Clinical Efficacy of Diphenylcyclopropenone in Alopecia Areata: Retrospective Data Analysis of 50 Patients

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Diphenylcyclopropenone (DPCP) is widely considered the most effective topical immunotherapy for refractory or extensive alopecia areata (AA), but questions regarding how long to try DPCP therapy before terminating and what factors are prognostic of therapeutic success still remain unanswered. In this retrospective study of 50 AA patients, we evaluated DPCP efficacy and identified patient factors predictive of therapeutic success/failure. The median duration of DPCP treatment was 3 years, with 47% patients experiencing their first regrowth in the first 6 months of DPCP therapy, 20% between 6 months–1 year, and 8% between 1–2 years. In our study, treatment success, defined as $\geqslant$50% terminal hair regrowth, was reached in 71% of alopecia totalis patients and in 56% of alopecia universalis patients. Three factors were statistically significant predictors of poor treatment outcome—extent of hair loss before DPCP treatment, history of thyroid disease, and extent of body hair involvement. Relapse was observed in 44% of patients and significantly associated with history of thyroid disease. Common side effects were itching, rash, and local lymphadenopathy. The results of this study support our belief that DPCP therapy is a viable treatment option, can be successfully accomplished at home, and should not be terminated before 2 years.

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INTRODUCTION

Alopecia areata (AA) is a non-scarring type of hair loss that affects both genders and all ethnicities. Calculated lifetime risk is ~2% of the population (Alkhalifah, 2013). The characteristic lesions are well-defined smooth round bald patches on the scalp or any other hair-bearing area of the body. This patchy pattern of hair loss may present at any age, but up to 66% of patients present before 30 years of age (Gilhar *et al.*, 2012). In some patients, AA can progress to alopecia totalis (total loss of scalp hair) or to alopecia universalis (total loss of all scalp and body hair).

The exact pathophysiology of AA remains poorly understood. Current evidence suggests that AA is an autoimmune disease with a genetic predisposition and an environmental trigger. A family history has been noted in 10–42% of cases, and triggers like emotional stress and trauma have also been correlated (de Andrade *et al.*, 1999). AA is associated with more than 20 HLA class I and class II alleles, as well as an increased overall risk for other autoimmune disorders like diabetes mellitus type 1, systemic lupus erythematous, and autoimmune thyroid disease (Alzolibani, 2011).

AA most commonly presents as minor patchy hair loss and usually resolves spontaneously. In ~7% of cases, alopecia area will evolve into a severe and chronic hair loss (Safavi *et al.*, 1995). Studies have shown that AA can cause devastating emotional distress in patients. Therefore, treatments, though optional, offer psychological support to foster increased self-esteem (Tucker, 2009). No cure or preventive treatment for AA has been established, and current treatments are directed towards halting disease activity. Corticosteroid (topical, local injections, and systemic) are the most popular and efficacious treatments for AA, but long-term application often leads to skin atrophy. Therefore therapies like topical immunotherapy, phototherapy, minoxidil, and anthralin are also being used. Topical immunotherapy is the best documented treatment for severe or refractory AA (Singh *et al.*, 2007).

Three topical sensitizers have been used in topical immunotherapy treatment for AA. Dinitrochlorobenzene was first to be used, but has been discontinued because of its possible mutagenicity. Squaric acid dibutylester and diphenylcyclopropenone (DPCP) are the two compounds still in use today. DPCP is considered as the most effective topical immunotherapy for AA treatment and is currently the preferred topical sensitizer owing to its low cost, stability in solution, and non-mutagenic properties. It has been in use since 1983. The exact

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Abbreviations: AA, alopecia areata; DPCP, Diphenylcyclopropenone

mechanism of action of DPCP is poorly understood, but it may include antigenic competition and decreased production of anti-hair-follicle antibodies (Tobin *et al.*, 2002). Regrowth rates observed with DPCP range from 33 to 83%, averaging at 50% (Cotellessa *et al.*, 2001; Aghaei, 2005; Avgerinou *et al.*, 2008). The repetitive application of DPCP induces an allergic contact dermatitis. Side effects of DPCP include persistent dermatitis, blistering, spread of contact eczema, lymph node enlargement, pigment changes, and secondary infection.

