Treatment options of Alopecia Areata and their Side Effects

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Abstract

Background:
Alopecia areata (AA) is a common form of non-scarring hair loss of scalp and/or body. Treatment is mainly focused to contain the disease activity. Corticosteroids are the preferred treatments in form of topical, intralesional, or systemic therapy.

Aim of work:
To discusses treatment options of alopecia areata and their side effects

Conclusion:
Corticosteroids are the main stay in the treatment of AA. The other treatments are minoxidil, immunotherapy, and PUVA.

Key Words: Corticosteroids, immunotherapy, intralesional, minoxidil.

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Introduction:

There is no curative or preventive therapy for AA. The main goal of treatment is to suppress the disease activity. Therapy efficacy is hard to assess because of the high rate of spontaneous remission and scarcity of randomized controlled trials. Furthermore, long-term outcomes have been not adequately followed (1).

Topical corticosteroids

Midpotent and potent topical corticosteroids in forms of lotions, creams, and ointments are widely used. Because of their pain free applications and wide margin of safety, they are treatments of choice in children (1).

In a half-head comparison trial established with 0.05% clobetasol propionate foam vehicle, **Tosti et al.** (2) found at least 50% regrowth of hair after 12 weeks of starting treatment. During the trial, blood levels of cortisol and ACTH were not affected.

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Lenane et al. (3) compared the use of twice daily treatment with clobetasol propionate 0.05% cream given in 2 cycles of six weeks on, six weeks off regimen for a total of 24 weeks, with hydrocortisone 1% cream used in the same regime. They found that clobetasol was more effective. Compared with only one third of the children in the hydrocortisone group, 85% of the children in the clobetasol group had at least 50% reduction in the surface area with AA.

Painful folliculitis and acneiform eruption of the face are the common side effects (more common with ointment formulation than foam), itching and burning. Striae, skin atrophy, telangiectasia and hypothalamic pituitary adrenal axis suppression can rarely be observed. The relapse rate varies from 37% to 63% after topical corticosteroid treatment has stopped and even with continuation of therapy (4).

Topical immunotherapy

Topical immunotherapy is the most effective treatment option for patients with chronic severe AA, with greater than 50% scalp involvement and refractory AA. The success rate is 50% to 60%, with a relapse rate up to 62% at a median period of 2.5 years (5).

No full understanding is reached regarding the mechanism of action of topical immunotherapy. Published suggested theories include antigenic competition, apoptosis induction of lymphocyte and alteration of the T cell response from the hair follicle to the epidermis. It aims to induce a low-grade chronic dermatitis by applying a contact allergen on the lesion to change the immune response and finally prompt hair regrowth (6).

The first topical sensitizer used in the treatment of extensive AA was dinitrochlorobenzene; however, it was forbidden because of its mutagenic effects. Squaric acid dibutylester (SADBE) and diphenylcyclopropenone (DPCP) are the two compounds still in use today. DPCP is favored since it is cheaper and more stable in acetone for storage (1).

Topical immunotherapy begins at first visit by the sensitization of the patient with 2% DPCP applied to a 5-cm circular area on the scalp. Two weeks later, a 0.001% DPCP solution is applied to the same half of the scalp. The concentration of DPCP is increased gradually each week to produce mild inflammation that manifests as pruritus and erythema lasting for 36–48 hour. After establishing the appropriate concentration for the patient, subsequent therapy is continued once weekly with the same concentration (6).

The possible complications of DPCP application are many and must be discussed with patients before application. Aside from the expected mild contact or allergic dermatitis, stronger reactions include vesicles, blistering, urticaria, lymphadenopathy, hyperpigmentation, or hypopigmentation. Generalized eruptions might occur and necessitate cessation of therapy (7).

Topical Minoxidil

Minoxidil (2, 4-diamino-6-piperidinopyrimidine-3-oxide) was originally developed as an antihypertensive drug (potent vasodilator) and its adverse effect was prominent hypertrichosis. Topical minoxidil has been mainly used as hair regrowing treatment in the late 1980s through incompletely understood mode of actions. Many mechanisms of action have been proposed, including vasodilatation, angiogenesis, opening of potassium channel, enhanced cell proliferation, inhibition of collagen synthesis, stimulation of vascular endothelial growth factor production and prostaglandin (PGE2) synthesis. In addition to its immunosuppressive effects which is reported by some studies (8).

There are a number of ways in which a drug may stimulate hair growth; it may increase the linear growth rate of hair, increase the diameter of the hair fiber, alter the hair cycle, either shortening telogen or prolonging anagen, or act through a combination of these effects. Present evidence suggests that minoxidil acts mainly on the hair cycle; it may also increase hair diameter (9).

Topical minoxidil solution is approved by FDA for the treatment of androgenetic alopecia, but it can be used in AA for both children and adults (10). In a double-blind placebo-controlled study, Price, (11) noticed an evidence for the effectiveness of using 3% topical minoxidil, twice daily in extensive. It was showed that application of 5% topical minoxidil in patients with extensive AA (75% or greater scalp hair loss) had superior efficacy compared to 1% concentration.

Clinical trials done by Price et al. (11) showed that the remarkable rapid increase in hair growth, measured by hair counts or hair weight, was greater in 5% topical minoxidil use in comparison to 2% topical minoxidil and placebo, respectively. The response of this rapidity can be explained by reversal of follicular miniaturization and that

minoxidil triggers follicles in the latent part of telogen into anagen.

