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RESEARCH ARTICLE
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FFECTIVENESS OF LIQUID NITROGEN CRYOTHERAPY FOR ALOPECIA AREATA

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ABSTRACT

Introduction: Alopecia areata (AA) is an autoimmune disease causing hair loss, which may adversely affect patients' quality of life. Liquid nitrogen cryotherapy has been suggested as a potential treatment, but its effectiveness is still under investigation.

Objective: This study aimed to evaluate the effectiveness of liquid nitrogen cryotherapy in promoting hair regrowth in patients with alopecia areata, comparing it to alternative treatments.

Materials and Method: A randomized controlled trial was conducted at Dermatology Department, Bolan Medical Complex Hospital Quetta, Pakistan from October, 2024 to March, 2025. Sixty patients, diagnosed with mild to moderate AA were randomized into two arms the cryotherapy with liquid nitrogen or non cryotherapy alternatives. Clinical and dermoscopy assessment of the efficacy of hair regrowth was done after six treatment sessions.

Results: The cryotherapy group registered an increment in hair regrowth of 60%, a significant increase from the 40% observed in the other treatment group. The cryotherapy group maintained an increase in visibility of follicular activity when tested by dermoscopy.

Conclusion: Cryotherapy using liquid nitrogen to treat alopecia areata can be very effective, and it can lead to significant regrowth and healthier follicles.

Keywords: *Alopecia areata, liquid nitrogen cryotherapy, hair regrowth, dermoscopy, autoimmune disorder, treatment efficacy.*

INTRODUCTION

Alopecia areata (AA) is a chronic autoimmune condition causing hair loss, mainly on the head, although it sometimes occurs in other body parts. It has a sudden onset and a round pattern of hair loss, in patches, often causing severe emotional stress and decreased quality of life. This condition is believed to be caused by a misdirected push by the immune system against hair follicles, leading to localized hair loss. The disorder presents in individuals of different ages, but it is most frequently seen in young adults. The global prevalence ranges from 0.1% to 0.2%. Several modalities of treatments have been evaluated, from immunosuppressive treatments to topical corticosteroids and phototherapy.

However, no standard treatment protocol has been verified to restore hair growth reliably, which drives further search for alternative procedures (1). LNC has emerged as an appealing option for controlling AA since it presents an easy, cost-effective, and safe approach to handling patients. The process behind cryotherapy involves applying cold temperatures to cause tissue damage, followed by inflammation that is believed to trigger immune mechanisms and promote hair regrowth.

Several clinical trials have assessed the effectiveness of LNC in managing AA, and it is evident that, though results may differ, the approach has promising effects. Clinical studies confirm cryotherapy as a treatment for hair regrowth, especially in mild to moderate AA(2). It is believed that freezing the affected regions during cryotherapy would stimulate the immune system, which might induce the restoration of the hair follicles. Comparative studies have examined how cryotherapy compares to corticosteroid injections and other means of therapy used to treat AA. Some studies have reported that cryotherapy may produce comparable results to intralesional corticosteroids, while others have shown that LNC may aid in better outcomes (3). The research by Aslam et al. (2022) indicated that LNC may be particularly effective for individuals with resistant AA who cannot recover with conventional corrections. Research results confirm the hypothesis that cryotherapy causes an inflammatory reaction that helps with hair regrowth in treated areas, just like results observed in previous studies (4). In a prospective study, the liquid nitrogen treatment was applied to affected scalp regions, and patients were monitored over several months to see whether the treatment helped new hair to grow (5).

In terms of other methods, cryotherapy brings unique benefits. Cryotherapy is an excellent example of a speedy and minimally invasive technique that can be administered on an outpatient basis. There are multiple applications of liquid nitrogen, which are done after a few-week interval on each procedure. Second, cryotherapy is usually less expensive than systemic treatments (oral corticosteroids, immunosuppressants), which are associated with serious side effects and require continuous medical administration (6). Furthermore, cryotherapy could be considered a safer alternative when the bodies respond poorly to other remedies. However, additional exploration is necessary to improve treatment management and the long-term effects of using LNC in AA patients (7). Research on LNC for AA has had mixed results regarding how well the treatment works. For instance, Gouda et al. (2021) studied the clinical efficacy of cryotherapy, noting its success in stimulating hair regrowth in particular for patients suffering from mild to moderate AA (3).

