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The Effectiveness of N-Acetyl Cysteine in Conjunction with Microneedling Compared to Microneedling Alone for the Treatment of Alopecia Areata

Eman M. Hassan, Miran K. Kassem

Dermatology, Venereology, and Andrology Department, Faculty of Medicine Benha University, Egypt.

Corresponding to:
Dr. Eman M. Hassan.
Dermatology, Venereology, and Andrology Department, Faculty of Medicine Benha University, Egypt.
Email:
EMAN.HASSAN01@fmed.bu.edu.eg

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Abstract:

Background: Alopecia areata (AA) is an autoimmune condition that causes non-scarring hair loss. Although several therapy options exist, many have considerable adverse effects and/or low efficacy. This encourages the ongoing creation of innovative treatments.

Objective: to evaluate the efficacy of N-acetyl cysteine (NAC) combined with microneedling (MN) versus microneedling (MN) alone in treating alopecia areata. **Patients and methods:** The comparative study of the intervention included fifty patients clinically diagnosed with AA and confirmed through dermoscopy. These patients were split into two groups. Group I (25 patients) underwent treatment with N-acetyl cysteine combined with microneedling (NAC-MN), and Group II (25 patients) underwent treatment with microneedling (MN). The patients were assessed utilizing the Severity of Alopecia Tool Score (SALT), the Hair Regrowth Scale (RGS), and dermoscopic evaluation. **Results:** The SALT score became statistically significantly lower after treatment compared to before treatment in Group I (NAC-MN) (P value < 0.001) than in Group II (MN) (P value < 0.035). Group I (n=15), which had 60% hair regrowth, had a statistically significantly higher Hair Regrowth Score (RGS 5) compared to group II (n=5), which had 20% regrowth (P value <0.001). **Conclusion:** N-acetyl cysteine may be considered an efficacious treatment for alopecia areata when used with microneedling as an adjunctive method for transepidermal delivery of active compounds. Minimal to no adverse effects were noted following microneedling in conjunction with NAC or microneedling independently. Further research is required on a large group of individuals with alopecia areata utilizing N-acetylcysteine as a topical therapy modality.

Keywords: Alopecia areata; microneedling; N-acetyl cysteine

Introduction

Alopecia areata (AA) is a complicated, long-lasting inflammatory skin condition that causes hair loss that is not always permanent. In clinical settings, AA presents in several forms, such as patchy alopecia, alopecia areata incognita (AAI), ophiasis, alopecia totalis (AT), and alopecia universalis (AU). A lot of clinical research shows that AA has a significant effect on mental health, causing problems including anxiety, insomnia, and low self-esteem, especially in extreme cases. Additionally, people with AA have a higher likelihood of having other health problems, such as autoimmune diseases, high blood pressure, and high cholesterol [(1)]. Immune dysregulation, hereditary predisposition, environmental variables, and epigenetic changes are all components of the complex pathophysiology of AA.

It is believed to arise from the loss of immune privilege at the hair follicle (HF), initiating a complex interaction among proinflammatory cytokines, including interferon-gamma (IFN-γ), interleukin 15 (IL-15), and interleukin 2 (IL-2). These signals are transmitted through Janus kinase (JAK) and signal transducers and activators of transcription (STAT), resulting in robust T cell activation and the execution of effector functions targeting the hair follicle [(2)].

Current therapies offer symptomatic relief; however, they are not effective in curing, thereby adding to the financial stress and a diminished quality of life for patients. Topical contact sensitizers like squaric acid dibutylester (SADBE) and diphenylcyclopropenone (DPCP) are part of conventional therapy, as are topical or systemic glucocorticosteroids. Systemic immunosuppressants, including cyclosporine (CsA), methotrexate, and azathioprine. As targeted therapy for AA, emerging medicines, particularly biologics and small-molecule medications like JAK and phosphodiesterase 4 (PDE4) inhibitors, show promise [(3)].

