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The Efficacy of Microneedling with Minoxidil Solution 5% for theTreatment of Alopecia Areata

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Abstract

Background: Alopecia Areata (AA) is an autoimmune disease of the hair follicle that presents as non-scarring alopecia both in the scalp and non-scalp areas. Minoxidil allows more oxygen, blood, and nutrient to the follicle with the aid of microneedling in treatment of alopecia areata.**Aim of the study:** The aim of this study was to assess the efficacy of combined use of microneedling with Minoxidil solution 5% in treatment of alopecia areata.**Patients and methods:**This study included 30 patients with alopecia areata divided into 2 groups Group I included 15 patients treated with microneedling weekly for eight weeks. Group II included 15 patients subjected to combined therapy with Microneedling and topical minoxidil solution 5% to affected areas weekly for eight weeks. Severity of disease was assessed in each patient using the severity of Alopecia Tool Score (SALT score). At the 12^{th} week, the efficacy of therapy was assessed on the basis of absolute change in the SALT score and physician's assessment. The percentage of hair regrowth, derived from change in baseline SALT score, was also graded into 6 grades (A0 with no changes to A5 with 100% regrowth).**Results:** There was a highly statistically significant increase in percentage of complete hair regrowth (grade A5)after therapy in group 2 compared to group 1. There was also a highly statistically significant increase in frequency of complete responseto minoxidil combined therapy in group 2 compared to group 1. No side effects of therapy were recorded in both groups.**Conclusion:**The present study suggests that combination therapy of minoxidil with microneedling could be an effective, safe, and promising option for the treatment of alopecia areata.**Keywords:**Alopecia Areata (AA), Microneedling, Minoxidil.

1. Introduction:

Alopecia Areata (AA) is an autoimmune disease of the hair follicle that presents as non-scarring alopecia both in the scalp and non-scalp areas. The etiology of this disease remains unknown; however, a current hypothesis implicates T-cell-mediated autoimmunity that affects hair follicles, as well as the up regulation of inflammatory cytokines,in the pathogenesis of disease [(1)]. The severity ranges from focal (patch-type AA) to total scalp hair loss (alopecia totalis) to entire body hair loss (alopecia universalis).[(2)]

Although the exact pathogenesis remains elusive, AA is thought to have a multifactorial etiology

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described as an interplay of genetic predisposition and environmental exposures. In patients with genetic susceptibility, stress, infection, and micro trauma have been documented to decrease immunosuppressive cytokines that normally maintain the immune privilege of the hair follicle.(3)

Scalp Microneedling is a procedure in which various micro-channels are created in the skin which has help in penetration and absorption of various agents into the skin. Microneedling is a promising and effective therapy for the treatment of Alopecia.(4)

Minoxidil (2, 4-diamino- 6-piperidinopyrimidine-3-oxide) is primarily an antihypertensive which causes vasodilatation(5). It is a potassium channel opener which causes hyperpolarization of the cell membranes. Minoxidil stimulates proliferation at the base of the hair bulb and differentiation above the dermal papilla. It stops hair loss. Many mechanisms of action include vasodilatation, angiogenesis, enhanced cell proliferation, and potassium channel opening.(6)

By widening the blood vessels, minoxidil allows more oxygen, blood, and nutrient to the follicle. This may cause the follicles in telogen phase to be shed and replaced by thicker hairs in a new anagen phase.(7)

The aim of this work was to assess the efficacy of combined use of microneedling with Minoxidil Solution 5% versus microneedling alone in the treatment of alopecia areata.

2. Patients and Methods:

2.1. The current study was conducted as a randomized controlled trial.It included 30 AA patients of both sexes selected from the Outpatient Clinic of Dermatology, Venereology and Andrology Department, Zagazig University Hospitals, during the period from June 2020 to February 2021 after obtaining the approval of the institutional review board (IRB) of Zagazig University.

Patients were classified randomly into 2 groups (15 patients in each group) according to treatment modality used:

- Group 1: patients were subjected to therapy with microneedling weekly for eight weeks.
- Group 2: patients were subjected to combined therapy with Microneedling and topical minoxidil solution 5% to affected areas weekly for eight weeks.

2.2. Healthy persons with chronic recurrent AA resistant to other lines of therapy wereincluded in this study.

2.3. Exclusion criteria included systemic or topical therapy in last 6 months, systemic diseases as hypothyroidism, diabetes, liver or renal impairment, or other autoimmune diseases as psoriasis and vitiligo,pregnancy, and lactation.

2.4. The patients who met the inclusion criteria and were suitable candidates for the study have been subjected to:

I. Medical consent was taken from all patients after counselling the benefits and possible adverse events of the treatment before the first session**.**

II. History taking:

A Proper history was taken

Analysis of the complaint:

-Onset, duration, course,

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-Past history: It included history of surgery, fever, illness, stress, anemia, and autoimmune diseases.
-History of drug intake, irradiation, chemotherapy, history of previoustreatment (e.g.,minoxidil), allergy to previous treatment.
-Family history: history of similar conditions.