Other studies suggest that patients with early-stage alopecia areata may improve from cryotherapy because there is evidence for significant shrinkage of hairless territory after several consecutive sessions (8). Conversely, the effectiveness of cryotherapy partly depends on the severity of the condition, a patient's age, and duration of the disease (9). One major limitation of the LNC is that patient results may differ hugely. Although the exact mechanism of cryotherapy in hair follicles is yet to be identified, it has been observed that the outcomes tend to depend on the details, such as the level of freezing applied and the general number of treatments administered (10). Cryotherapy is superior for treating patients with localized hair loss patches compared to those with extensive or longer-standing alopecia areata, as shown in clinical studies (11). However, as established by a systematic review conducted by Lim and Lee (2023), treatment with cryotherapy seemed to help AA patients initiate hair regrowth when the disease began to develop, although their effects were modest among those with longstanding or severe hair loss (9).

Additionally, the efficacy of cryotherapy may vary due to individual genetic makeup, the health of the immune system, and the consistency with which a patient follows through with the treatment. While the primary results are positive, more large-scale randomized controlled trials are needed to determine the impact of LNC on the long-term course of annular acne. Most of the previous research has few study subjects, short follow-up, and heterogeneous research approaches. Consequently, more studies need to be conducted to establish the most effective cryotherapy schedule, optimal duration of treatment, and the appropriate groups of patients (12). Some studies have also considered cryotherapy in combination with topical corticosteroids or immunomodulators. This combination strategy is based on the concept that cryotherapy can augment the absorption and efficiency of other medications, thus leading to improved hair regrowth results (13).

According to a study that Iraji et al. (2024) published, when cryotherapy and betamethasone were combined, there were better results in treating alopecia areata, particularly in patients with a more developed disease (8). This evidence can help create new treatment strategies, which may increase the potential of cryotherapy when it is used alone. Furthermore, liquid nitrogen cryotherapy is recognized as an effective treatment strategy for patients with alopecia areata in cases of localized or early phases of the disease. However, preclinical evidence shows that cryotherapy can help regenerate hair, and more clinical trials are needed to refine the application methods and track any long-term benefits. Due to its low cost, noninvasive nature, and feasibility in being incorporated within other treatment schemes, cryotherapy represents a valid management approach for AA. More research would significantly contribute to the management of alopecia areata in the form of liquid nitrogen cryotherapy (14)(15).

Objective: The objective of this study is to evaluate the effectiveness of liquid nitrogen cryotherapy in treating alopecia areata, assessing hair regrowth outcomes and comparing its efficacy to other therapeutic options.

MATERIALS AND METHODS

Design: Randomized Controlled Trial.
Study setting: A study carried out at Dermatology Department, Bolan Medical Complex Hospital Quetta, Pakistan**.**
Duration: The study was carried over a six-month duration, from October, 2024 to March, 2025.
Inclusion Criteria: Adult participants in the age range of 18 – 50 years and confirmed diagnosis of alopecia areata were eligible for the study. Eligible participants need to have a confirmed diagnosis of mild to moderate alopecia areata, and no previous treatment should have been performed during the last three months.

Exclusion Criteria

The study excluded patients with extensive alopecia areata, such as alopecia totalis or universalis. Furthermore, patients with histories of major systemic illnesses, pregnant patients, or participants taking immunosuppressive treatment were not included in the study.

Methods

The study groups were divided into two different groups by random selection. While a group of participants received a liquid nitrogen cryotherapy, the members of the other group underwent a contrasting treatment, usually intralesional corticosteroid injections. Participants received cryotherapy in liquid nitrogen by spraying the cryogen on the affected regions of the scalp, and it usually takes 10 to 15 minutes per session. The procedure required applying the therapy every two weeks, which meant six sessions. Assessment in the clinic was conducted at the onset, after 3rd treatment, and at the end of the study period. Both clinical inspection and dermoscopy were applied to assess the growth of hair regrowth. The primary endpoint was quantified as the overall hair regrowth, and secondary endpoints were evaluated based on patient perception of hair density and overall quality of life. The research used statistical methods to determine how effective liquid nitrogen cryotherapy was in comparison to other treatments, taking into account the age of patients, the number of years with alopecia, and the severity of the condition.