Numerous inflammatory disorders have been linked to dysregulated autophagy levels. By considering the regulation of autophagy, novel therapeutic options could potentially be developed. Cysteine may regulate autophagy, shielding cells from oxidative stress-induced harm. The pathophysiology of AA is secondary to psychiatric problems, which are frequently associated with it. N-acetylcysteine has received approval for its therapeutic efficacy in psychiatric diseases. Research indicates that N-acetylcysteine exhibits beneficial therapeutic responses in AA situations [(4)].

Aim of the study:

Our goal is to assess the effectiveness of N-acetyl cysteine (NAC) combined with microneedling (MN) compared to microneedling (MN) alone in treating alopecia areata.

Patients and Methods:

Patients' Criteria

Fifty male and female patients with alopecia areata who were diagnosed clinically and dermoscopically were included in this intervention comparison study. They were recruited from the Dermatology, Venereology, and Andrology outpatient clinic of Benha University Hospital from February to July 2025. Our local Ethics Committee approved the study (RC 5-2-2025), and all the steps followed the Helsinki Declaration of 1975 and its update in 2000. Every patient gave written consent that they understood. The minors agreed, and their parents signed consent documents.

The inclusion criteria were patchy hair loss of less than 50% of the scalp and no treatment for alopecia, either topical or systemic, one month before and during the study, except that the sessions were conducted in the hospital.

The exclusion criteria include systemic diseases known to affect hair growth (e.g., thyroid disorders), recent treatment with similar interventions within the last 3 months, a history of scalp surgery within the past year, and known skin diseases

affecting the scalp (e.g., psoriasis, dermatitis); patients currently using medications that influence hair growth (e.g., chemotherapy agents, immunosuppressive drugs) or with significant scalp infections or open wounds at the treatment site, conditions that cause bleeding, as well as long-term use of blood-thinning medications. Pregnant and breastfeeding women are also excluded.

Patients Evaluation

All patients underwent history taking and local clinical and dermoscopic examination of the lesion(s). The Severity of Alopecia Tool (SALT) grades alopecia areata by assessing hair loss in four scalp regions, yielding a score from 0 (no loss) to 100 (total loss) [(5)]. The SALT score at the beginning, at every visit, and at the final stretch of the study, as well as the hair regrowth scale, were used to determine how well the treatment worked [(6)].

To evaluate the overall progress, the global evaluation score [(6)] was utilized, considering the density and extent of regrowth measured by the SALT Score: A0 indicates nothing has changed or additional loss, A1 indicates 1-24% regrowth, A2 indicates 25-49% regrowth, A3 indicates 50-74% regrowth, A4 indicates 75-99% regrowth, and A5 indicates 100% growth back. The following 6-point semi-quantitative score was used to assess the level of clinical improvement: RGS 0 (re-growth <10%), RGS 1 (11%-25%), RGS 2 (26%-50%), RGS 3 (51%-75%), RGS 4 (re-growth ≥75%), and RGS 5 (re-growth =100%), as per the Regrowth Scale (RGS) [(7)].

During each visit and follow-up, the patients were checked for evidence of hair regrowth using both clinical and dermoscopic methods. The iPhone 11 Pro Max's 12-megapixel camera was used to capture sequential digital photos (clinical and dermoscopic) of the areas of alopecia before the therapy started, during the treatment sessions, and at the conclusion of the treatment. Dermlite DL4™ was utilized to evaluate disease activity prior to and following treatment. Two separate investigators looked at the pictures.

Treatment Protocol

All patients applied topical anesthetic cream (Pridocaine® [lidocaine 2.5%/prilocaine 2.5%], GNP Pharmaceuticals) under occlusion for 30 minutes before the procedure.

The patients were divided into two groups randomly using a closed envelope method.