III. General medicalexamination.

IV. Detailed Dermatological examination:

1) Dermatological examination of scalp was done including:

- Site
- size
- Number of AA lesions
- Severity assessment by Severity of Alopecia Tool score (SALT score)

In SALT score the scalp is divided into 4 areas namely, Vertex-40% (0.4) of scalp surface area; right profile of scalp-18% (0.18) of scalp surface area; left profile of scalp-18% (0.18) of scalp surface area; Posterior aspect of scalp-24% (0.24) of scalp surface area. Percentage of hair loss in any of these areas is percentage of hair loss multiplied by the percent of surface area of the scalp in that area. SALT score is the sum of percentage of hair loss in all above-mentioned areas (Bhat et al., 2014).

- The disease severity was classified by SALT subclasses based on extend of scalp hair loss:

S0 = no hair loss

S1 = hair loss <25% of scalp

S2 = hair loss 25% - 49% of scalp

S3 = hair loss 50 – 74% of scalp

S4 = hair loss 75 – 99% of scalp

S5 = 100% hair loss

2) Dermatological Examination had been done for all.

V. Digital photography of the lesions of hair loss.

The Lesions were photographically documented for results evaluation, using a digital camera. The photographs were taken at weeks 0 (at start of therapy), 2, 4, 6, 8 with 2 weeks interval and re-evaluated after 12 weeks.

Procedure:

Microneedling was performed using an automated Microneedling pen (Ultima A6) equipped with a disposable tip cartridge containing 36 micro-needles, and we adjusted the needles to 1.5 mm in length with the maximal piston stroke speed.

After disinfection with alcohol solution, we applied the electric dermapen perpendicularly to the scalp, held it with light pressure for 3 seconds in circular manner over the affected area until mild erythema or pinpoint bleeding was noted which was considered as the end point of the procedure.

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Group 1:
Patients subjected to Microneedling weekly for eight weeks.
Group 2:
Patients subjected to combined therapy with Microneedling and topical minoxidil solution 5%. After Microneedling we applied 1 ml minoxidil mesotherapy on the affected areas and rub it gently then Microneedling again. The procedure performed weekly for 8 weeks.
After 12thweek, the efficacy of therapy was assessed in both groups and compared. on the basis of absolute change in the SALT score and the percentage regrowth derived from change in baseline SALT score.

Absolute change in SALT score = SALT score at baseline – SALT score after 12 weeks.
Percent scalp hair regrowth based on SALT score = 100× (Baseline SALT score − SALT score at 12 weeks)/ Baseline SALT score.
Assessment of percentage hair regrowth was graded into following 6 grades:

- A0 = no change or further loss of hairs
- A1 = 1–24% regrowth
- A2 = 25–49% regrowth
- A3 = 50–74% regrowth
- A4 = 75–99% regrowth
- A5 = 100% regrowth.[(8)]

2.6. Statistical analysis:
For data analysis, Statistical Package for Social Science (SPSS) version 24.0was used.The following tests were used. Chi square test,Mann Whitney test and Paired Wilcoxon test,the threshold of significance is fixed at 5% level (P-value): *P value of >0.05 indicates non-significant results. P value of <0.05 indicates significant results.

3. Results:
The mean age in Group 1 was 9.6 and in Group II 18.13. Regarding sex 60% of Group I were male, 40% in Group II were male. There were no statistical significance differences between the studied groups in age or sex distribution **(Table 1).**

The mean disease duration among Group I was 0.5 years while in Group II it was 0.85 years. The median salt score in all groups was 10 and also the median number of patches in all groups was 1. Most cases in all groups were S1(SALT score) (100% in Group I & 93.3% in Group II) also all lesions in Group I and Group II and was Patchy in type. Only 1 case in each group had previous treatment (minoxidil). There wasno statistically significant difference between the studied groups in clinical data of patients**(Table 2).**

In group I, 40% of patients after therapy showed hair regrowth of grade A2, 26.7% of grade A1, 20% of grade A3, 6.7% of grade A4 and 6.7% of grade A0. While in group II, 46.7% of patients showed hair regrowth of grade A5, 20% of grade A4, 20% of grade A2 and 13.3% of grade A0. There was a highly statistical significance increase in frequency of A5 response among Group II

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compared to Group I **(Table 3).**

In group I 6.7% of patients showed no response, 86.7% showed partial response and 6.7% showed complete response. While in Group II 13.3% was non responded, 20% were partially responded,66.7 %were completely responded. There was a highly statistical significance increase in frequency of complete response among Group II compared to Group I (p value 0.002*)**(Table 4).**

All cases in Group I & II had no side effects. There were no statistical significance differences between the studied groups in side effects of treatment **(Table 5).**

Table (1): Demographic data of the studied groups

	Variable	**Group I (M) (*n*=15)**		**Group II (M+M) (*n*=15)**		**KW**	**P**
Age: (years)	*Mean ± SD*	9.6 ± 10.7		18.13 ± 9.46			
	Median	6		12		2.56	0.28
	Range	4 - 47		7 – 33			NS
	Variable	**No**	**%**	**No**	**%**	**χ^2**	**p**
Sex:	*Female*	6	40	9	60	5	0.08
	Male	9	60	6	40		NS

Table (2): Clinical data of the studied groups.

