Diphenylcyclopropenone Treatment Outcomes for Alopecia Areata

Supenya Varothai, M.D., Rattapon Thuangtong, M.D., Daranee Sonmek, B.N.S., Thanawan Iamphonrat, M.D.

Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

ABSTRACT

Objective: To ascertain (1) Diphenylcyclopropenone (DCP)'s efficacy in treating alopecia areata (AA), alopecia totalis (AT), and alopecia universalis (AU) in Thai patients; and (2) prognostic factors.

Materials and Methods: We retrospectively reviewed the medical records of patients with AA, AT, and AU who were administered DCP at Siriraj Hospital, Bangkok, Thailand. The median response and relapse times of the 3 groups were evaluated. Factors affecting outcomes were investigated.

Results: Fifty-nine cases were enrolled (AA, 22; AT, 9; AU, 28), with women predominating in each group. The overall response was 61% (AA, 78.6%; AT, 66.7%; AU, 50%). The median response time was 58 weeks, with a significantly longer time for AU than AA ($P = 0.006$). Factors significantly influencing response to DCP, evaluated by multivariate analysis, were older age at onset ($P = 0.02$), disease duration before DCP initiation ($P = 0.003$), and treatment duration to initial hair regrowth ($P = 0.001$). The overall relapse rate was 63.9%, with a median of 39 weeks between response and relapse. The most common side effect was blistering (73.7%).

Conclusion: DCP is effective and safe for treating extensive AA. Favorable prognostic factors are low disease severity, late disease onset, short duration before DCP treatment, and short duration to initial response. As the relapse rate is high, maintenance therapy should be considered.

Keywords: Alopecia areata; Diphenylcyclopropenone; Diphencyprone; DCP; DPCP; Topical immunotherapy; Prognosis (Siriraj Med J 2023; 75: 121-131)

INTRODUCTION

Alopecia areata (AA) is an autoimmune disorder affecting hair follicles. There are several types of nonscarring alopecia, consisting of a focal area of patchy hair loss (patchy AA), complete scalp hair loss (alopecia totalis, AT), and entire scalp hair with body hair loss (alopecia universalis, AU). While limited forms of the disease may recover spontaneously or respond well to intralesional corticosteroid therapy, the extensive forms (AT, AU) often resist treatment modalities. Topical immunotherapy is the most effective therapeutic option with the best safety profile for treating severe, chronic AA. The mechanism of action of topical immunotherapy is inconclusive. It is supposed that contact sensitizers induce a new population of inflammatory cells. These cells have an inhibitory effect on the preexisting autoimmune reaction of hair, which promotes the regrowth of hair.

Three contact sensitizers have been used exclusively to treat AA: dinitrochlorobenzene, squaric acid dibutyl ester, and diphenylcyclopropenone (DCP). In our hair clinic, due to the mutagenic effects of dinitrochlorobenzene and the instability of squaric acid dibutyl ester, we use DCP as the standard treatment for AT, AU, and recalcitrant cases of extensive AA. "Recalcitrant cases of extensive AA" are defined as the presence of either more than a 30% loss of scalp hair or the ophiasis type of AA ("ophiasis AA") and failure of intralesional corticosteroid therapy. The application method was adopted from the standard

Corresponding author: Supenya Varothai
E-mail: supenya_var@gmail.com
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ORCID ID:http://orcid.org/0000-0002-3740-0425
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protocol described previously.[1] Unlike the unilateral application of the original regimen, we painted DCP on all of the affected areas. The literature[2] has reported that the efficacy of DCP varies widely, from 5% to 85%, and the published evidence for prognostic factors (especially in Asians) is limited. In addition, the application of DCP is time-consuming. It is therefore essential to have certainty of treatment outcomes and prognostic factors. Treatment can be adjusted with that knowledge, and patients can be adequately advised.

The primary purpose of this study was to ascertain the efficacy of DCP treatment for patients with AA, AT, and AU. The secondary objectives were (1) to determine the side effects and relapse rate of the therapy and (2) to identify factors influencing its outcomes.

MATERIALS AND METHODS

We retrospectively reviewed the medical records of patients diagnosed with AA, AT, and AU who initiated DCP treatment at the Hair Clinic of the Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, between January 1999 and July 2007. Before this research began, its protocol was approved by the Siriraj Institutional Review Board, Siriraj Hospital, Mahidol University, Bangkok, Thailand, in August 2011. Patients who received treatment for at least 6 months were included, and the data were continuously recorded for up to 2 years. Patients were excluded if they were lost to follow-up for more than 3 months.