A Dermapen (Dr. Pen ULTIMA A6™) with disposable tips with thirty-six needles was used under aseptic conditions, featuring a 1.5 to 2.5 mm needle length. On AA patches, the Dermapen was moved four to five times in each of the following directions: diagonally, vertically, and horizontally. Pinpoint bleeding was the end point of the procedure. In **Group I** (NAC-MN), which included twenty-five patients, we applied N-Acetyl Cysteine solution (Rotacystiene® soln. 20% [200 mg/ml]) before, during, and after microneedling with dermapen. **Group II** (MN), which included twenty-five patients, had microneedling done alone. After the procedure, all patients were told to avoid washing their scalp for the rest of the day and to use topical antibiotic cream twice daily for 5 days afterward. Both groups participated in sessions every two weeks for a total of six sessions and were monitored for four weeks afterward.

Statistical analysis

We used SPSS v26 (IBM Inc., Chicago, IL, USA) to complete the statistical analysis. An unpaired Student's t-test was used to compare the two groups' quantitative parametric variables, which were reported as mean and standard deviation (SD). The Mann-Whitney test was used to look at quantitative non-parametric variables, which were shown as the median and interquartile range (IQR). Qualitative variables were represented as frequency and percentage (%) and analyzed using the chi-square or Fisher's exact test as appropriate.

Results

The mean (± SD) age was 32.96 (±13.02) years in Group I and 30.92 (±11.49) years in Group II. Regarding sex, 12 (48%) patients were males in Group I, and 13 (52%) patients were females, the same number found in Group II. Age and sex were statistically insignificant between the two groups. The duration of the alopecia areata, family history, recurrence, stress, and course were statistically not significantly different between the two groups. The number of lesions was statistically insignificantly different between the two groups. Dermoscopic examinations showed black dots, broken hair, and exclamation hair, which were statistically not significantly different between the two groups before treatment. Also, yellow dots and circular hair before treatment were not statistically different between the two groups. At the same time, after treatment, they significantly improved in Group I compared with Group II (*P* value = 0.010 and 0.012, respectively) (Table 1). Before treatment, Group I had a statistically significant amount of vellus hair (P value=0.029) compared to Group II. After treatment, Group II had a smaller amount of vellus hair (P value=0.002). Upright-growing hair before treatment was statistically insignificantly different between the two groups. All patients in both groups improved after treatment.

In Group I, black dots, yellow dots, broken hair, exclamation hair, vellus hair, circular hair, and upright-growing hair were statistically significantly improved after treatment compared to before treatment (*P* value < 0.05) (Figure 1).

In Group II, black dots, yellow dots, broken hair, vellus hair, and circular hair were statistically insignificantly different before and after treatment. Exclamation hair and upright-growing hair were statistically significantly improved after treatment compared to before treatment (*P* value < 0.05).

The Regrowth Score (RGS 5) was statistically significantly higher in Group I (n=15) at 60% compared to Group II (n=5) at 20%, with a *P* value of less than 0.001 (Table 2).

The SALT score before treatment was statistically insignificantly different between the groups. It became statistically significantly lower after treatment compared to before treatment in both Group II (Figure 2) (*P* value < 0.035) and Group I (Figure 3) (*P* value < 0.001) (Table 3).

Table 1. Dermoscopic examination of the studied groups

		Group I (n=25)	Group II (n=25)	P value
Black dots	Before treatment	24(96%)	21(84%)	0.345
	After treatment	9(36%)	16(64%)	0.089
P# compared to before treatment		<0.001*	0.197	
Yellow dots	Before treatment	13(52%)	12(48%)	0.773
	After treatment	1(4%)	9(36%)	0.010*
P# compared to before treatment		0.005*	0.566	
Broken hair	Before treatment	21(84%)	20(80%)	0.712
	After treatment	10(40%)	15(60%)	0.257
P# compared to before treatment		0.003*	0.217	
Exclamation hair	Before treatment	13(52%)	17(68%)	0.386
	After treatment	1(4%)	5(20%)	0.191
P# compared to before treatment		0.005*	0.001*	
Vellus hair	Before treatment	25(100%)	19(76%)	0.029*
	After treatment	8(32%)	22(88%)	0.002*
P# compared to before treatment		<0.001*	0.461	
Circular hair	Before treatment	5(20%)	9(36%)	0.344
	After treatment	22(88%)	13(52%)	0.012*
P# compared to before treatment		<0.001*	0.392	
Upright growing hair	Before treatment	8(32%)	5(20%)	0.520
	After treatment	25(100%)	25(100%)	-----
P# compared to before treatment		<0.001*	<0.001*	