RESULTS

Sixty patients with alopecia areata were involved in the study, 30 were randomly allocated to artificial freezing with liquid nitrogen cryotherapy, and 30 participated in the alternative treatment. In the beginning, both groups were similar in terms of age, gender, and duration of disease. The study was composed of patients with an average age of 32.5 years and who aged between 18 and 50 years. Over half of the patients were male (60%), and most (70%) had a disease duration of less than a year.

Table 1: Baseline Characteristics of Participants

Characteristic	Liquid Nitrogen Cryotherapy (n=30)	Alternative Treatment (n=30)	p-value
Mean Age (years)	33.1	31.9	0.450
Gender (Male %)	60%	60%	1.000
Disease Duration (months)	8.2	7.8	0.630

At the end of the research, it was apparent that both groups achieved meaningful hair regrowth. The cryotherapy group showed more hair regrowth than patients receiving alternative therapy treatment. Patients in the cryotherapy treatment group registered an average of 60% improvement in hair regrowth as compared with the 40% by those in the alternative treatment group.

Table 2: Hair Regrowth Percentage After Treatment

Group	Percentage of Hair Regrowth (%)	p-value
Liquid Nitrogen Cryotherapy	60%	0.005
Alternative Treatment	40%	

In addition to clinical tests, a dermoscopic examination of hair follicle activity was performed. The results showed that cryotherapy significantly increased follicular activity and that 70% of the treated areas responded, while only 45% was the case in the other treatment group. The cryotherapy treatment produced an increased number of active hair follicles per unit area.

Table 3: Dermoscopic Evaluation of Hair Follicle Activity

Group	Active Hair Follicles (%)	p-value
Liquid Nitrogen Cryotherapy	70%	0.002
Alternative Treatment	45%	

Using patient-reported outcome measures shows that the cryotherapy group significantly improved quality of life, noticing a 30% decrease in alopecia-related distress. In contrast, the alternative treatment group reported a 15 percent results loss. Both groups had mild to moderate side effects, and transient redness and scabbing were the most common complaints in the cryotherapy group, which resolved shortly after the treatment. The findings report that liquid nitrogen cryotherapy exceeds other alopecia areata therapies, with respectable improvements of hair regrowth reported as measured through clinical and dermoscopic tests.

DISCUSSION

Results of this study highlight the efficacy of liquid nitrogen cryotherapy in treating alopecia areata (AA), especially in cases of mild to moderate disease presentation. Cryotherapy was observed to have produced markedly enhanced hair regrowth and follicular activity in the current study compared to the control group, which mainly relied on intralesional corticosteroids. These results correspond to previous studies addressing cryotherapy in AA, suggesting that liquid nitrogen therapy can provide substantial therapeutic gains to AA patients. Alopecia areata an autoimmune disorder undermines hair follicle activity and results in superficial, circular hair loss. Alopecia areata's basal cause is an immune system attack on hair follicles, primarily emphasizing follicles in the anagen phase. In the efforts to control AA, researchers have proposed several strategies, among them the use of topical corticosteroids, systemic immunosuppressive drugs, and phototherapy. Despite different options, no treatment has proven effective across all patients.

Liquid nitrogen cryotherapy has recently become a minimally invasive and straightforward treatment for AA. Cryotherapy's functioning mechanism is to initiate focused inflammation in the skin that might stimulate hair follicle replacement and increase immune activity. The use of cold induces a

response of the immune system, which leads to the movement of inflammatory cells needed for hair follicle regeneration and the stimulation of new hair growth (1). The findings correspond to the previous works that discussed the possible advantages of cryotherapy in treating AA. Aslam et al. (2022) showed that liquid nitrogen cryotherapy greatly affected hair. Consistent with these findings, Gouda et al. (2021) also observed positive results for cryotherapy, which was more valuable in localized alopecia areata patients, suggesting that cryotherapy could be of exceptional help for patients with limited disease scope (3).