Demographic data were recorded. Personal data (history of atopy, vitiligo, autoimmune thyroid diseases, and family history of AA) were reviewed. Details of the following were collected:

1. The course and degree of hair loss
2. Age at onset
3. Previous treatment modalities
4. Disease duration when treatment began
5. Treatment duration to a proper eczematous reaction
6. Duration and DCP concentration for the initial response.

The number of treatments corresponded to the duration of therapy as the treatment protocol required DCP to be applied weekly. Details of examinations of the area of involvement, nail changes, and general skin were evaluated.

The patients were classified into 4 groups based on disease severity: AA, AT, AU, and ophiasis AA (the recalcitrant form of AA). All cases were also classified as "responder" or "nonresponder." "Responders" were patients who achieved cosmetically acceptable hair regrowth of more than 75% of the affected area. Consentaneously, all reviewed cases were assessed under two board-certified dermatologists (SV and RT) with united approval. Further investigations were conducted on the duration needed to achieve a response and the time to relapse for the responders. Factors associated with the responders were also investigated.

Statistical analysis

Descriptive statistics were applied to demographic and personal data and treatment history. Kaplan–Meier survival analysis was used to calculate the median response and median relapse times. Univariate and multivariate analyses were used to determine factors affecting treatment. To this end, the following were considered using Kaplan–Meier and Cox regression: sex, presence of atopy, previous treatment modalities, age at onset, severity of scalp involvement, nail involvement, duration of hair loss before DCP application, duration of treatment to reach proper eczematous reaction, duration of treatment to obtain initial hair regrowth, and concomitant treatment.

RESULTS

Demographic data

A summary of the demographic data is presented in Tables 1 and 2. Data were collected from 59 patients; most (50) were women. After classifying the severity of scalp involvement as AA, AT, AU, and ophiasis AA, AU was found most frequently (47.5%), followed by AA (23.7%), AT (15.3%), and ophiasis AA (13.6%). According to the medical records, none had a positive family history of AA. Seven patients had a history of atopy, and approximately half had AU. Two patients had vitiligo, and both were classified as having ophiasis AA. According to their histories, thyroid function tests, or thyroid antibody tests, no patients had autoimmune thyroiditis. Approximately 60% of the cases had nail abnormalities in the form of nail pits.

Most of the patients had previously received other treatments, and 2 had undergone DCP treatment prior to the episode studied. The age at onset of the disease ranged from 3.8 to 68.8 years (median = 26.6), and the age at the initiation of DCP treatment ranged from 11.9 to 63.4 years (median = 29.4). The duration from disease onset to initiation of DCP treatment was 0.1 to 19.9 years (median = 2.3). Generally, there were no statistically significant differences in the demographic data of the 4 clinical groups. One exception was a history of previous intralesional steroid injections ($P = 0.01$). The other was the age at initial DCP treatment of the AU group; it was significantly younger than that of the ophiasis AA group ($P = 0.02$).

TABLE 1. Demographic data.

Factors	Groups; number (%)					*P* value
	Total	AA	AT	AU	Ophiasis AA	
	59 (100.0)	14 (23.7)	9 (15.3)	28 (47.5)	8 (13.6)	
Female	50 (84.7)	11 (22.0)	7 (14.0)	25 (50.0)	7 (14.0)	0.74
Family history of AA	0	0	0	0	0	-
A history of atopy	7 (11.9)	0	2 (28.6)	4 (57.1)	1 (14.3)	-
Vitiligo	2 (3.4)	0	0	0	2 (100.0)	-
Autoimmune thyroiditis	0	0	0	0	0	-
Pitting nail	11 (57.9)	1 (9.1)	3 (27.3)	6 (54.5)	1 (9.1)	0.49
Previous IL steroids	21 (35.6)	7 (33.3)	6 (28.6)	4 (19.0)	4 (19.0)	0.01*
Previous topical steroids	31 (52.5)	8 (25.8)	5 (16.1)	14 (45.2)	4 (12.9)	0.98
Previous oral steroids	27 (45.8)	9 (33.3)	4 (14.8)	12 (44.4)	2 (7.4)	0.35
Previous IM steroids	29 (49.2)	5 (17.2)	5 (17.2)	16 (55.2)	3 (10.3)	0.54
Previous topical minoxidil	12 (20.3)	1 (8.3)	1 (8.3)	8 (66.7)	2 (16.7)	0.42
Previous DCP	2 (3.4)	0	0	2 (100.0)	0	0.78
Median age of onset (min, max; years)	26.6 (3.8,62.8)	26.3 (8.1,62.8)	27 (14.7,35.5)	24.7 (3.8,44.4)	42.9 (9.0,54.7)	0.08
Median age at initial DCP treatment (min, max; years)	29.4 (11.9,63.4)	28.7 (14.0,63.4)	31.5 (18.5,35.8)	27.2 (11.9,47.2)	46.4 (19.3,62.1)[3]	0.02*
Median duration from onset to initial DCP treatment (min, max; years)	2.3 (0.1,19.9)	0.9 (0.1,19.9)	2.4 (0.4,13.6)	2.7 (0.2,13.5)	4.2 (0.2,13.9)	0.39

