Case Series
MVP Journal of Medical Sciences, *Vol 7(2), 288-294, July-December 2020*
ISSN (Print) : 2348–263X
ISSN (Online) : 2348-2648
DOI: 10.18311/mvpjms/2020/v7i2/24570

Unresponsive Alopecia Areata Treated Successfully with Liquid Nitrogen Cryotherapy: A Study of Five Patients

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Abstract

Introduction: Alopecia Areata (AA) is one of the most common form of hair loss seen in dermatology. Treatment failures can occur with almost every conventional therapy, either singly or in combination. **Aims and Objectives:** To study the clinical profiles and management outcome of Liquid Nitrogen Cryotherapy (LNC) for the treatment of unresponsive cases of AA. **Materials and Methods:** A prospective study was conducted on five patients who showed no response to conventional topical treatment for six months. The subjects were enrolled in the study after written consent. Clinical photographs were recorded at each visit. Patients were given 3-5 sittings of LNC at 2 week intervals. Each session consisted of dual freeze thaw cycles of 15 seconds each, with a cryospray technique following application of topical anaesthetic cream. Suitable antibiotics and anti-inflammatory agents were prescribed post-operatively for five days. The clinical response was evaluated by using regrowth scale at 4th week and 8th week. Final end point evaluation of patient post 3 months after the last treatment session was done to observe sustained regrowth of hair. **Results**: Five patients were recruited, out of which three patients showed an excellent response, 1 each had a satisfactory response and a fair response respectively. Commonly seen adverse effects were slight pain, erythema, edema, erosion, crusting, dyspigmentation/hypopigmentation, which were transient and did not require withdrawal of treatment. **Conclusion**: Liquid Nitrogen Cryotherapy is a cheaper, easily available with transient adverse effects and can be worth trying in unresponsive Alopecia Areata.

Keywords: Alopecia Areata(AA), Liquid Nitrogen Cryotherapy (LNC), Unresponsive

1. Introduction

Alopecia Areata (AA) is one of the most common form of non-scarring hair loss accounting for 25% of all the alopecia cases[1,2]. Etiopathogenesis of AA consists of autoimmunity, genetic predisposition and environmental factors[2]. If AA is not treated, it can progress to Alopecia Totalis (AT) or Alopecia Universalis (AU) in 5–10% patients[2]. There are different treatment modalities like topical corticosteroids, intralesional steroids, minoxidil, tacrolimus, contact sensitizers, irritants, photochemotherapy, immunomodulators like methotrexate, alefacept, azathioprine, systemic Janus Kinases, Signal Transducer and Activator of

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Transcription (JAK/STAT) pathway inhibitors and tumor necrosis factor-alpha inhibitors (TNF-α)[3]. Although AA is a commonly encountered disease, its course and prognosis is unpredictable and the available treatment is also not uniform. Cryotherapy has been used as a mechanical intervention in treatment of AA. It exerts cold inflammation over. It exerts cold inflammation over the lesional skin and helps in vasodilatation and immunosuppressive effect over the causative activated immune system and thus helps in Alopecia Areata. There are anecdotal reports of treatment with cryotherapy in AA.

2. Aims and Objectives

To study the clinical profiles and management outcome of Liquid Nitrogen Cryotherapy(LNC) for the treatment of unresponsive cases of AA.

3. Materials and Methods

We conducted a prospective study on five patients to treat the unresponsive AA with LNC who showed no response to various modalities of treatment taken for 6 months.
Ethical committee clearance was taken. Thorough history and clinical evaluation with clinical pre and post photographs were recorded. The subjects were counselled in detail about the modality of treatment and written consents were taken. Topical local anesthetic cream (2.5%lidocaine and 2.5% prilocaine) was applied 1hr prior to therapy.

3.1 Inclusion Criteria

- Age more than 18 years.
- Unresponsive AA not responding to other modalities of treatment taken for 6 months.

3.2 Exclusion Criteria

- Associated autoimmune diseases such as thyroid disorders, vitiligo, diabetes mellitus.
- Intolerance to cold (cryoglobulinemia, cryofibrinogenemia, cold urticaria, mixed cryoglobulinemia).
- Active secondary infection like warts, herpes or bacterial infection.
- Patients not willing to follow the protocol.

We used a handheld cryo unit containing liquid nitrogen with a 1mm brass spray tip. At a distance of 2 cm from the alopecic patch, lesion was sprayed with liquid nitrogen. Dual freeze-thaw cycles of 15 seconds each, such 2 cycles were sprayed in a paint brush-like manner from one end of lesion moving up and down across each lesion. The end point was considered as development of uniform frost over the patch at the treatment site. Patients were given 3-5 sittings of LNC at 2 weeks interval. The patients were given systemic antibiotic, anti-inflammatory drugs, topical mupirocin ointment for five days post procedure to prevent secondary infection and no other treatment modality was given in between the follow up period. The clinical response was evaluated by using regrowth scale at 4^{th} week and 8^{th} week [1] (Table 1).

Final end point evaluation of patient post 3 months after the last treatment session was done to observe sustained regrowth of hair.

