Liquid nitrogen cryotherapy in the treatment of alopecia areata: an Egyptian study

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Introduction
Alopecia areata (AA) is a common cause of nonscarring alopecia that occurs in a patchy, confluent or diffuse pattern. It may involve loss of hair from some or all areas of the body, usually from the scalp. The aim of this study was to evaluate the effect of cryotherapy in the treatment of AA.

Patients and methods
Through a nonrandomized and nonblinded study, 17 patients with 20 recalcitrant patchy AA lesions were recruited at the outpatient dermatology clinic, Assiut University Hospital, between August 2014 and September 2016. The lesions were treated with liquid nitrogen cryotherapy spray once weekly for 6 weeks. The lesions were sprayed for 2–3 s, until it became slightly frozen. After the frozen area was thawed (~3–5 s), a second spray was done in the same manner. The lesions were assessed by direct scalp observation for the size and hair regrowth and by taking photographs. The therapeutic response of the lesions to cryotherapy was evaluated in relation to the age of the patients, the size of the lesions, and the duration of the disease.

Results
A positive therapeutic response was noted in 13 (65%) lesions. By studying the clinical response to cryotherapy in relation to the age of the patients, we found that 53.8% of the lesions which responded to cryotherapy were in patients aged more than 30 years compared with 46.2% in patients aged less than 30 years. Lesions less than or equal to 3 cm have shown a better clinical response than those of more than 3 cm (76.9%). The clinical response of AA lesions was better (84.6%) when the disease duration was less than 6 months.

Conclusion
Superficial cryotherapy with liquid nitrogen is a therapeutic option with a good treatment outcome. It has the privilege of being simple, convenient, short-term and office-based technique, especially in mild to moderate recalcitrant AA.

Keywords:
alopecia areata, liquid nitrogen cryotherapy, treatment

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Introduction

Alopecia areata (AA) is a T-cell mediated autoimmune disease characterized by a patchy, nonscarring hair loss affecting the scalp and other body parts. In the most frequent and benign forms, patients have one or more discrete round patches of hair loss that often resolves within a few weeks or months. The rare and severe forms of AA with complete and persistent hair loss seem to occur more frequently in children and young adults, especially those with a history of atopy or family history of alopecia and in adults with autoimmune disorders [1].

The etiology of AA has eluded investigators for years, and therefore a multitude of associations have been proposed by researchers in the field of trichology [2]. Patients with AA have an increased frequency of autoantibodies to follicular structures; however, there is little consistency in which follicular structures are labeled by the antibodies [3].

One of the most intriguing features of hair biology is the immune privilege of the anagen hair follicle (HF) that is characterized by an immunosuppressive milieu around the hair bulb. The unique microenvironment of this immune-privileged site protects the organs from deleterious immune reactions and loss of function [4]. The HF immune privilege is present during anagen but is lost during the resting (telogen) and regression (catagen) phases of the hair cycle. Collapse of HF immune privilege is thought to contribute to the development of AA, in which pigment-producing anagen hair bulbs are attacked by inflammatory cells [5].

Patients and methods

Through a nonrandomized and nonblinded study, 17 patients with 20 recalcitrant patchy AA lesions were recruited at the outpatient dermatology clinic, Assiut University Hospital, between August 2014 and September 2016. The experimental design was approved by the Institutional Ethics and Research Committee of Faculty of Medicine, Assiut University, Egypt.

Inclusion criteria

The following were the inclusion criteria:
(1) Age older than 14 years
(2) AA covering less than 25% of scalp areas
(3) Absence of any severe medical illness
(4) No simultaneous immune suppressive therapy and discontinuation of any other treatment for at least 4 weeks.

Exclusion criteria

The following were the exclusion criteria:
(1) Pregnancy and lactation
(2) History of bleeding tendency or any documented hypersensitivity to the procedure (e.g., intolerance to cold).

Twenty AA lesions were treated with superficial liquid nitrogen cryotherapy spray once weekly for 6 weeks. A cryogun was used to spray the lesion with liquid nitrogen for 2–3 s till the appearance of mild frost. After the frozen area was thawed (~3–5 s), a second spray was done in the same manner.

Before each session, patients were assessed by direct scalp observation for the size of the lesion, hair regrowth, and by taking photographs, and any adverse effects were recorded.

According to the extent of terminal hair growth, lesions were grouped into four categories [6]:
(1) Excellent response (>75% terminal hair regrowth)
(2) Good response (50–75% terminal hair regrowth)
(3) Moderate response (25–50% terminal hair regrowth)
(4) Poor response (<25% terminal hair regrowth).