* $P < 0.05$ was statistically significant.

Abbreviations: AA, alopecia areata; AT, alopecia totalis; AU, alopecia universalis; DCP, diphenylcyclopropenone; IL, intralesional; IM, intramuscular

Notes: 1: Statistically significant compared with AA
2: Statistically significant compared with AT
3: Statistically significant compared with AU
4: Statistically significant compared with ophiasis AA

Treatment data

A "proper eczematous reaction" was defined as at least 2 days of eczematous reaction. The duration of treatment to reach a proper eczematous reaction varied from 1 to 50.6 weeks (median = 5 weeks). The median time to achieve a proper eczematous reaction was the shortest for patients with AU (3.3 weeks), followed by AT (5 weeks) and AA (6.9 weeks). It was the longest for patients with ophiasis AA (7.4 weeks). There were no statistically significant differences between the groups (P = 0.48). The median DCP concentration at the proper eczematous reaction was 0.001% for all groups.

The treatment duration needed to obtain initial hair regrowth ranged from 4 to 70.1 weeks (median = 11 weeks). The median durations for AA, AT, AU, and ophiasis AA were 8, 10.1, 14.1, and 22.5 weeks, respectively. The duration of treatment required to obtain initial hair regrowth for the AA group was significantly shorter than that for the ophiasis AA group (P = 0.03). The maximum DCP concentration was 1% for the AT and AU groups, but it was lower for the AA and ophiasis AA groups (0.5% and 0.35%, respectively). However, there were no significant differences among the 4 groups (P = 0.06). Almost all patients did not receive any other treatment

TABLE 2. Treatment data.

Factors	Groups; number (%)					*P* value
	Total	AA	AT	AU	Ophiasis AA	
	59 (100)	14 (23.7)	9 (15.3)	28 (47.5)	8 (13.6)	
Median duration of treatment to first eczema (min, max; weeks)	5 (1.0,50.6)	6.9 (1.0,10.0)	5 (1.1,19.9)	3.3 (1.0,50.6)	7.4 (1.0,29.6)	0.48
Median DCP concentration at first eczema (min, max)	0.001 (0.00001,1.0)	0.001 (0.00010,0.35)	0.001 (0.00001,0.1)	0.001 (0.00001,1.0)	0.00055 (0.0001,0.35)	0.41
Median duration of treatment to initial hair regrowth (min, max; weeks)	11 (4.0,70.1)	8 (4.0,50.7)	10.1 (6.1,21.9)	14.1 (5.0,64.3)	22.5 (9.9,70.1)[1]	0.03*
Median Maximum DCP concentration	1 (0.001,2.0)	0.5 (0.001,2.0)	1 (0.01,1.5)	1 (0.01,2.0)	0.35 (0.001,1.0)	0.06
Median DCP concentration at cosmetic hair regrowth (min, max)	0.1 (0.0001,2.0)	0.1 (0.0001,1.5)	0.1 (0.0001,1)	0.1 (0.0001,2.0)	0.1 (0.001,0.5)	0.85

* $P < 0.05$ was statistically significant.

Abbreviations: AA, alopecia areata; AT, alopecia totalis; AU, alopecia universalis; DCP, diphenylcyclopropenone

Notes: 1: Statistically significant compared with AA
2: Statistically significant compared with AT
3: Statistically significant compared with AU
4: Statistically significant compared with ophiasis AA

modality during DCP treatment. The exceptions were 7 patients (11.9%) who received topical minoxidil (Table 2).