Table1. Percentage of hair regrowth using regrowth scale with liquid nitrogen cryotherapy

Score	Regrowth	Response
0	<10%	No response
1	11–25%	Poor
2	26–50%	Fair
3	51–75%	Satisfactory
4	≥75%	Excellent

4. Results

The present study was conducted on five patients of unresponsive AA cases. Out of 5 patients, there were 3 male patients and 2 female patients, aged between 19 and 32 years with a disease duration ranging from 1 to 2 years with 25%-50% of scalp involvement with only one patient involving beard area (Table2).

The positive therapeutic response was interpreted as regrowth of terminal hairs within the alopecic patches at the 4th and 8th week. Three patients (60%) showed an excellent response out of which two patients (40%) showed response at the 6th week, one patient (20%) showed response after two sitting (4th week), with no further requirement of LN cryotherapy sitting and one patient each (20%) showed satisfactory and fair response at the 8th week (Table3). Commonly seen adverse effects were slight pain, erythema, edema, erosion, crusting, dyspigmentation/ hypopigmentation, which were transient and did not require withdrawal of treatment.

Table 2. Clinical profiles of patients

Sr. No.	Age	Sex	Anatomical location	Number of patches	Duration of the disease	Previous treatment taken
1	30	Female	Vertex	2	10 months	Intralesional and topical steroids, topical tacrolimus.
2	20	Male	Occiput	4	13 months	Topical steroids and tacrolimus.
3	32	Female	Vertex	1	9 months	Intralesional and topical steroids,phenol.
4	28	Male	Temporal	2	12 months	Systemic and topical steroids.
5	19	Male	Beard	1	24 months	Intralesional and topical steroids,anthralin.

Table 3. Management outcome of patients

Sr.no	Age/sex	Percentage of regrowing hair on follow-up at the 8th week (%)	Response at the 8th week	Sustained regrowth of terminal hair at 3 months after the last session
1	30/F	≥75%	Excellent	Present
2	20/M	≥75%	Excellent	Present
3	32/F	≥75%	Excellent	Present
4	28/M	51–75%	Satisfactory	Present
5	19/M	26–50%	Fair	Present

5. Discussion

Alopecia Areata is a known autoimmune disease which can be seen in association with other autoimmune disorders such as vitiligo, diabetes mellitus and thyroid disorders.The massive T cell infiltrations around hair follicles, the presence of antibodies against parts of the hair follicle and hair shaft and therapeutic response to immunosuppressive agents all indicate the involvement of the immune system in the pathology of Alopecia Areata. The available therapies are directed to correcting or modulating the immune response.

Cryotherapy can act either singly or by combination of the which mechanisms resulting in regrowth of hair in AA[4]. After cryotherapy, initially there is vasoconstriction and then during the thaw period, there is significant vasodilation as the temperature attained is 0° Celcius[5]. This is hypothesized to cause regrowth of follicular hair. Also local edema and inflammation can occur post cryotherapy which is known to play a role in inducing vasodilatation[6]. Another speculation is that cryotherapy causes partial damage to keratinocytes of which hair follicle keratin 16 and trichohyalin are the main targets, further decreasing damage in perifollicular infiltrate. Tissue Langerhan cells are also altered which could further alter the antigen presentation process. Other theories suggest temporary paralysis of melanocytes[7,8].

In our study, we used longer duration of cryotherapy freeze-thaw cycle of 15 seconds each, at shorter interval that was every 2 weeks between the sessions and got excellent results. But studies done by Gita et al used 2–3 seconds freeze cycle and 3–5 seconds thaw cycle along with short duration of interval in between sessions and got comparable results[9]. However study conducted by Hyung *et al.*, when treated alopecic patch with cryotherapy at an interval of more than 3 weeks got poor results[10].

We conducted this study on unresponsive AA patients who earlier were treated with topical, intralesional and oral steroids and now got excellent response with cryotherapy. Similar study conducted by Radmanesh *et al.* also suggested cryotherapy as an alternative method for unresponsive AA[11].

Gita et al. in her study compared efficacy of LNC versus topical betamethasone lotion and concluded that both have similar efficacy and thus cryotherapy can be reserved for resistant, isolated AA cases, children or anyother individual on immunosuppresive agents apart from steroids[9]. However Amirnia *et al.* found poor response to cryotherapy when compared to intralesional triamcinolone, but suggested that cryotherapy still can be used as monotherapy to induce hair regrowth in special circumstances[12].