Results

Overall, 13 (76.5%) male and four (23.5%) female patients with age range from 14 to 42 years, were recruited from the outpatient clinic of Dermatology Department, Assiut University Hospital [Table 1].

Positive therapeutic history of topical steroids and minoxidil with temporary or no response has been reported in nine (52.9%) patients. Six (35.2%) patients had a past history of AA.

The results of lesions treated with cryotherapy showed the following (Figs. 1–3):
(1) Five (25%) lesions showed an excellent response (>75% terminal hair regrowth) at the end of the treatment course (6 weeks). Two of them showed complete hair regrowth
(2) Six (30%) lesions showed a good response (50–75% terminal hair regrowth) at the end of treatment course
(3) Two (10%) lesions showed a moderate response (25–50% terminal hair regrowth). One of them showed white hair and discontinued the treatment course at the fifth week.

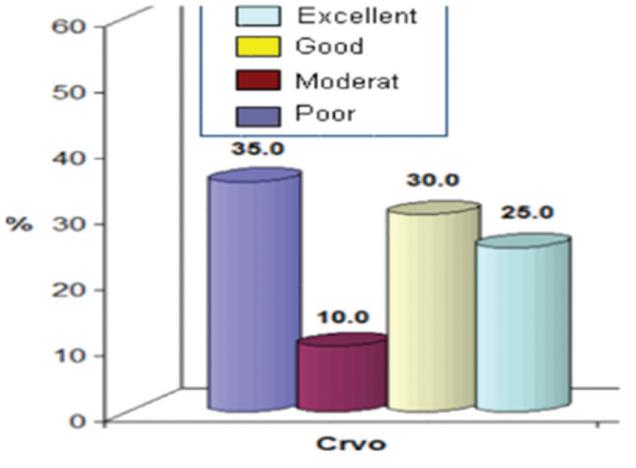
By studying the clinical response to cryotherapy in relation to the age of the patients, we found that 53.8% of the lesions that responded to cryotherapy were in patients aged more than 30 years compared with 46.2% in patients aged less than 30 years [Table 2]. Lesions less than or equal to 3 cm have shown a better clinical response than those of more than 3 cm (76.9%), but the difference was not statistically significant [Table 3].

Regarding the clinical response to cryotherapy in relation to the disease duration, the clinical response

Table 1 Demographic data of patients with alopecia areata

Item	*n* (%)
Age	
Mean±SD	26.55±8.54
Median (range)	25.5 (14.0-42.0)
Sex	
Male	13 (76.5)
Female	4 (23.5)
Duration of alopecia areata	
<6 months	14 (70.0)
≥6 months	6 (30.0)

Figure 1



Clinical response of alopecia areata to cryotherapy.

of AA lesions was better (84.6%) when the disease duration was less than 6 months [Table 4].

Discussion

AA is a chronic inflammatory disease of the HF usually manifesting as round or ovoid patchy areas that show sudden hair loss with discrete borders [7]. It is a challenging problem in dermatology. Neither the efficacy of the available therapies nor the course and the prognosis of the disease is predictable [4]. Considering all the limitations and the risk-benefit balance, treatment options are limited especially with mild to moderate AA [8].

Although cryotherapy has been reported for the treatment of AA, it is not popular in this field. In previous reports, the authors conducted a research on cases with limited involvement or in combination with other modalities [9].

Cryotherapy leads to local edema, inflammation, and blister formation; hence, like other sensitizers and irritants, it increases the local blood flow [6].

Table 2 Response of alopecia areata to treatment according to the age of the patients

Age	Response [*n* (%)]	Poor response [*n* (%)]	*P*
<30 years	6 (46.2)	5 (71.4)	0.374
≥30 years	7 (53.8)	2 (28.6)	

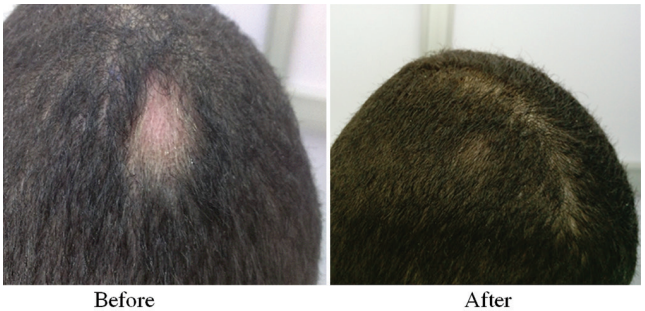
Table 3 Response of alopecia areata to treatment according to the size of the lesion

Size of the lesion	Response [*n* (%)]	Poor response [*n* (%)]	*P*
≤3 cm	10 (76.9)	2 (28.6)	0.787
>3 cm	3 (23.1)	5 (71.4)	

Table 4 Response to treatment according to the duration of the disease

Duration of the disease	Response [*n* (%)]	Poor response [*n* (%)]	*P*
<6 months	11 (84.6)	3 (42.9)	0.122
≥6 months	2 (15.4)	4 (57.1)	

Figure 2



Before After

Alopecia areata lesion, 1.5 x 2 cm, in 27 years old male patient treated by cryotherapy showing an excellent response after 6 session.