* Significant as *P* value ≤ 0.05

Table 2. Regrowth Score (RGS) of the studied groups

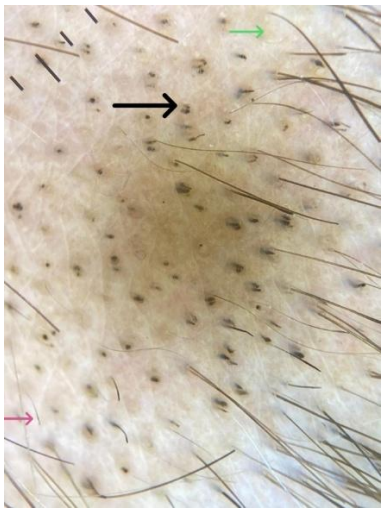
		Group I (n=25)	Group II (n=25)	*P* value
RGS	**RGS 2**	0(0%)	5(20%)	**0.050***
	RGS 3	1(4%)	7(28%)	**0.048***
	RGS 4	9(36%)	8(32%)	0.765
	RGS 5	15(60%)	5(20%)	**<0.001***

* Significant as *P* value <0.05 RGS: Regrowth score, RGS2 (26-50%), RGS3 (51-75%), RGS4 (>75%), RGS5 (100%).

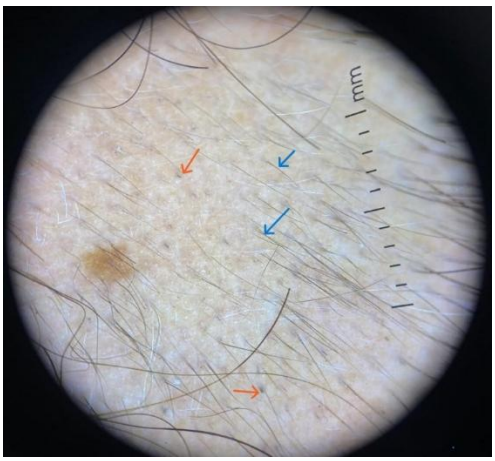
Table 3. SALT score of the studied groups

		Group I (n=25)	**Group II (n=25)**	***P* value**
SALT score	**Before treatment**	3.02±1.52	2.43±1.86	0.231
	After treatment	0.24 ±0.55	1.44±1.31	**0.001***
***P*# compared to before treatment**		**<0.001***	**0.035***	

* Significant as *P* value <0.05, SALT: Severity of Alopecia Tool.



(a)



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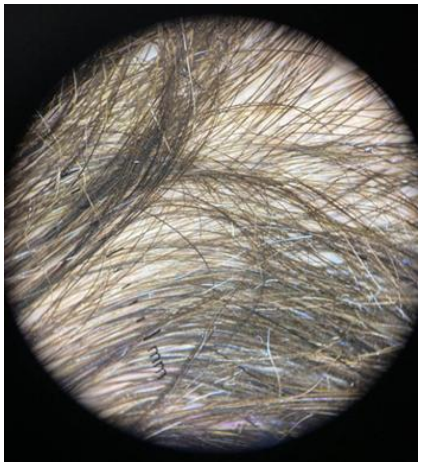

(c)

Figure 1. (a) Dermoscopy of alopecia areata before treatment shows black dots (black arrow), yellow dots (green arrow), and exclamation mark hair (red arrow). (b) Dermoscopy of alopecia areata after 4 sessions of NAC combined with MN shows upright growing hair (blue arrows) and black dots (orange arrows). (c) Dermoscopy of alopecia areata at the end of the study, one month after the last sixth session.