Small sample size was the limitation of our study and a larger multicentric study with LNC on unresponsive

A) Pre-operative

B) 3 months post 4th sitting

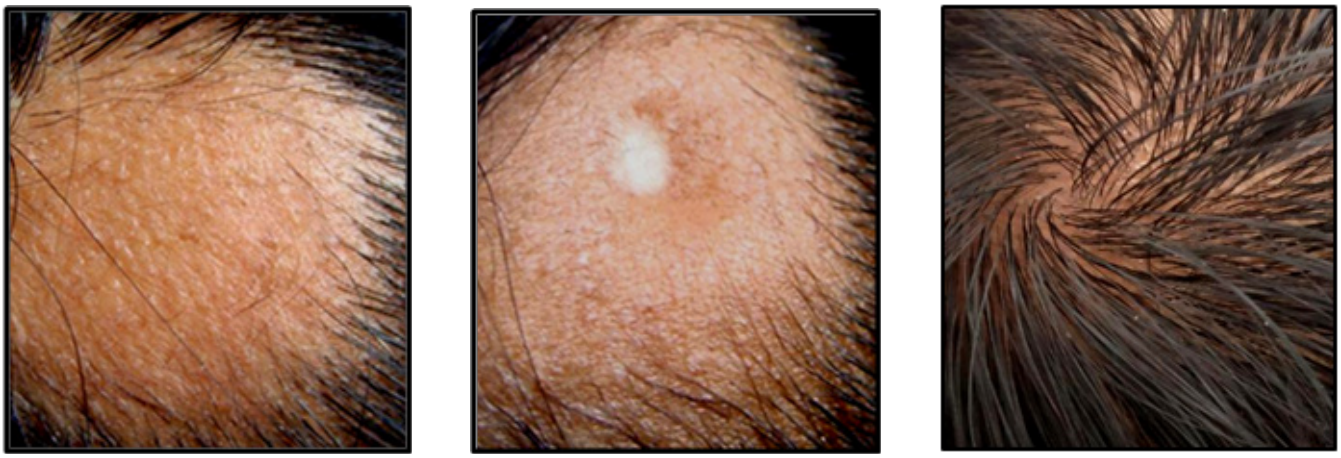
Figure 1. Showing excellent response in 4 sittings with LNC.

Alopecia Areata cases would give us better insight about its effectiveness.

Unresponsive AA is common in clinical practice and treatment failures are known to occur with almost every conventional therapy whether used singly or in combination. There should be availability of alternative therapeutic approaches, which should be suitable for administration, with minimal transient side effects and should be able to produce sustainable hair regrowth. We tried LN cryotherapy as a monotherapy in patients who did not respond to other modality of treatment and excellent to good results were observed in these patients. We believe that LN cryotherapy is a cheap, easily available option and can be worth trying in the management of unresponsive AA.

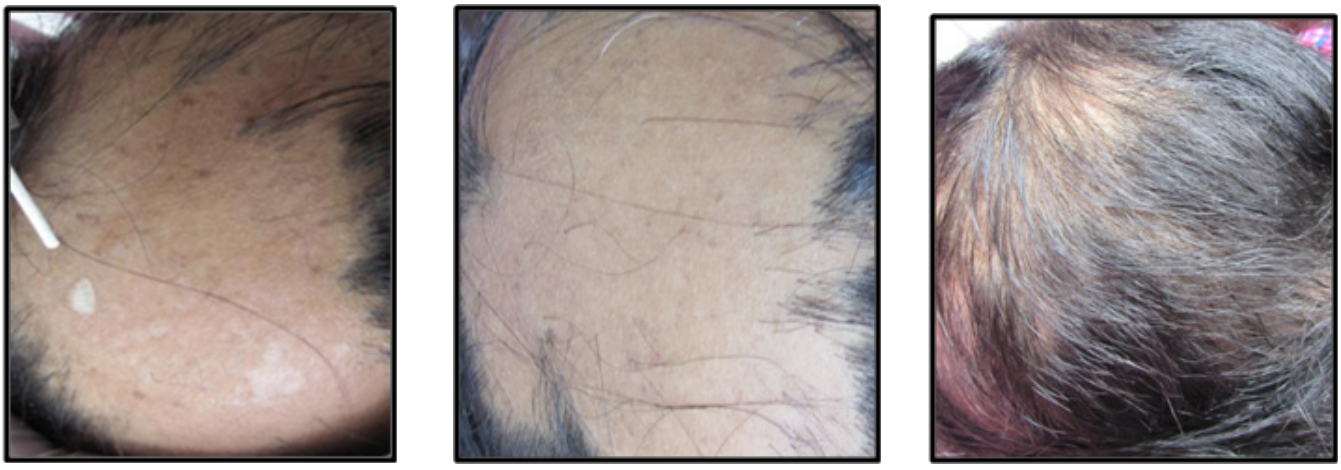
6. Conclusion

LN cryotherapy can be worth trying modality in the treatment of unresponsive AA cases.



A) Pre-operative B) Intra-operative C) 3 months post 2nd sitting

Figure 2. Showing excellent response in 2 sittings with LNC.



A) Pre-operative B) Intra-operative C) 3 months post 4th sitting

Figure 3. Showing excellent response in 4 sittings with LNC.

A) Pre-operative B) Intra-operative C) 3 months post 5th sitting

Figure 4. Showing satisfactory response post 5th sitting,

A) Pre-operative B) Erosion post cryotherapy C) 3 months post 5th

Figure 5. Showing fair response post 5th sitting.

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How to cite this article: Zawar V, Bharati JS, Pawar M, Kumavat S and Das J. Unresponsive Alopecia Areata Treated Successfully with Liquid Nitrogen Cryotherapy: A Study of Five Patients. MVP J. Med. Sci. 2020; 7(2):288-294.