In the present study, the hair regrowth rate in patients on cryotherapy was, on average, 60%, exceeding the 40% recorded in those on the alternative treatment. A difference of that nature indicates that cryotherapy is capable of causing more optimal outcomes than the normative ways. Observations of increased follicular activity in the dermoscopy of the cryotherapy group highlight the beneficial effect of cryotherapy on hair growth. Dermoscopy is an essential technique for assessing the state of hair regrowth and follicles by providing high magnification views of the scalp and roots of hair. The superiority of cryotherapy, as shown by the 70% response rate in the cryotherapy group, compared to 45% in the alternative treatment group, demonstrates better pump capability of the hair follicles. Studies have reported information on cryotherapy causing an increase in blood flow in hair follicles, which helps regenerate follicles through inflammatory actions, which is relevant in these results (4). Cryotherapy showed efficacy, although many factors, such as the extent of the disease, the time interval between procedures, and the patient's immune system, greatly influence. The patients involved in the study did have mild to moderate alopecia areata, and perhaps, for individuals with more advanced disease stages such as alopecia totalis or universalis, one might expect different treatment responses. From the study by Lim and Lee (2023), cryotherapy causes more hair growth within the affected region, while cases are poor for patients with extensive alopecia (5). The findings showed that patients who experienced a more minor to moderate hair loss gained more from cryotherapy than those with extensive alopecia. Proper diagnosis and assessment of patients are vitally crucial for successful cryotherapy outcomes.

Despite having encouraging results, it is essential to recognize the limitations of cryotherapy. The most significant problem concerning the use of cryotherapy is that its results are inconsistent. The effectiveness of this treatment is very variable in patients, and some patients do not even show desired hair regrowth. These differences in effectiveness with the treatment may be caused by individual immune system function, genetic makeup, and the ability of the scalp to heal after cryotherapy. Although cryotherapy is believed to be a safe procedure, it has been noted to sometimes have side effects such as erythema, scabbing, and discomfort in the area affected, as reflected in the research. The side effects were usually mild and disappeared quickly, consistent with prior studies claiming that cryotherapy had minimal side effects (6). The monetary matter of cryotherapy must also be considered. Liquid nitrogen cryotherapy is usually cheaper than such procedures as systemic corticosteroids or immunosuppressants, though the charge for several sessions can increase their overall cost for patients.

Cryotherapy may not be commonplace in some areas due to the necessity for special equipment and individuals with the skills involved. Nevertheless, the potential of cryotherapy as a treatment should be balanced with its availability and long-term costs before it is taken into widespread clinical use. This study showed significant gains in quality of life reported within the cryotherapy group, relating to a 30% reduction in distress for alopecia as reported by patients. The findings are based on previous studies that focus on the mental health benefits of hair regrowth in patients of AA. Losing hair has a considerable psychological impact on AA with varying consequences such as self-consciousness, anxiety, and depressive symptoms. Finally, treatments that can successfully restore hair can improve the physical appearance of the patient, as well as their emotional health. The study highlights the importance of the emotional well-being alongside medical management in patients suffering from alopecia areata, since it concerns more than looks.

Finally, liquid nitrogen cryotherapy appears to be a promising approach for alopecia areata, particularly in localized or mild disease cases. Results of better regrowth of hair, greater follicular activity, and better reported patient quality of life suggest that cryotherapy could provide an

alternative to conventional modes of treatment. Still, other studies, including carefully planned randomized controlled trials with prolonged observation intervals, are needed to define the optimal treatment parameters, evaluate the long-term efficacy of cryotherapy, and investigate its possible synergism with other therapies. With the evolution of dermatology, the use of cryotherapy in treating alopecia areata could become the standard technique, offering patients a safe, effective, and readily available method for restoring hairs.

CONCLUSION

According to the results of the study, it can be stated that liquid nitrogen cryotherapy distinguishes itself as one of the most viable options for alopecia areata, causing significant increases in hair regrowth and follicle activity when compared to other therapies. Patients receiving cryotherapy exhibited significantly increased rates of hair regrowth and stronger clinical signs of active hair follicles when examined using dermoscopy, highlighting the ability of the therapy to promote hair regrowth. Moreover, participants reported a more life-providing quality of life after receiving treatment, which meant a reduction in distress caused by alopecia. Although cryotherapy is promising, there is optimization of the therapy for patients with localized mild to moderate alopecia areata, and there are also highly variable responses in individuals. Although the procedure was generally well-tolerated, patients had temporary erythema and scabbing, which resolved rapidly. Additional studies using larger populations with prolonged observation intervals will be required to confirm these outcomes and improve the treatment protocols. Overall, cryotherapy is a good alternative in terms of treating alopecia areata.

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