Response to treatment

As mentioned above, the "response to treatment" was defined as cosmetically acceptable hair regrowth or a hair regrowth of more than 75%. Sixty-one percent of cases responded to treatment. The treatment duration to obtain a response ranged from 5 weeks to 24 months, with a median response time of 58 weeks after the initiation of treatment. In terms of disease severity, 78.6% of the AA cases responded to DCP with a 28.9-week median response time. For AT, 66.7% responded with a 52.1-week median response time. For patients with AU and ophiasis AA, 50.0% and 62.5% responded, with median response times of 93.4 and 58 weeks, respectively. The median response time of the AU group was significantly longer than that of the AA group (P = 0.006; Table 3 and Figs 1a and 1b). The DCP concentration required to achieve a treatment response was 0.1% for all groups (Table 2).

Prognostic factors

Univariate analysis—demographic data

Age at onset of alopecia and duration from disease onset until the initiation of DCP treatment had significant effects on treatment responses (P = 0.04 and 0.003, respectively). After being categorized, late-onset patients (20 years or older) had a significantly better response rate than younger patients. The duration from disease onset to the initial DCP treatment was divided into 3 groups: less than 1 year, 1 to 3 years, and more than 3 years. A shorter duration was found to be associated with better outcomes. The other demographic factors of the responders and nonresponders (sex, history of atopy, nail abnormality, and age at initial DCP treatment) did not differ significantly. The previous treatment modalities also did not generally affect the outcomes. However, an exception was that the patients who had received prior intralesional steroids were significantly more responsive to DCP than those who had not (P = 0.02; Tables 4a and 4b).

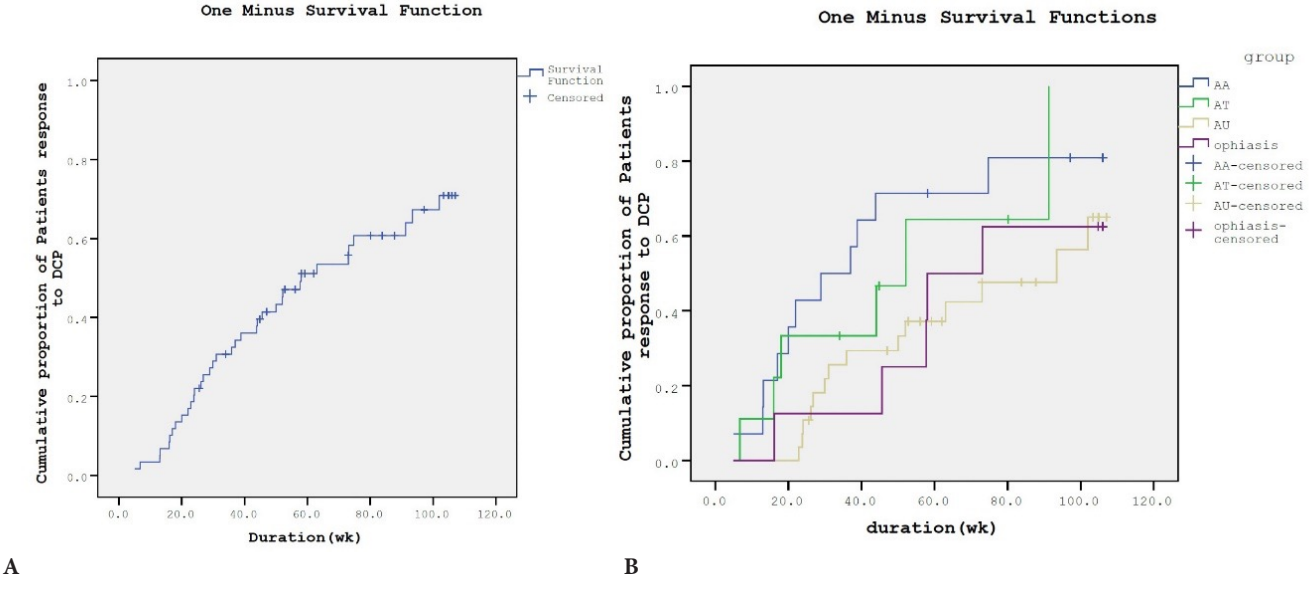
TABLE 3. Median response times.

Groups	Total N	Response N (%)	Median response time (weeks)	*P* value
Overall	59	36 (61.0)	58	0.03*
AA	14	11 (78.6)	28.9[3]	0.006*
AT	9	6 (66.7)	52.1	
AU	28	14 (50.0)	93.4	
Ophiasis AA	8	5 (62.5)	58	

* P < 0.05 was statistically significant.

Abbreviations: AA, alopecia areata; AT, alopecia totalis; AU, alopecia universalis

Notes: 1: Statistically significant compared with AA
2: Statistically significant compared with AT
3: Statistically significant compared with AU
4: Statistically significant compared with ophiasis AA



A B

Fig 1. **(A)** The overall cumulative proportions of responses. **(B)** The cumulative proportions of response, classified by disease severity.