	Variable	**Group I (M) (*n*=15)**		**Group II (M+M) (*n*=15)**		**KW**	**P**
Duration: (years)	*Mean ± SD*	0.55 ± 1.01		0.85 ± 1.31			
	Median	0.17		0.33		2.41	0.30
	Range	1 m – 4 y		1m – 5 y			NS
SALT score:(%)	*Mean ± SD*	9.27 ± 1.58		12.6 ± 10.27			
	Median	10		10		2.69	0.26
	Range	5 - 10		6 – 48			NS
Number of patches:	*Mean ± SD*	1.07 ± 0.26		1.47 ± 1.81			
	Median	1		1		3.67	0.16
	Range	1 - 2		1 – 8			NS
	Variable	**No**	**%**	**No**	**%**	**χ^2**	**p**
AGS:	*S1*	15	100	14	93.3		
	S2	0	0	1	6.7	5.34	0.50
	S3	0	0	0	0		NS
	S4	0	0	0	0		
Type:	*Patchy*	15	100	15	100	2.05	0.36
	Ophiasis	0	0	0	0		NS
Previous treatment:	*No*	14	93.3	14	93.3	0	1
	Minoxidil gel	1	6.7	1	6.7		NS

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Table (3): Response to treatment among the studied groups according to SALT score.

Variable		Group I (M) (*n*=15)		Group II (M+M) (*n*=15)		χ^2	P
		No	%	No	%		
Response:	*A0*	1	6.7	2	13.3		
	A1	4	26.7	0	0		
	A2	6	40	0	0	**27.1**	**0.003**
	A3	3	20	3	20		*
	A4	1	6.7	3	20		
	A5	0	0	7	46.7		

Table (4): Response to treatment among the studied groups

Variable		Group I (M) (*n*=15)		Group II (M+M) (*n*=15)		χ^2	P
		No	%	No	%		
Response:	*No*	1	6.7	2	13.3		
	Partial	13	86.7	3	20	**16.6**	**0.002**
	Complete	1	6.7	10	66.7		*

Table (5): Side effect to treatment among the studied groups

Variable		Group I (M) (*n*=15)		Group II (M+M) (*n*=15)		χ^2	P
		No	%	No	%		
Irritation:	*No*	15	100	15	100	2.05	0.36
	Yes	0	0	0	0		NS
Abnormal hair	*No*	15	100	15	100	-----	---
growth:	*Yes*	0	0	0	0		
Redness:	*No*	15	100	15	100	-----	---
	Yes	0	0	0	0		
Scale:	*No*	15	100	15	100	-----	---
	Yes	0	0	0	0		

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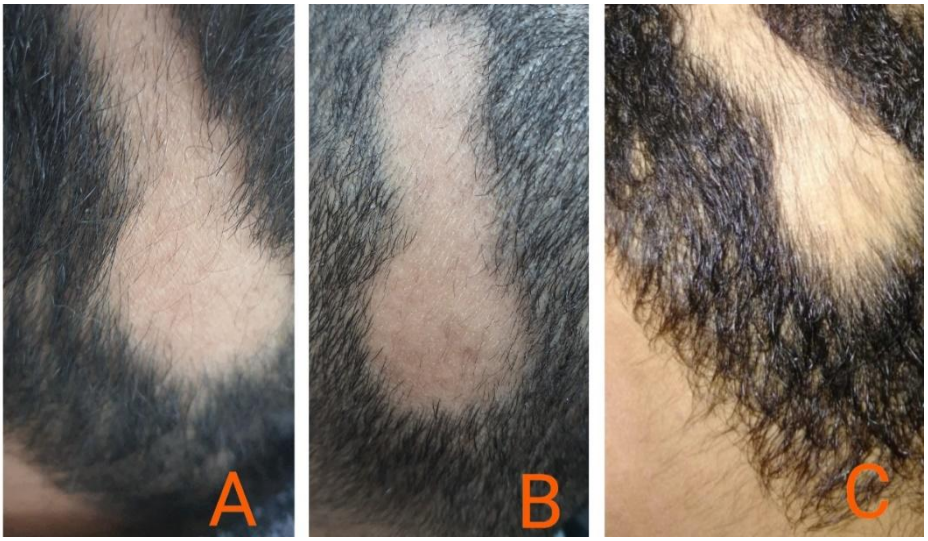

Photo (1) From Group I A: Alopecia areata before treatment, B: During treatment with Microneedling alone at 6thweek, C: After therapy showing no response.