(a) (b)

Figure 2. Alopecia areata before (a) and after (b) the sixth session of treatment with MN.

(a) (b)

(C)

Figure 3. (a) Alopecia areata before treatment. (b) Alopecia areata immediately after a session of NAC combined with MN shows bleeding points. (c) scalp one month after the last sixth session.

Discussion

A comprehensive strategy to control AA is essential, incorporating topical and systemic medications, psychological therapy, and lifestyle modifications to achieve long-term remission of the condition. Although incomplete remission and relapses are frequent, recognized first-line treatment options include topical, intralesional, and oral corticosteroids; topical and oral minoxidil; cyclosporine; and various immunotherapy medications [8].

N-acetyl cysteine (NAC) has potent antioxidant activity and is an oxygen radical scavenger. NAC is a lately employed, safe, and easy-to-take over-the-counter supplement that is well-tolerated by most people and demonstrates some indication of efficacy for chronic hair and skin conditions [9].

Microneedles create multiple minor injury points on the skin's surface. This can help new blood vessels form, cells grow, and drugs get into the body quickly. Research indicates that microneedle acupuncture can induce the synthesis of Wnt proteins, specifically Wnt3a and Wnt10b, which have been demonstrated to turn on dermal papilla stem cells and promote hair development [10, 11].

Our study assessed the effectiveness and safety of microneedling combined with N-acetyl cysteine compared to microneedling alone for treating alopecia areata. This study was the first to use NAC as a local application through microneedling to treat AA.

Demographic information and personal traits of the studied groups showed that their age, sex, family history, and duration were not statistically significantly different, in line with Meguid et al. [12].

Dermoscopic examination of patients showed black dots, yellow dots, exclamation mark hair, and broken hair, which were statistically insignificant before treatment between the two groups. These findings are also reported in the study done in Egypt by Ahmed et al. [13].

Our study showed that group I (MN with NAC) was more effective, having statistically significant vellus hair, exclamation hair, upright-growing hair improvement, and the highest regrowth score of hair in AA. This is in line with El Sayed et al. [14], who found that N-acetyl cysteine (NAC) significantly improved most of the trichoscopic features of androgenetic alopecia [14]. In the current study, dermoscopic results were in accordance with the research of EL Mulla et al. [15], who reported improvements in dermoscopic findings in alopecia areata after treatment.

In the current research, the SALT score was statistically significantly lower in Group I treated with MN combined with NAC, in accordance with Popova and Mancuso [9], who thought about giving NAC to people with trichotillomania because it might help and has few adverse effects. They said that their patient had less desire to twirl his hair and that his hair had completely grown back after 6 months of treatment with NAC [9].

When microneedling is used alone in treating alopecia areata, our results showed clinical and dermoscopic improvements. This agrees with Aboeldahab et al. [16] and Abdallah et al. [17]. Giorgio et al. [18] found no effect from MN alone in AA subjects.

One limitation of this study is its small sample size and short follow-up period, which may limit how widely the findings can be applied and our understanding of long-term treatment efficacy and safety.

Conclusion

N-acetyl cysteine can be considered an effective treatment for alopecia areata when combined with microneedling as an adjunct to enhance the transepidermal delivery of active ingredients. Minimal or no side effects were observed after microneedling combined with NAC or microneedling alone. More research is

needed on a larger patient sample with AA using NAC as a topical treatment.

Author contributions

EMH: Conceptualized, designed and conducted the research, drafted, and submitted the article. MKMK: Cooperate in drafting and final revision of the article.

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Nil

Conflict of interest

There is no conflict of interest.

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