Review Article

Complementary and Alternative Therapies for Alopecia Areata

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Alopecia areata (AA) is a chronic autoimmune disease of the hair follicle, resulting in nonscarring hair loss. While initial therapy for AA often consists of topical and intralesional corticosteroids, some patients may also turn to complementary and alternative medicine (CAM) for additional treatment. This narrative review aims to summarize recent complementary and alternative therapies for AA.

INTRODUCTION

Alopecia areata (AA) is a chronic autoimmune disease of hair follicles, resulting in patches of nonscarring hair loss. In severe cases, AA can cause complete hair loss of the scalp (alopecia totalis) or entire body (alopecia universalis). This condition can significantly impact an individual's quality of life, often affecting emotional and mental health.[1,2] Therefore, treatment for AA focuses on halting disease progression and stimulating hair growth.

Until the approval of oral baricitinib in 2022, there was no consensus guideline or FDA-approved conventional medication for treating AA.[3] Baricitinib is an oral janus kinase (JAK) inhibitor that, while showing impressive efficacy, is currently only approved for adults with severe AA and has a number of potentially concerning side effects including infections, increased risk of death, increased cancer risk, blood clots, and increased risk of major adverse cardiovascular events.[3] Other conventional therapies include topical corticosteroids, diphenylcyclopropenone, or topical minoxidil, which may be associated with atrophy, pruritus, and dermatitis.[3] Moreover, reported efficacy of these treatments remain modest according to a network meta-analysis, which outlined response rates of topical corticosteroids (67.9%; 50.1%), diphenylcyclopropenone (63.4%; 87.9%), and topical minoxidil (61.2%; 55.5%) for mild and moderate-to-severe AA.[4]

Given the variable efficacy of existing therapies and their associated side effects, some patients may also turn to complementary and alternative medicine (CAM). Though the quality of evidence for some CAM therapies remains fairly limited, this narrative review aims to summarize the proposed mechanism, efficacy, and adverse events of recent complementary and alternative therapies for AA.

METHODS

A literature search was conducted in the Pub-Med, EMBASE, and Cochrane Central Register of Controlled Trials databases using the following Medical Subject Heading (MeSH) terms: (alopecia) and (complementary, alternative, integrative, traditional, homeopathic, natural, acupuncture, acupressure, massage, vitamin, cryotherapy, aromatherapy, hypnosis, biofeedback, phytotherapy, herb, herbal, or oil). Upon restricting the search results to full text and performing deduplication, our search yielded 375 articles. The contents of each article were manually reviewed, and the article was subsequently included if it was published in English, conducted on human subjects with AA, and featured complementary or alternative therapies as the primary intervention. Upon screening, 228 articles were excluded for failing to mention alopecia areata and complementary/alternative medicine in the article, 78 for publication type (e.g. commentary, protocol, conference report, guidelines, review), and 25 for being written in a non-English language. A remaining total of 44 articles were then included in our review, and references of included articles were further screened for pertinent literature.

TECHNIQUES

ACUPUNCTURE

Acupuncture is the practice of inserting one or more needles into specific sites on the body for therapeutic purposes and is one of the most frequently used methods of com-

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plementary medicine.[5,6] Acupuncture points on the body, ear, head, or even tongue can be stimulated using different types of acupuncture needles, electricity, laser, heat, or pressure.[7,8] Acupuncture has already been used to treat various skin disorders[5,7] and may mitigate hair loss in AA by reducing inflammatory activity against the hair bulb. Acupuncture may also stimulate hair follicles, warm local collaterals, and activate blood circulation.[8]

While our literature search yielded no randomized control trials for acupuncture in AA, we were able to find case reports worth examining. In one such report, a 22 year-old Chinese female with a ten year history of alopecia totalis (AT), a severe and treatment-resistant form of AA that manifested as a total loss of scalp hair, achieved clinical benefit from being treated with electroacupuncture.[9] Her scalp hair was completely absent with no clear inciting factor. She was treated with electroacupuncture by incorporating transverse needle insertion at points GB20 (located at the nape of the neck) and GV16 (located at the nape of the neck midline) for 30 minutes once per week. After three sessions, she experienced a 25% regrowth, and after eight sessions there was 55% regrowth and more pigmented terminal hair. After 4 months of treatment, the patient had 70% hair regrowth.

In another case report, a 52 year-old female patient experienced AA with hair loss at the top region of the head in association with stress at work.[10] The hair in the GV20 region (located at the top of the head) was white, sparse, and had a reduction in hair follicles. She was treated with wrist and ankle acupuncture for 30 minutes twice a week, in addition to plum blossom needle tapping, application of Psoralea solution, and moxibustion.[10] After 6 weeks of treatment, small black hairs gradually grew into the GV20 area and after 12 weeks of treatment, longer hairs had grown in. Six months later, no new lesions could be found. Though the results of this case are positive, these findings must be interpreted with caution, as it is difficult to judge the effect of acupuncture alongside other concurrent treatments.

