Current Treatments for Alopecia Areata

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Selection of a therapy for a patient with alopecia areata (AA) is frequently based on the age of the patient, disease extent, perhaps disease duration, patient expectations, cost of therapy in terms of time commitment, and financial resources, as well as the results of screening laboratory studies that rule out the presence of other co-morbidities such as anemia, low iron stores, thyroid abnormalities, low vitamin D, or other autoimmune diseases. Although there is currently no cure for AA and no universally proven therapy that induces and sustains remission, many therapies are available which can be of benefit to both affected children and adults. Before selecting a treatment for patients with extensive long-standing AA, a scalp biopsy may provide useful information about the degree of inflammation and follicle differentiation. Recent clinical and translational research observations with the systemic Janus kinase (JAK) inhibitors and interleukin-2 (IL-2) have excited the clinical and AA patient communities and have led to clinical trials, as well as to the off-label use of these more expensive and targeted systemic therapies.

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CURRENT TREATMENTS

Most physicians generally prefer topical therapy for AA but current treatment of patchy and extensive AA can include many modalities as summarized in Tables 1 and 2, respectively (Delmere *et al.*, 2008; Hordinsky, 2011; Castela *et al.*, 2014; Craiglow and King, 2014; Xing *et al.*, 2014). However, in a recent analysis of the biomedical literature database, PubMed using the terms ''randomized controlled trials'' and ''alopecia areata'' only 29 trials, which strictly met these criteria were found. These studies and treatments (Table 3) were reviewed and analyzed using the American College of Physicians guideline grading system (Hordinsky and Donati, 2014). The assessment was that the majority of these studies were only of moderate quality. At the same time, a number of treatments were found to be effective, e.g., topical and oral corticosteroids and the sensitizing agents diphenylcyclopropenone (DPCP) and dinitrochlorobenzene. Most studies though had major limitations that hindered the interpretation of study results. Until robust clinical research studies are completed, there will be ongoing debate regarding established therapies, as well as the risks and benefits, cost, and sustainability of new approaches. This is particularly true in the case of children with AA where there has been very little clinical research.

TREATMENT OF AA IN CHILDREN WITH THERAPIES COMMONLY USED IN ADULTS: TOPICAL, INTRALESIONAL (IL), ORAL, OR INTRAVENOUS STEROIDS, TOPICAL MINOXIDIL, LIGHT AND IMMUNOTHERAPY

Issues with the current pediatric literature for AA are that few studies are controlled and there is no way to prove that treatment is better than placebo/natural course of the disease. Moreover, measuring outcomes is not standardized and often not detailed and many studies include no follow-up. As with adults, topical steroids are often the first-line approach for limited patchy AA. Lenane *et al.* (2014) demonstrated that higher potency topical steroids might be most beneficial for pediatric AA patients. Clobetasol propionate 0.05% cream and hydrocortisone 1% cream were compared in 42 patients and the investigators found that the clobetasol group had a statistically significant greater amount of regrowth after 24 weeks. A 2004 case series also showed better responses to high-potency steroids. Of 4 patients, 2 were treated with clobetasol and both had complete resolution after about 9 months. Despite widespread use, there still is not much more data in children with AA.

The use of intralesional (IL) steroids is a mainstay of therapy of AA for adults, although the concentration and total dose to be safely delivered continue to be debated. In children, the use of IL steroids is more limited most likely because of fear of injections and pain. There is data though from a 2002 chart review from Singapore which showed that 160/248 (65%) of children had >50% improvement after 12 weeks, 211/248 (85%) with >50% improvement after 24 weeks; however, 32 stopped injections because of pain (Tan *et al.*, 2002). There are also no good studies in children on the use of oral corticosteroids. Interestingly, both trials and chart reviews have been published on the administration of high-dose pulse methylprednisolone in children with the key points being that this approach may be useful in acute crises of hair loss but is associated with a high relapse rate and need for careful monitoring (Kiesch *et al.*, 1997; Sharma and Muralidhar 1998; Hubiche *et al.*, 2008).

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Abbreviations: AA, Alopecia Areata; DPCP, diphenylcyclopropenone; IL, intralesional; JAK kinase, Janus kinase family protein tyrosine kinase

Table 1. Common treatments for patchy alopecia areata

Topical or intralesional corticosteroids
Minoxidil solution: 2% or 5%
Anthralin
Combination therapy
Steroids in shampoo formulations
Topical immunotherapy

Table 2. Treatments for extensive alopecia areata

Corticosteroids
Topical
Intralesional
Pulsed methylprednisolone
Oral
Topical minoxidil
Topical immunotherapy
DPCP
SADBE
Anthralin
Phototherapy
Psoralen plus UVA light
Narrow-band UVB light
Laser therapy—excimer laser/fractional photothermolysis laser
Photodynamic therapy
Immunosuppresive agents
Methotrexate
Cyclosporine
Prostaglandin analogues
Biologics
JAK inhibitors
Combination therapy

Abbreviations: DPCP, diphenylcyclopropenone; SADBE, squaric acid dibutylester.

