Clinics in Dermatology (2016) **34**, 628–632

ELSEVIER

Clinics in Dermatology

Phototherapy for alopecia areata

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Abstract Phototherapy is a useful therapeutic method for various skin diseases due to its modulatory effect on the cutaneous immune system. Alopecia areata is a dermatosis characterized by partial or complete hair loss. Collapse of the immune privilege of the hair follicle, which induces noncicatricial alopecia, is an important factor in its etiology. Several forms of phototherapy are used in dermatology.

Introduction

Phototherapy is a modality that uses ultraviolet (UV) light to treat various skin diseases. In this review, the author provides indications and therapeutic results of different wavelength phototherapy used in the treatment of alopecia areata (AA). These include broadband UVB, narrowband UVB (NBUVB), excimer laser, excimer lamp, PUVA, and UVA-1.

AA is a disease of the hair follicle that is considered a model of autoimmune disease. Hair loss can occur in single or multiple areas and, less frequently, in a diffuse total or universal form.[1] The immune system has been implicated in its pathogenesis through loss of the immune privilege of the hair follicle.[2] This process involves various cells and factors, including Langerhans cells, CD4 and CD8 T cells, natural killer cells, and their receptors and mediators.[3,4] Research suggests that there is a predominance of T-lymphocytes with a TH-1 profile.[5] Factors that favor its development include genetic predisposition,[6,7] an association with HLA-DQ3,[8] and stress.[9,10] Despite recent progress, its pathogenesis has not been satisfactorily elucidated.

AA affects about 1.7% of the population in the United States.[11] It predominates in the pediatric and young adult population, but it can occur at any age.[1] UV light decreases the presence and activity of Langerhans cells and the immune network. It suppresses proinflammatory reaction type 1, interleukin (IL)-12, interferon gamma, and IL-8. It increases the production of IL-1, IL-6, prostaglandin E2, and tumor necrosis factor-α.[12] UV light decreases DNA synthesis and induces p53 tumor suppressor gene expression.[13]

Its action on Langerhans cells, CD4/CD8 T, natural killer-lymphocytes, and their receptors makes phototherapy a potential option for AA.[14] Currently, first-line treatment includes topical and intralesional corticosteroids with a reported efficacy of 50% to 70%.[1,15] In patients who do not respond, other therapies are available, such as topical minoxidil, anthralin, tacrolimus, and pimecrolimus. Sometimes, systemic corticosteroids, cyclosporine, methotrexate, and sulfasalazine are employed.[1,16,17] Contact dermatitis inductors, such as dinitrochlorobenzene, diphenylcyclopropenone,[18] and squaric acid dibutylester,[19] have been used with some success in selected and recalcitrant cases of total alopecia (AT). Dinitrochlorobenzene is not currently recommended as it was shown to be mutagenic in *Salmonella typhimurium* in the Ames test.[20,21] Recently, to facitinib, a janus-kinase inhibitor, was used to treat psoriasis in a patient with concomitant alopecia universalis (AU) of 8 years' duration. The patient experienced complete hair regrowth, including the scalp, eyebrows, and eyelashes, after 8 months of treatment.[22]

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http://dx.doi.org/10.1016/j.clindermatol.2016.05.014
0738-081X/

Narrowband UVB

NBUVB has been used in several skin diseases, including psoriasis, vitiligo, mycosis fungoides, cutaneous pruritus, and atopic dermatitis.[23–27]

Its efficacy was evaluated in a retrospective study of 25 patients with AA.[28] Initially, phototherapy was administered three times weekly at a dose of 200 mJ/cm^2 in skin phototypes II and at 300 mJ/cm^2 in skin phototypes III. Treatment continued with a dose increase of 20% in each session up to a maximum of 1800 mJ/cm^2. Once acceptable results were obtained, the dose and frequency of treatment was gradually reduced.