CRYOTHERAPY

Cryotherapy, or the general use of low temperatures as a medical therapy, may serve as another alternative therapy for recalcitrant alopecia areata. Various studies on cryotherapy for AA postulate that cold-induced inflammation may alter the immunologic processes and structural components of hair follicles responsible for AA.[11] In one cross-sectional, non-randomized, non-blinded study of patients with alopecia areata (n=44), hairless areas were treated with a closed contact CO_2 system with metallic probes for an average of 10-15 seconds.[11] At follow-up, varying degrees of hair growth were detected in 23 (52.5%) patients by week 4 and 29 (65.9%) patients by week 8. Upon further stratification of the response rates after 8 weeks, 15 (34.09%) patients achieved hair growth over 50-75% of treated areas, while 2 (4.55%) patients demonstrated hair growth over >75% of treated areas. Treatment-related adverse events were limited to 18 cases of partial leukotrichia, 14 cases of varying degrees of post-inflammatory hypopigmentation, and 2 cases of post-inflammatory hyperpigmentation.[11] However, these complications were resolved six months after follow-up, suggesting cryotherapy may serve as an effective alternative therapy for patients with AA who do not respond to conventional therapies such as topical or intralesional steroids.

HYPNOSIS AND MINDFULNESS PSYCHOTHERAPY

Hypnosis is a widely used complementary or alternative therapy in many dermatologic diseases.[12] Patients with AA often have psychological comorbidities of anxiety and depression that can affect one's quality of life. In a prospective cohort study, participants with longstanding severe (defined as over 75% hair loss) alopecia areata completed 10 sessions of individual 1-hour hypnotherapy sessions over six months. After those sessions, the patients showed improved scores on assessments of anxiety and depression. In the sessions, patients underwent 20 minutes of personalized discussions on stress, quality of sleep, self-esteem and anxiety followed by 40 minutes of self-hypnosis that included a variety of suggestions to improve their self-esteem and to decrease shame and anxiety in public. Patients also received a 20-minute self-hypnosis exercise to perform daily.

They quantified the scores of psychological well-being, physical quality of life, mental quality of life, and dermatology specific quality of life using a variety of psychological and quality of life scales. Significant differences in scores after hypnosis were seen on the psychological well-being ($p=0.001$), mental quality of life ($p=0.001$), and dermatology quality of life ($p=0.001$) scales. The positive psychological benefits of hypnotherapy were maintained six months after the end of treatment.[13] While eight patients showed non-significant regrowth of terminal hair after six months of treatment, the clinical efficacy of hypnotherapy for treatment of alopecia is still unknown.[14] A limitation of this form of therapy for AA is that hypnosis and mindfulness therapy require highly motivated patients to complete the treatment.

TOPICAL AGENTS

ESSENTIAL OILS

Aromatherapy may have a role in treating AA. Aromatherapy for AA involves the topical application of essential oils derived from plants, flowers, and wood resins. A randomized, double-blind, placebo-control trial (RDBPCT) by Hay et al. showed that daily topical application of a combination of cedarwood, lavender, thyme, and rosemary oil within a carrier oil significantly decreased areas of hair loss at 3- and 7-month assessments by scored photographic assessments ($P = 0.008$) and areas of hair loss computerized calculations of transparent film mappings ($P = 0.05$) compared to vehicle control.[15] In another RDBPCT by Özmen et al,, patients in the treatment group showed significant differences from control in hair growth rate ($p=0.001$), clinical assessment ($p=0.001$,) and extent of affected area ($p=0.007$) after twelve weeks of topical application of rosemary, thyme, lavender, evening primrose oil and cedrus in a carrier oil.[16] In both

studies, participants went without any other conventional interventions (topical medications or intralesional steroids).

In regards to limitations, the technique for the randomization process used in the trial by Hay et al. was not mentioned and the disease duration for patients was not reported.[17] Furthermore, essential oil(s) specifically responsible for alleviating disease severity remain unknown, as both trials used a combination of essential oils. It is possible that only one or two of the agents in the mixture is responsible for the improvement seen in these patients. Allergic contact dermatitis from aromatherapy was observed in one (2%) patient in the Özmen trial while no adverse events were reported in the Hays trial.

Despite these limitations, aromatherapy with a combination of essential oils including cedarwood, lavender, thyme, rosemary, evening primrose and cedrus oils may be an effective, relatively safe, and inexpensive complementary or alternative treatment to conventional treatments for AA.