Univariate analysis—treatment data

One factor was found to influence the treatment outcomes: the duration of treatment needed to obtain initial hair regrowth (P = 0.01). Patients who achieved initial hair regrowth before 12 weeks of treatment had significantly better outcomes (Tables 4a and 4b). The duration of treatment to reach a proper eczematous reaction did not affect the treatment outcomes. The responder and nonresponder groups also had no significant difference in their DCP concentrations at the proper eczematous response (P = 0.16, 0.19, respectively).

Multivariate analysis

Multivariate analysis was performed using Cox regression to determine the prognostic factors that independently affected treatment outcomes and to calculate the hazard ratio of each factor. Factors that significantly influenced the response to DCP were age at onset (P = 0.02), disease duration before the initial DCP treatment (P = 0.003), and treatment duration until initial hair regrowth (P = 0.001). The hazard ratio was 3.13 for patients with ages at onset of 20 or older. This finding meant that these patients responded to treatment

TABLE 4a. Univariate analysis of categorical variables.

Factors	Total	Response	Median survival time				*P* value
			Median	Standard error	95% Confidence interval Lower Bound	Upper Bound	
Sex							0.41
Female	50	29	73.0	13.5	46.5	99.5	
Male	9	7	52.0	12.1	28.2	75.8	
A history of atopy							0.54
No	11	8	52.1	22.6	7.9	96.4	
Yes	7	4	44.0	14.8	15.0	73.0	
Unknown	41	24	73.0	13.4	46.7	99.3	
Nail							0.41
Normal	8	5	50.0	17.8	15.2	84.8	
Pitting	11	5	73.1	12.2	49.2	97.0	
Unknown	40	26	52.0	8.5	35.3	68.7	
Previous intralesional steroids							0.02*
No	38	20	73.1	9.3	55.0	91.3	
Yes	21	16	38.9	10.0	19.2	58.5	
Previous topical steroids							0.19
No	28	16	74.7	11.7	51.8	97.7	
Yes	31	20	50.0	9.5	31.4	68.6	
Previous oral steroids							0.90
No	32	18	58.0	8.4	41.6	74.4	
Yes	27	18	73.0	14.9	43.7	102.3	
Previous intramuscular steroids							0.52
No	30	19	52.1	7.6	37.3	67.0	
Yes	29	17	63.0	24.1	15.7	110.3	
Previous topical minoxidil							0.52
No	47	31	57.7	8.7	40.6	74.8	
Yes**	12	5	-	-	-	-	
Previous DCP							0.26
No	57	36	57.7	8.7	40.6	74.8	
Yes**	2	0	-	-	-	-	
Concomitant minoxidil							0.40
No	52	31	58.0	13.3	31.8	84.2	
Yes	7	5	52.1	39.5	0.0	129.5	
Age at onsetγ							0.02*
< 20 years**	17	7	102.0	-	-	-	
≥ 20 years	40	27	44.0	8.9	26.5	61.5	
Duration from onset to initial DCP treatmentγ							<0.001*
< 1 year	15	14	23.9	5.1	13.9	33.8	
1–3 years	18	11	57.7	23.8	11.1	104.3	
> 3 years**	24	9	-	-	-	-	
Duration of treatment to initial hair regrowthγ							0.007*
≤ 12 weeks	30	24	38.9	5.6	27.9	49.8	
> 12 weeks	22	10	93.4	16.7	60.6	126.2	

* P < 0.05 was statistically significant.
**The number of responders were less than half the total number of patients; thus, the median survival time could not be evaluated.
γ The data for this factor were incomplete.
Abbreviation: DCP, diphenylcyclopropenone

TABLE 4b. Univariate analysis of continuous variables.