These 25 patients with advanced alopecia were divided into two groups: 15 patients with patchy AA and the other 10 patients with AT/AU. Four patients (22.2%) with extensive AA and two (20%) with AT/AU had excellent hair growth. Four of these six patients additionally received a monthly intramuscular injection of corticosteroids; however, it was not clear whether they belonged to the extensive AA or to the AT/AU group. Three patients had a good response to phototherapy, one of whom received treatment with corticosteroids. Four patients had a moderate response, two received only phototherapy, and two received combined therapy. Twelve patients had poor hair regrowth, including one receiving monthly corticosteroids. The average number of sessions was 46 with a cumulative dose of 63.9 J/cm^2. From these results, the authors concluded that NBUVB was not effective for severe AA. The authors of this contribution selected a group of patients with severe disseminated AA and AU who were recalcitrant to previous treatments. The drawback of this study is that it was retrospective and included concomitant administration of monthly intramuscular corticosteroids in some patients, making it difficult for evaluation.

Another report[29] from Glasgow, Scotland, evaluated the efficacy of NBUVB in various dermatoses in children (<16 years), including six with AA. Phototherapy was applied only on affected areas for an average of 20 sessions, and in most patients there was a dose increase of 20% at every session. Five of the six patients (83%) showed no improvement. Two patients had regrowth at the end of treatment but could not maintain it for more than 2 to 3 months. The drawback is that phototherapy was administrated on 77 patients with various skin diseases, of whom only six had AA. A defined methodology for the administration and assessment of clinical response to NBUVB in AA was not described, nor were details on its administration. No prospective studies of NBUVB were found in the literature reviewed.

Topical PUVA

The efficacy of topical PUVA for AA was evaluated in 149 patients using a toxic dose of UVA.[30] Multiple patches of alopecia were found in 124, and 25 had AT or AU. All patients reported a history of resistance to topical corticosteroids, minoxidil, or dinitrochlorobenzene and cryotherapy. A solution of 8-methoxypsoralen at 0.1% was administered on the alopecic areas of the scalp 20 minutes before UVA radiation. UVA dose was based on the patient's skin phototype (6-20 J/cm^2, average 12 J/cm^2). The dose given was between two and five times the minimal erythema dose. Avoidance of sun exposure for 3 days was recommended. The treatment was administered once every 3 months until terminal hair appeared.

In patients with AT (n = 25), 14 (56%) had a good (>50% hair growth) response. Two patients developed this response after a single session, eight after three sessions, three after four sessions, and one after six. The remaining 11 patients (44%) received four to seven sessions, but only nonterminal hair was detected. The mean number of sessions was three and the mean total UVA dose was 42 J/cm^2.

In the AA group (124 cases), five (4%) did not have hair growth, 14 (11%) had partial growth of white hair that subsequently disappeared, and 105 (85%) had good to excellent hair growth. Of these 105 patients, 86 developed regrowth after one session (9-18 J/cm^2), 12 required two sessions (16-34 J/cm^2), and seven patients needed three sessions (24-54 J/cm^2). In the AA group, the mean administered dose was 15 J/cm^2. The side effects detected were slight erythema in the next few days, and a burning sensation in 11 patients. Only one patient had a bullous reaction.

Patients with alopecia totalis presented hair regrowth 6 to 8 weeks after the last UVA irradiation. Clinical control was continued 2 years after treatment. Three patients had a partial relapse after 10, 14, and 17 months, respectively. Regrowth was obtained in one patient after two courses of treatment. The remaining cases presented regrowth after the application of 8-methoxypsoralen and sunlight exposure during 1 month. Regarding treated cases of AA, five cases presented recurrence of hair loss after a period of 10 months to 2 years of treatment. Complete regrowth occurred after a second course of treatment or after sunlight exposure 12 to 16 hours after 8-methoxypsoralen application.

The authors consider that phototherapy with a topical and phototoxic dose of PUVA given every 3 months could represent an alternative in the management of AA, AT, and AU. None of the patients had a previous therapeutic response to corticosteroids, minoxidil, dinitrochlorobenzene, and cryotherapy, but the possibility of spontaneous hair growth must still be considered.

This study did not specify the treatments used before the study or the precise operative definition of resistant AA. Still, the results are interesting and should be ratified in prospective controlled studies in patients with AA recalcitrant to first-line treatments.

In a prospective study, 35 patients with AA (age range 13-52 years) who were recalcitrant to treatment with topical and/or systemic therapy at least 6 months before their inclusion in the protocol[31] were treated with a phototoxic dose of UVA 20 minutes after topical application of a 0.1% solution of 8-methoxypsoralen. The wavelength was 315 to 400 nm with an initial dose of 6 J/cm^2 every 3 months, increasing 1 J/cm^2