PRIMULA OBCONICA

The leaves and flowers of *Primula Obconica*, a plant native to China, can act as an irritant and increase blood circulation at the site of application.[18] In a case series of five patients, hair regrowth was observed after sensitization to *Primula Obconica* and application to the scalp two times per week. In the first patient, sensitization to *Primula Obconica* occurred after six weeks of wearing a leaf continually against the skin. Thereafter, application of *Primula Obconica* to the scalp twice a week led to the observation of hair regrowth at 1 month; more evident results occurred by 2 months.[18] While the results seem optimistic in this case series, the limited sample size of this study warrants further study of *Primula Obconica* as a topical agent that relies on contact sensitization for treating AA.

HERBAL LOTION

Herbal extracts can also be incorporated into lotions and sprays to serve as alternative therapies for AA. One such example is a herbal lotion containing *salvia miltiorrhiza radix* (SMR).[19] A study found that when SMR is removed from the herbal lotion formulation, effectiveness on hair regrowth decreased by 10%, and the speed of hair growth was much slower.[20] However, despite its ability to introduce hair regrowth, SMR can cause contact sensitization if present in concentrations greater than 2%.[19]

Another herbal extract known as *Urginea maritima* (white squill) is commonly used in Iranian traditional medicine and has been topically applied to treat patients with AA. In a 12-week randomized double-blind trial (n=42) comparing 0.05% clobetasol lotion and 2% white squill extract in treating AA, participants applied either topical 0.05% clobetasol lotion or 2% white squill lotion twice daily to alopecia patches and were evaluated using semi-quantitative regrowth scores (RGS) every two weeks.[20] After 3 months of treatment, moderate re-growth of terminal hairs (defined as ⩾50%) was observed in 45% and 55% of patients treated with 2% white squill lotion or 0.05% clobetasol lotion, respectively. The mean size of affected areas were decreased from 974 to 766 cm^2 in squill group and 985 to 726 cm^2 in clobetasol group.[20] However, there were no statistically significant differences in mean hair growth rates between the two groups, suggesting that both treatments may facilitate hair regrowth. Itching and burning was reported in 10% (n=2) and 40% (n=4) of patients, respectively, treated with white squill, while only mild irritation was reported by 40% (n=8) of patients treated with clobetasol.[20]

From these early findings, *Urginea maritima* (white squill) and *salvia miltiorrhiza radix* (SMR) are two herbal agents thus reported that may be used in an herbal formulation as a complementary or alternative AA treatment for patients who desire a non-conventional treatment.

GARLIC AND ONION

Garlic extract may also be used as a topical therapy for AA. While the exact mechanism of how garlic induces hair growth remains unclear, some studies have attributed its hair growth effect to the antibacterial and sterilizing properties of allicin (main component of garlic), induction of vasodilation, or modulation of the immune system.[21] In a RD-BCT by Hajheydari et al., participants (n=40) were treated twice daily for three months with either 0.1% betamethasone valerate cream and 5% topical garlic gel, or 0.1% betamethasone valerate cream alone. By the third month, individuals treated with topical corticosteroids and garlic gel demonstrated significantly greater total and terminal hairs than those treated with the betamethasone cream alone ($P=0.001$).[22] Furthermore, the size of hairless patches significantly decreased ($P=0.04$), and no adverse events were observed throughout the duration of this study.[22] When recommending garlic extract as a topical therapy for AA, clinicians should be aware that some patients may be deterred by the odor of garlic; however, there are currently no reports in the literature of garlic odor being an issue with this therapy.

Another complementary therapeutic that patients may explore is onion juice, which shares chemical similarities with garlic. However, the mechanism of action of onion juice in treating AA remains highly contested. Some report that onion can induce contact dermatitis, while others state that onion extract can inhibit cutaneous allergic reactions and stimulate hair regrowth through antigenic competition. Regardless of its mechanism, however, an 8-week single-blind, placebo-controlled trial (n=62) demonstrated that topical application (twice daily) of onion juice compared to tap water results in statistically significant hair regrowth ($P<0.0001$).[23] By week 2, re-growth of terminal coarse hairs was observed in patients treated with onion juice. By week 4, 17 patients (73.9%) treated with onion juice demonstrated hair regrowth with an additional 3 patients by week 6. Interestingly, hair regrowth was significantly higher among males (93.7%) compared to females (71.4%) ($P<0.0001$). Adverse events related to application of onion juice were limited, with only mild erythema reported in 14 patients (60.8%) treated with crude onion juice.[23] When recommending onion juice as a topical therapy for

AA, clinicians should be aware that some patients may be deterred by the odor of onions; however, there are currently no reports in the literature of odor being an issue with this therapy.