Factors	HR	95.0% CI for HR		*P* value
		Lower	Upper	
Age at onset (years)	1.03	1.00	1.06	0.04*
Age at initial DCP treatment (years)	1.01	0.99	1.04	0.30
Duration from onset to initial DCP treatment (years)	0.84	0.75	0.94	0.003*
Duration of treatment to first eczema (weeks)	0.95	0.88	1.02	0.16
Number of treatments at first eczema	0.94	0.86	1.03	0.19
DCP concentration at first eczema	0.43	0.04	5.05	0.50
Duration of treatment to initial hair regrowth (weeks)	0.97	0.95	0.99	0.02*
Number of treatments at initial hair regrowth (weeks)	0.94	0.91	0.98	0.01*

*P < 0.05 was statistically significant.
Abbreviations: DCP, diphenylcyclopropenone; HR, hazard ratio

3.13 times better than younger patients. Durations of disease before the initial DCP treatment of less than 1 year were associated with the best prognoses, while longer durations corresponded to worse outcomes. The hazard ratio was 3.81 for durations less than 1 year but 1.07 for 1 to 2 years. Finally, patients who needed less than 12 weeks to obtain initial hair regrowth responded significantly better than those who needed more than 12 weeks (hazard ratio = 4.66; Table 5 and Figs 2-4).

Side effects

Approximately 30% of the patients experienced side effects from the therapy. The most common side effect was blistering (23.7%); all other effects were uncommon (1%-4%; Table 6). Localized effects consisted of blistering and lymphadenopathy, while generalized effects were generalized eczema, angioedema, and urticaria.

Relapse

The overall relapse rate was 63.9%. In our group analysis, the relapse rate was highest for ophiasis AA (100%), followed by AT (66.7%), AU (57.6%), and AA (54.5%). The overall median relapse time was 39 weeks after achieving a response to DCP. There were no statistically significant differences in the median relapse times of the 4 groups (Table 7).

TABLE 5. Multivariate analysis.

Factors	HR	95.0% CI for HR		*P* value
		Lower	Upper	
Age at onset (years)				
< 20	1.00 (reference)			
≥ 20	3.13	1.16	8.39	0.02*
Duration from onset to initial DCP treatment (years)				
< 1	3.81	1.56	9.28	0.003*
1–2	1.07	0.43	2.68	0.89
≥ 3	1.00 (reference)			
Duration of treatment to initial hair regrowth (weeks)				
≤ 12	4.66	1.89	11.52	0.001*
> 12	1.00 (reference)			
Previous intralesional steroids				
No	1.00 (reference)			
Yes	1.38	0.65	2.96	0.40

*P < 0.05 was statistically significant.

