeva, M., Witol, A., Mufti, A., Maliyar, K., & Yeung, J. (2021). Alopecia areata related paradoxical reactions in patients on dupilumab therapy: a systematic review. *Journal of Cutaneous Medicine and Surgery*, 25(4), 451-452.
- XII. Olamiju, B., & Craiglow, B. G. (2021). Combination oral minoxidil and spironolactone for the treatment of androgenetic alopecia in adolescent girls. *Journal of the American Academy of Dermatology*, 84(6), 1689-1691.
- XIII. Amor, K. T., Ryan, C., & Menter, A. (2010). The use of cyclosporine in dermatology: part I. *Journal of the American Academy of Dermatology*, 63(6), 925-946.
- XIV. Messenger, A. G., McKillop, J., Farrant, P., McDonagh, A. J., Sladden, M., Hughes, J., ... & Mohd Mustapa, M. F. (2012). British Association of Dermatologists' guidelines for the management of alopecia areata 2012. *British journal of dermatology*, 166(5), 916-926.
- XV. Gupta, P., Verma, K. K., Khandpur, S., & Bhari, N. (2019). Weekly azathioprine pulse versus betamethasone oral mini-pulse in the treatment of moderate-to-severe alopecia areata. *Indian Journal of Dermatology*, 64(4), 292.
- XVI. Açıkgöz, G., Çalışkan, E., Tunca, M., Yeniay, Y., & Akar, A. (2014). The effect of oral cyclosporine in the treatment of severe alopecia areata. *Cutaneous and Ocular Toxicology*, 33(3), 247-252.
- XVII. Rossi, A., Muscianese, M., Piraccini, B. M., Starace, M., Carlesimo, M., Mandel, V. D., ... & Fortuna, M. C. (2019). Italian Guidelines in diagnosis and treatment of alopecia areata.
- XVIII. Ramos, P. M., Anzai, A., Duque-Estrada, B., Melo, D. F., Sternberg, F., Santos, L. D. N., ... & Mulinari-Brenner, F. (2021). Consensus on the treatment of alopecia areata—Brazilian Society of Dermatology. *Anais Brasileiros de Dermatologia*, 95, 39-52.
- XIX. Ellis, C. N., Brown, M. F., & Voorhees, J. J. (2002). Sulfasalazine for alopecia areata. *Journal of the American Academy of Dermatology*, 46(4), 541-544.
- XX. Nasimi, M., Ghandi, N., Abedini, R., Mirshamsi, A., Shakoei, S., & Seirafi, H. (2019). Efficacy and safety of anthralin in combination with diphenylcyclopropenone in the treatment of alopecia areata: a retrospective case series. *Archives of Dermatological Research*, 311(8), 607-613.