Our study showed that 25% of cryotherapy patients showed a good response (>75% terminal hair regrowth), and this is in agreement with Gita and Mohammadreza [10] who compared the efficacy between cryotherapy with liquid nitrogen and topical 0.1% betamethasone in treatment of AA and found good results in 23% of the patients treated with cryotherapy.

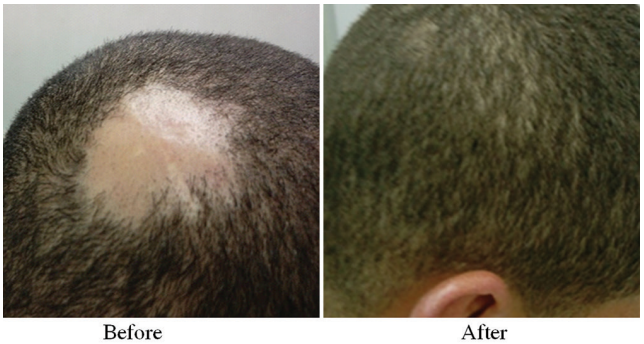
In our study, the overall clinical response of AA lesions treated with cryotherapy was 65% and that was quite similar to the results of Jun *et al.* [11], where 60.9% of the patients were classified as responders. Similarly, Hong *et al.* [12], in their Korean study done on 153 patients with AA, 68.6% of patients showed a therapeutic response after 12 weeks of treatment with superficial cryotherapy using liquid nitrogen.

Regarding the cryotherapy technique, the study of Lei *et al.* [13], on patients with AA using a different cryotherapy technique (a cotton swab) once weekly for 4 weeks, showed 97.2% improvement compared with 65% in our study. This could be explained by the large number of the studied patients and the different cryotherapy technique.

Another study using a different cryotherapy technique was done in 2013 by Radmanesh and Azar-Beig [6] on 44 patients with AA or alopecia totalis treated with a closed contact CO_2 system for 8 weeks. In spite of the closed contact technique and the longer duration of therapy, their study showed a positive therapeutic response in 29 (65.9%) of 44 patients compared with 65% in our study after 6 weeks using superficial cryotherapy.

When analyzing our results according to the age of the patient, the clinical response of AA lesions to cryotherapy was less in patients aged younger than 30 years (46.2%). Similarly, according to the results of Jun *et al.* [11], the treatment response to cryotherapy was the lowest in the teenagers. In contrast, Hong

Figure 3



Before After

Alopecia areata lesion, 4 x 3 cm, in 20 years male patient treated by cryotherapy, showing an excellent response after 6 sessions.

et al. [12], reported that patients older than 50 years have a relatively poor response.

Regarding the size of the lesions, in our study, 80% of AA lesions that responded to treatment (excellent to good response) were less than 3 cm in diameter. This was superior to the results obtained by Gita and Mohamedriza [10] where 45% of AA lesions (<2.5 cm) showed a good response.

According to the duration of the therapy, in our study, by using liquid nitrogen spray once weekly for 6 weeks, the clinical improvement was observed in 65% of the involved lesions. This was superior to the results of Lee *et al.* [14], where the percentage of improvement was 22.4% following 6 months of treatment duration, and the results of Jun *et al.* [11], where 60.9% of patients showed a clinical improvement following 18.6 weeks (2-week treatment interval). This was also consistent with the results of Hong *et al.* [12], where there was an improvement in 86.6% of the patients following 12 weeks of therapy.

In contrast, Zawar and Karad [15], in their study done on 11 patients with recalcitrant AA, reported better results; 80% of their patients showed a clinical response. These patients were treated with superficial liquid nitrogen cryotherapy every 2 weeks for maximum five sessions. These superior results may be explained by the longer duration of therapy and the longer freeze and thaw cycles (15 s each compared with 3–4 s in our study).

Conclusion

Superficial cryotherapy with liquid nitrogen is a therapeutic option with a good treatment outcome. It has the privilege of being a simple, convenient, short-term, and office-based technique.

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Conflicts of interest

There are no conflicts of interest.

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