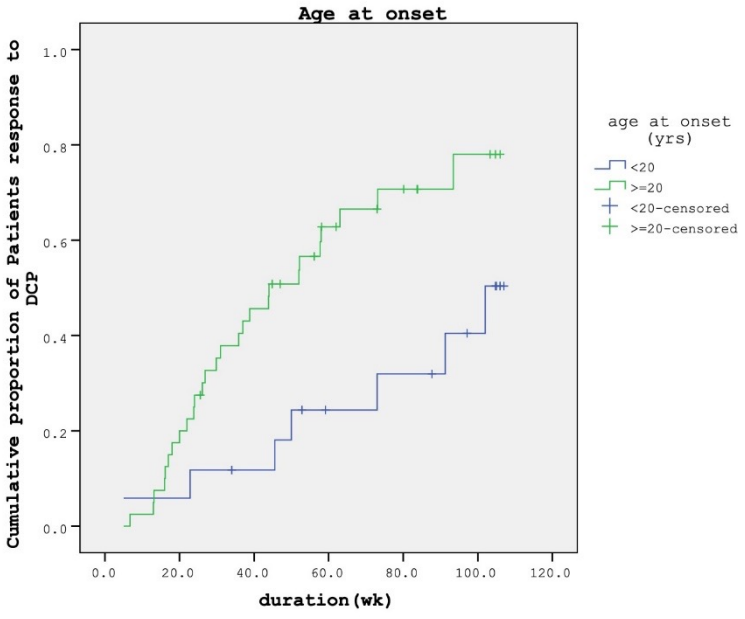


Fig 2. The cumulative proportions of response, classified by age at onset

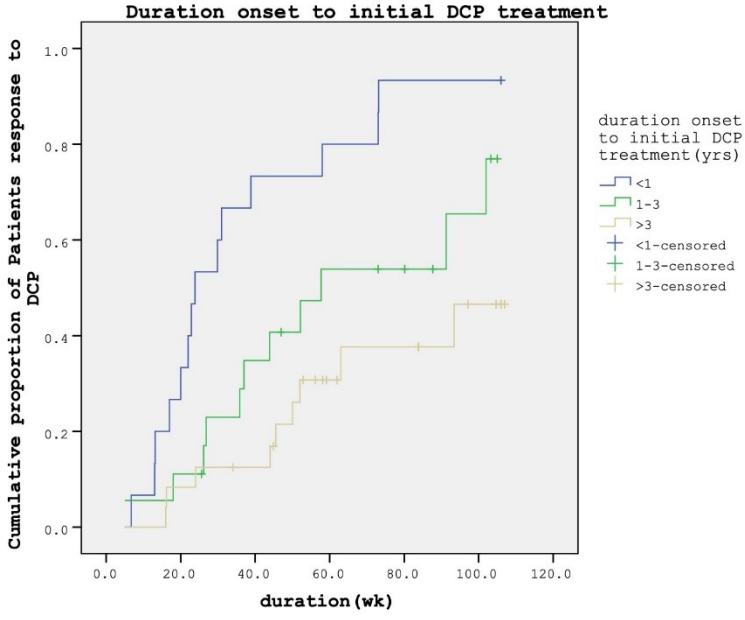


Fig 3. The cumulative proportions of response, classified by disease duration before initial DCP treatment

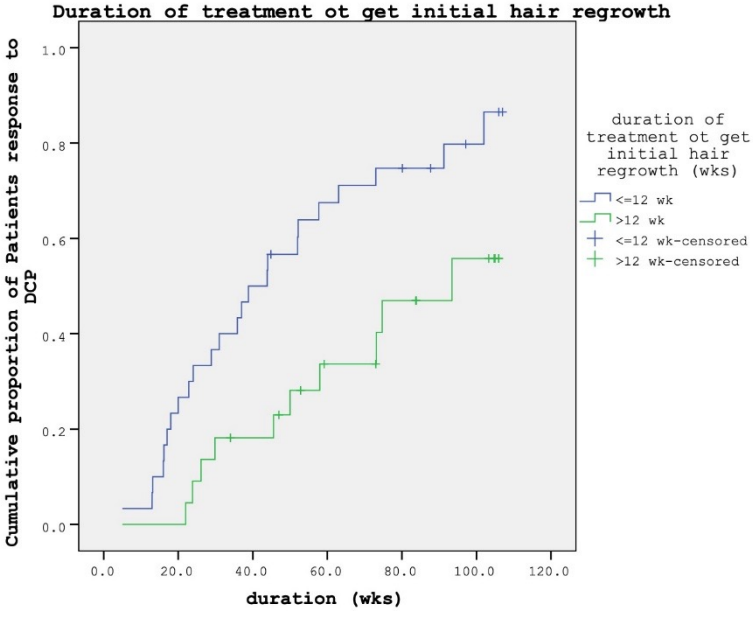


Fig 4. The cumulative proportions of response, classified by duration of treatment needed to obtain initial hair regrowth

TABLE 6. Side effects.

Side effects	Number (%)
No	40 (67.7)
Yes	19 (32.3)
Blistering	14 (23.7)
Generalized eczema	2 (3.4)
Angioedema	1 (1.7)
Lymphadenopathy	1 (1.7)
Urticaria	1 (1.7)

TABLE 7. Relapse rate.

Group	Total	Response N (%)	Median relapse time				*P* value
			Median	Standard error	95% Confidence interval Lower Bound	Upper Bound	
Overall	36	23 (63.9)	39.0	4.5	30.1	47.9	0.27
AA	11	6 (54.5)	52.0	4.1	44.0	60.0	
AT	6	4 (66.7)	30.0	14.9	0.8	59.2	
AU	14	8 (57.1)	39.7	11.2	17.8	61.6	
Ophiasis AA	5	5 (100)	29.9	10.8	8.7	51.0	

Abbreviations: AA, alopecia areata; AT, alopecia totalis; AU, alopecia universalis

DISCUSSION

The organ-specific autoimmune disease AA is associated with the activation of T lymphocytes around hair follicles. The disease causes various degrees of nonscarring alopecia and significant psychosocial problems. The underlying mechanism of DCP is not yet fully understood. However, many hypotheses explain its action, such as antigenic competition, perifollicular lymphocyte apoptosis, and peribulbar CD4/CD8 lymphocyte ratio changes. Effective treatment modalities are intralesional corticosteroids, systemic corticosteroids, and contact immunotherapy with DCP. Alkhalifah et al. reviewed the therapeutic options and found that contact immunotherapy was effective for extensive AA in an intracontrolled, half-head study.[2] At our clinic, DCP contact immunotherapy is the standard treatment for patients with AT, AU, and recalcitrant extensive AA (more than a 30% loss of scalp hair) who have not responded to systemic corticosteroids for at least 12 weeks.