Hordinsky and Donati (12) reviewed eight randomized controlled studies about the rational for use topical minoxidil of different concentration in AA. They elicited that positive results were found in studies in which patients had already responded to oral corticosteroids. Minoxidil 5% lotion was found statistically significant in comparison with latanoprost and betamethasone solution in treatment of AA.

The use of intradermal delivery of minoxidil was found to provide a higher efficacy over its topical application. Deepak and Shwetha (13) applied minoxidil intradermally together with triamcinolone acetonide through a scalp roller for cases of resistant and extensive AA and reported a good success rate.

In general, 5% topical minoxidil is rarely used as a monotherapeutic agent but usually it is combined with many other treatments such as topical or intralesional steroids, prednisone, anthralin, or DPCP. Treatment complications include local irritation, allergic contact dermatitis, or, occasionally, increased facial hair growth. Minoxidil foam, which does not contain propylene glycol, has less irritating effects than topical solution (14).

Anthralin

Anthralin, 0.5–1%, short contact therapy is used as an alternative treatment although evidence for its efficacy depends on case series without controls. Anthralin 1% cream is applied daily for 15 or 20 minutes and then washed. The contact time is increased by 5 min weekly up to one hour or to the time required to cause a low-grade dermatitis. Once the contact time sufficient to produce the mild dermatitis is found, subsequent therapy is continued daily for the established period of time. Anthralin should be applied at least three months before evaluating therapy response (11).

Side effects include severe irritation, folliculitis, regional lymphadenopathy, and staining of skin, clothes and fair hair. Patients should avoid eye contact with anthralin, and the treated area should be protected from the sun (14).

Intralesional corticosteroids (ILCS)

The intralesional corticosteroids are commonly used in treatment of AA and considered as the first-line treatment for patchy AA involving < 50% of the adults scalp. In extensive AA, intralesional steroids are used as adjunctive therapy to systemic treatment. In addition, ILCS are suitable for AA patients with active inflammation; patients with positive hair pull test and patients with exclamation point hair (15).

Injections are made every 4–6 weeks into the deep dermis using a 0.5-inch long 30-gauge needle. For lesions of the scalp, 0.1 mL of triamcinolone acetonide at concentration of 5 mg/ mL is injected at 1-cm intervals. ILCs application is also effective for beard and eyebrow AA at a concentration of 2.5 mg/ml. Maximum dose of triamcinolone acetonide should be limited to 3 mL for scalp, 0.5 mL for each eyebrow and 1 mL for beard (16).

Initial hair regrowth is usually observed within four to eight weeks and ILCs should be discontinued, if there is no improvement in six months. In some patients, resistance to steroid therapy can be explained by a decreased expression of thioredoxin reductase 1, an enzyme that activates the glucocorticoid receptor in the outer root sheath. Recently, studies showed that using of three micro needle device (TMD) may be beneficial for the treatment of AA as it provides superior clinical efficacy without apparent increase of adverse effects compared with conventional needles (8).

The most common observed side effect is atrophy, which may be prevented by avoiding superficial injections, and reducing the concentration and volume of injections. Hypopigmentation, depigmentation, and telangiectasia are other adverse effects (16).

Systemic glucocorticosteroids

Systemic corticosteroids have been used since 1952 in the treatment of AA; however, relapse rates are high upon dose reductions. Long-term daily treatment with oral corticosteroids will produce favorable results in a part of the patients (9).

It is also sometimes possible to observe a “rebound” effect, with the occurrence of the disease in a more severe form and resistant to therapy (17).

Proposed therapeutic protocols with systemic steroids include pulse regimens, as monthly intramuscular injections of 40 mg of triamcinolone acetonide (half dose in children), intravenous infusions of methylprednisolone 500 mg/day for 3 consecutive days a month for 3 months (10 mg/kg

in children); oral prednisolone 300 mg/day for 1 day a month for 4 months (5mg/kg in children); oral dexamethasone 5 mg per day for 2 consecutive days/week for 6 months (1/2 dose in children) (18).

Chronic administration of systemic corticosteroids is often required to maintain hair regrowth, and it is always associated with severe long term side effects, such as osteoporosis, obesity, diabetes, adrenal insufficiency, immuno-suppression, acne, dysmenorrhea and some irreversible effects such as cataract, glaucoma, aseptic necrosis of the femoral head. Corticosteroid pulse therapy seems to have less of a side effect profile than daily or alternate day oral regimens (17).

Immunosuppressive treatment

Immunosuppressive agents namely sulfasalazine, methotrexate, and cyclosporine can be used in the treatment of AA. Sulfasalazine therapy can be an alternative treatment option in persistent AA cases. Studies have shown favorable treatment response, but a high relapse rate. The most common side effects include nausea, vomiting, headache, fever, and rash; less commonly hematologic abnormalities and hepatotoxicity can develop (19).

Severe forms of AA resistant to conventional topical and systemic treatments may respond to methotrexate. In a retrospective study, a 15–25 mg weekly dose of methotrexate with or without 10–20 mg prednisolone daily was reported to be effective in 64% of cases. Cyclosporine has been used alone or in conjunction with corticosteroids variable response rates. Use of cyclosporine is limited because of side effects and high relapse rate. Side effects include nephrotoxicity, immune suppression, hypertension, and hypertrichosis of body hair (14).

Conclusion:

AA is the common form of hair loss affecting the quality of life of many patients. There is paucity of controlled studies regarding effective treatments of AA. Corticosteroids are the main stay in the treatment of AA. The other treatments are minoxidil, immunotherapy, and PUVA. Newer therapies are focused at T-cell mechanisms and NK-cell activating ligands.

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