ORAL AGENTS

HERBS/PHYTOTHERAPY

Phytotherapy refers to the use of plants or herbs to treat disease. In an effort to find treatment with long lasting effects and minimal side effects, phytotherapy has become a popular alternative to conventional AA treatments. In a network pharmacology analysis of 20 medicinal herbs by Leem et. al., the main components associated with key proteins in alopecia included acetylcholinesterase (27 compounds), PLA2G1B (14 compounds), LPCAT1 (six compounds), NTE5 (five compounds), fibroblast growth factor receptor 2 (FGF-2, four compounds), FR-beta, and -gamma (four compounds each), NNMT (four compounds), QPRT (four compounds), and DAB adaptor protein 2 (three compounds).[24] These target proteins further implicated the disease process of alopecia areata to pathways associated with glycerophospholipid metabolism, choline metabolism, endocytosis, nicotinate/nicotinamide metabolism, ether lipid metabolism, RAS signaling pathway, glutamatergic synapse, purine metabolism, and pyrimidine metabolism in the hair follicle cycle.[24] While the exact mechanism of phytotherapy in treating AA may vary by herb, phytotherapy can be generally associated with the management of hair cycles, keratinocyte proliferation, apoptosis, angiogenesis, hormones, and inflammation.[25]

Some formulas are being marketed as innovative botanical products that can be used at home to regrow hair. Brevilin A is a molecule that is derived from the medicinal plant *Centipeda minima*. Brevilin A has shown strong inhibition of JAK-STAT signaling *in vitro* and *in vivo*. The JAK-STAT pathway is a common target for AA management; inhibition of this pathway is likely beneficial by suppression of T lymphocytes and stimulation of the anagen hair phase.[26] The simultaneous use of systemic (300mg/day) and topical (2% cream twice a day) brevilin A for 18 months was tested on participants with alopecia universalis, alopecia totalis, ophiasis pattern (a symmetric, band-like hair loss pattern of the occipital, temporal and parietal regions of the scalp), and male androgenetic alopecia. Overall, the treatment was well tolerated, and no treatment-related adverse effects reported. They observed a clinical improvement in Severe Alopecia Tool (SALT) scores but did not achieve statistical significance. The treatment may have worked better in multifocal AA (3 out of 4 patients). However, these results must be approached with caution, as the study is limited by its low sample size and lack of a control group.[26]

KOREAN RED GINSENG

Korean red ginseng (KRG) is a herbal preparation used to prevent hair loss and promote hair growth.[27] A previous study reported that KRG promoted recovery of hair follicles through a combination of proliferation and apoptosis of cells in mouse hair follicles.[28] Ginsenosides are a main component of KRG because of its anti-allergic and anti-inflammatory effects which could be linked to the ability to promote hair regrowth.[29] In one comparison trial, a control group of patients treated for AA with corticosteroid intralesional injection (ILI) was compared with another group treated with corticosteroid ILI while taking KRG. At 12 weeks of treatment, the group taking KRG showed statistically significant improvement compared to the control group (4-point scale scores of 3.6±0.6 vs. 3.1±0.5; $p<0.05$) in a blinded expert panel assessment of global photographs taken at week 0 and week 12 . The hair density and thickness also improved more in the group taking KRG compared to control; however, there were no statistically significant differences.

PEONY & GLYCYRRHIZIN

Total glucosides of peony capsule (TGPC), extracts from the root of the peony plant, and compound glycyrrhizin tablets (CGT), extracts from the root of the licorice plant, are forms of traditional Chinese medical therapy believed to help with AA because of their anti-inflammatory and immunosuppressive properties.[30] In a randomized control trial, children were allocated in a treatment group given oral TGPC plus CGT or a control group of CGT alone for twelve months. At twelve months, both treatment (Before treatment: 6.4±1.1; 12^{th} month after treatment: 1.5±0.9; $P<0.01$) and control groups (Before treatment: 6.6±1.3; 12^{th} month after treatment: 2.4±1.3; $P<0.01$) demonstrated statistically significant improvement in AA severity score compared to baseline. However, the scores of alopecia areata severity were much lower than those of the control group by 12 months ($P<0.05$). No severe adverse events were observed and there was no statistically significant difference in adverse events between groups. In a separate randomized control trial, TGPC was compared with CGT.[31] After three months, the group treated with TGPC demonstrated a 68.18% cured and markedly effective rate while the group treated with CGT demonstrated a cured and markedly effective rate of 71.43%. The rate of adverse reactions were similar in both groups, with 13.64% with TGPC and 16.67% with CGT.

CONCLUSION

Alopecia areata can significantly impact a patient's quality of life, often affecting their emotional and mental health. When traditional forms of treatment fail to address their underlying condition, some patients may turn to complementary and alternative therapies for relief. Through a variety of mechanisms such as down-regulating the immune response, exerting anti-inflammatory effects, or creating conditions favorable for hair regrowth, integrative therapies hold promise for patients who may not respond to or desire traditional treatments. While additional research is required to understand the true efficacy of these complementary and alternative therapies, patients with AA may

continue to explore these treatment options given their favorable safety profile.

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