According to the demographic data of our study, women greatly predominated (84.7%). This finding was inconsistent with most other studies, which reported that women and men were equally susceptible to the disease.[6] The epidemiological study by Kyriakis et al. showed that women had a higher prevalence of AA than men, but only marginally (women = 53.7%; men = 46.3%).[7] Our results possibly indicate that Thai women are considerably more concerned about appearance than Thai men.

The reported efficacy of DCP has varied from 5% to 85%.[1] This extensive range may result from differences in patient demographics, the baseline extent of hair loss, treatment guidelines and protocols, the definitions of response to treatment, and the duration of the follow-up period to evaluate treatment outcomes. Consequently, we used the definition of a response given by published guidelines.[8] In our study, the overall cumulative response was 61% within 24 months of follow-up, and the median response period was 58 weeks. This overall response was

close to the rate recently reported by El-Zawahry et al. (55.7%).[9] In a group of studies with baseline extents of hair loss and response definitions similar to our work, we noted that investigations with short evaluation periods had lower response rates. Hull et al. found a 35.7% rate in research that defined a response as terminal hair with patchy AA, cosmetic acceptance, or terminal hair over the scalp at 8 months.[10] A study by Sotiriadis et al. revealed that 39.5% of patients achieved greater than 80% hair regrowth at the 6-month follow-up visit.[11]

In contrast, studies with longer evaluation durations (12-32 months) had noticeably higher treatment response rates (38%-77.9%).[9,12–15] The cumulative response also increased over time, as found by the current investigation and 2 other studies.[9,13] Therefore, we propose that a 6-month evaluation period may be too short to effectively determine the response to treatment. We also suggest that an extended duration of treatment should be used to avoid prematurely denoting patients as nonresponders. This approach would be particularly beneficial for patients with AU, who had the longest median response time in the present work.

Moreover, our analysis showed that the duration and number of treatments needed to obtain initial hair regrowth in patients with ophiasis AA were longer than those of the other patients. The duration was also statistically significantly longer than that for patients with AA. Therefore, it is essential to inform patients with ophiasis AA that they will need to be prepared to wait a minimum of 5 months after treatment before hair regrowth becomes apparent.

Some studies have investigated prognostic factors for treatment outcomes. A large prospective study by van der Steen et al. demonstrated that the type of AA before treatment, the disease duration before therapy, and the presence of nail changes were significant prognostic factors.[16] However, when these investigators performed re-evaluations at the 19-month follow-up, only the type of AA and the disease duration remained significant.[17] A study by Gordon et al. found that the presence of nail changes, a long duration of AA, and a history of atopy were adverse prognostic factors.[14] A large retrospective study by Wiseman et al. also found a positive correlation between the degree of AA and the age at onset of the disease.[13] In contrast, Avgerinou et al. did not identify any significant prognostic factors.[12]

According to the disease severity classifications used in our study, the AA group had a significantly better prognosis than the AU group. Initially, we set out to analyze the prognostic factors for each of the 4 groups. Unfortunately, the number of patients in each group was too small to allow accurate calculations. Consequently, we performed univariate and multivariate analyses to determine the overall prognostic factors. The multivariate analysis found that outcomes were significantly affected by age at onset of the disease, the duration before the initiation of DCP treatment, and the duration of treatment needed to obtain initial hair regrowth. Our results were consistent with previous studies. However, more information was obtained by the present work, especially in terms of the DCP concentration required for a proper eczematous response and the finding that the maximum concentration did not affect treatment outcomes. Furthermore, we calculated the hazard ratios of these factors to obtain more information. Earlier studies did not use this approach.

Approximately one-third of our patients suffered side effects from DCP, most of which were blistering. All cases improved after discontinuing DCP and topical steroid and oral antihistamine treatments. The other side effects were generalized eczema, angioedema, lymphadenopathy, and urticaria. Approximately 60% of the responders had relapses, with a median relapse duration of 39 weeks. We observed that relapses usually occurred when we stopped DCP treatment. The relapse rate of approximately 60% was close to those of other studies.[12,13] Ohlmeier et al. found that the relapse rate once DCP therapy was stopped was higher if DCP was not tapered. These investigators recommended that DCP should not be abruptly stopped but instead be reduced gradually to maintain remission and avoid the risk of relapse.[18] Further extensive studies should be performed to explore this aspect.

In conclusion, DCP is an effective and safe treatment modality for extensive AA, with an overall response rate of 61%. The factors associated with a good prognosis are low disease severity, older age at disease onset (20 or older), a short period from onset to initial DCP treatment, and a short duration of treatment to obtain initial hair regrowth. However, as the relapse rate is high, maintenance therapy should be considered.

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