Table 3. Randomized, controlled studies on the treatment of alopecia areata

Anthralin
Antidepressants
Biologics
Calcineurin inhibitors
Corticosteroids (topical and systemic)
Minoxidil
Prostaglandin analogs
Sensitizers
Miscellaneous: topical and oral drugs (including aromatherapy, photodynamic therapy, azelaic acid, garlic gel, bexarotene, triiodothyronine, inosiplex, and total glucosides of paeony)

As with adults, topical immunotherapy may benefit children with chronic and extensive AA but requires frequent visits, may be more difficult for children to tolerate and at this time, there is no Food and Drug Administration (FDA) formulation approved for use in the USA (Hull *et al.*, 1991; Salsberg and Donovan, 2012). Topical minoxidil is used in children to enhance anagen differentiation but noteworthy is that there are no pediatric trials or chart reviews; only case reports are available for review.

HOLISTIC MANAGEMENT OF PEDIATRIC AND ADULT AA

Management of childhood AA is complicated by the child's psychosocial well-being, as well as parental anxiety, frustration, guilt, and expectations. In some cases, no treatment may be an option for both children and adults.

FUTURE

Numerous treatments are available for adults and children with AA but most studies supporting use of these treatments in children have been completed in adults. More research needs to be done for pediatric AA using the Alopecia Areata Investigational Guidelines (both on novel new treatments and established adult treatments) with detailed outcome measurements along with follow-up data (Olsen *et al.*, 1999). The new clinical and translational research observations and clinical trials with the Jak inhibitors and IL-2 have excited the clinical and AA patient communities and all look forward to moving from the trials and off-label use to focused use of these medications either orally, systemically, or topically in a coordinated, cost effective, safe manner in both children and adults.

CONFLICT OF INTEREST

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REFERENCES

Castela E, Le Duff F, Butori C *et al.* (2014) Effects of low-dose recombinant interleukin 2 to promote T-regulatory cells in alopecia areata. *JAMA Dermatol* 150:748–51

Craiglow B, King BA (2014) Killing two birds with one stone: oral tofacitinib reverses alopecia universalis in a patient with plaque psoriasis. *J Investig Dermatol Symp Proc* 134:2988–90

Delmere FM, Sladden MJ, Dobbins HM *et al.* (2008) Interventions for alopecia areata. *Cochrane Database of Syst Rev* 2:CDO 04413

Hordinsky M (2011) Treatment of alopecia areata. ''What is new on the horizon?'' *Dermatol Ther* 24:364–8

Hordinsky M, Donati A (2014) Alopecia areata: an evidence-based treatment update. *Am J Clin Dermatol* 15:231–45

Hubiche T, Léauté-Labrèze C, Taïeb A *et al.* (2008) Poor long term outcome of severe alopecia areata in children treated with high dose pulse corticosteroid therapy. *Br J Dermatol* 158:1136–7

Hull SM, Pepall L, Cunliffe WJ (1991) Alopecia areata in children: response to treatment with diphencyprone. *Br J Dermatol* 125:164–8

Kiesch N, Stene JJ, Goens J *et al.* (1997) Pulse steroid therapy for children's severe alopecia areata? *Dermatology* 194:395–7

Lenane P, Macarthur C, Parkin PC *et al.* (2014) Clobetasol propionate, 0.05%, vs hydrocortisone, 1%, for alopecia areata in children: a randomized clinical trial. *JAMA Dermatol* 201:47–50

Olsen E, Hordinsky M, McDonald-Hull S *et al.* (1999) Alopecia areata investigational assessment guidelines. National Alopecia Areata Foundation. *J Am Acad Dermatol* 40:242–6

Salsberg JM, Donovan J (2012) The safety and efficacy of diphencyprone for the treatment of alopecia areata in children. *Arch Dermatol* 148: 1084–5

Sharma VK, Muralidhar S (1998) Treatment of widespread alopecia areata in young patients with monthly oral corticosteroid pulse. *Pediatr Dermatol* 15:313–7

Tan E, Tay YK, Giam YC (2002) A clinical study of childhood alopecia areata in Singapore. *Pediatr Dermatol* 19:298–301

Xing L, Dai Z, Jabbari A *et al.* (2014) Alopecia areata is driven by cytotoxicT lymphocytes and is reversed by JAK inhibition. *Nat Med* 20:1043–5