In this study we aimed to evaluate the clinical efficacy, tolerability, and prognostic factors of DPCP therapy to identify patient and treatment factors predictive of therapeutic success.

RESULTS

The demographic and clinical data are depicted in Table 1. The study included 50 subjects with AA. All patients had undergone prior treatments for AA including intralesional steroids (82% of patients), topical steroids (64%), topical minoxidil (46%), and oral steroids (44%). After sensitization with 2% DPCP solution, 1 of the 50 patients failed to develop erythema or mild eczematous response to DPCP and was classified as anergic. This patient was excluded and 49 patients were available for the final analysis.

None of the patients discontinued DPCP therapy because of adverse effects, but side effects were reported by 23 patients (47%). Ten patients (20%) experienced lymph node swelling, 11 experienced blistering (22%), 11 experienced spreading of contact eczema (22%), and 11 experienced severe itching (22%). Of the patients who experienced side effects, the majority experienced at least two. Two patients (4%) experienced all four side effects.

In our study, the duration of DPCP treatment ranged from 6 months to 15 years, with a median of 3 years. The first clinical evidence of hair regrowth was detected at a median duration of 5 months after the onset of DPCP therapy (range: 1–46 months). Those who experienced more than 50% regrowth saw regrowth after an average of 7 months whereas those who had minimal response experienced their first regrowth after an average of 14 months. Statistical analysis did not establish significant association between the time to first regrowth and treatment outcome ($P = 0.063$).

The initial concentration of DPCP used post-sensitization ranged from 0.0001 to 1% with a median of 0.001%. The first detectable eczematous scalp reaction was elicited at a median concentration of 0.01% (range 0.0001–1%). The first detectable terminal hair regrowth was elicited at a median concentration of 0.001% (range 0.000001–0.0.1%). The highest concentration of DPCP used ranged from 0.001 to 7% with a median of 0.1%.

Treatment success ($\geqslant$50% terminal hair regrowth) was reached in 66% of cases. Nineteen patients (39%) achieved complete regrowth (>90% terminal hair), 13 patients (27%) had partial regrowth (50–90% terminal hair), 7 patients (14%) had minimal regrowth (<50% terminal hair), and 11 patients (22%) had no regrowth (0–10% terminal hair). Statistical analysis established a significant association between the extent of hair loss before DPCP treatment and treatment outcome ($P = 0.020$, odds ratio = 3.34). This suggests that the odds of achieving at least 50% terminal hair regrowth was 3 times more likely in those with severe loss (50–74%) than in those with total loss (75–100%) and about 3 times more likely in those with moderate loss (25–49%) than in those with severe loss (50–74%). In this study, $\geqslant$50% terminal hair regrowth was achieved in 52% of those with total hair

Table 1. Demographic and clinical data[1]

Demographic data	
Number of patients	50
Anergic patients (not assessed in the further analysis)	1
Gender (M/F)	14 (28)/36 (72)
Race	
Caucasian	46 (92)
Black	3 (6)
Asian	1 (2)
Age at disease onset (years)	
Median	21
Range	3–59
Age of beginning of therapy (years)	
Median	37.5
Range	10–61
Disease duration before treatment (years)	
Median	5
Range	2 months–45 years
Clinical data	
Type of alopecia areata	
Patchy	9 (18)
Totalis	14 (29)
Universalis	25 (51)
Ophiasis	1 (2)
Extent of scalp hair loss	
Total (75–100%)	25 (51)
Severe (50–74%)	15 (31)
Moderate (25–49%)	8 (16)
Mild (0–24%)	1 (2)
Comorbidities	
Thyroid dysfunction	25 (51)
Atopy	27 (55)
Anemia	14 (29)
PCOS	3 (6)
Nail changes	10 (20)
Body hair involvement	35 (71)
Positive family history	
Alopecia areata	11 (22)
Autoimmune disease	31 (63)

Abbreviation: PCOS, polycystic ovary syndrome.
[1]Values in parentheses are expressed as percentages.