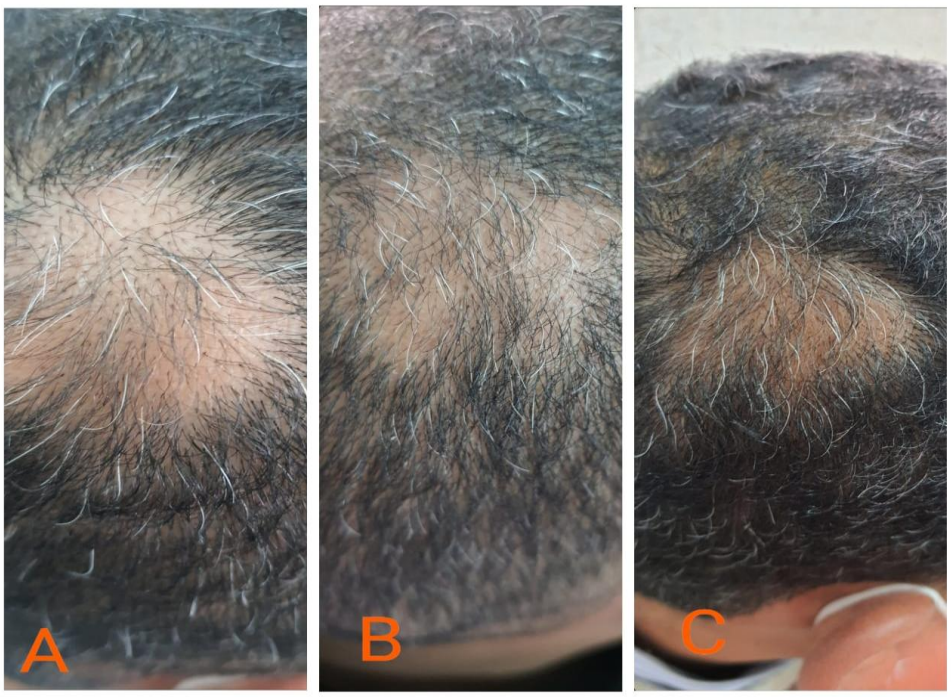

Photo (2) From Group I A: Alopecia areata before treatment, B: During treatment with Microneedling alone at 6th week, C: After therapy showing partial response.

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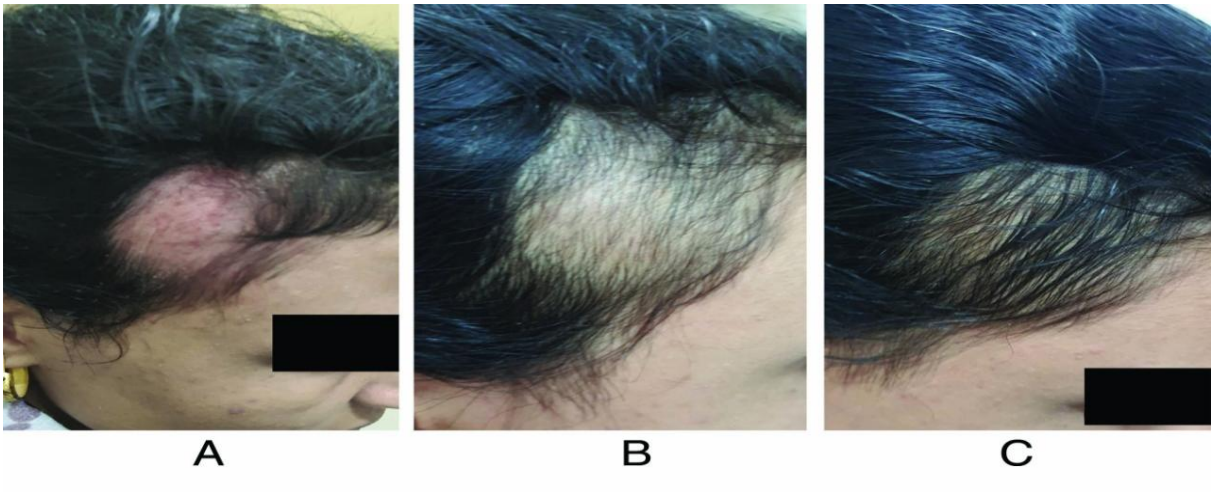

Photo (3) From Group II A: Alopecia areata before treatment, B: During treatment with Combined Microneedling with Minoxidil 5 % at 6th week, C: after therapy showing complete response.

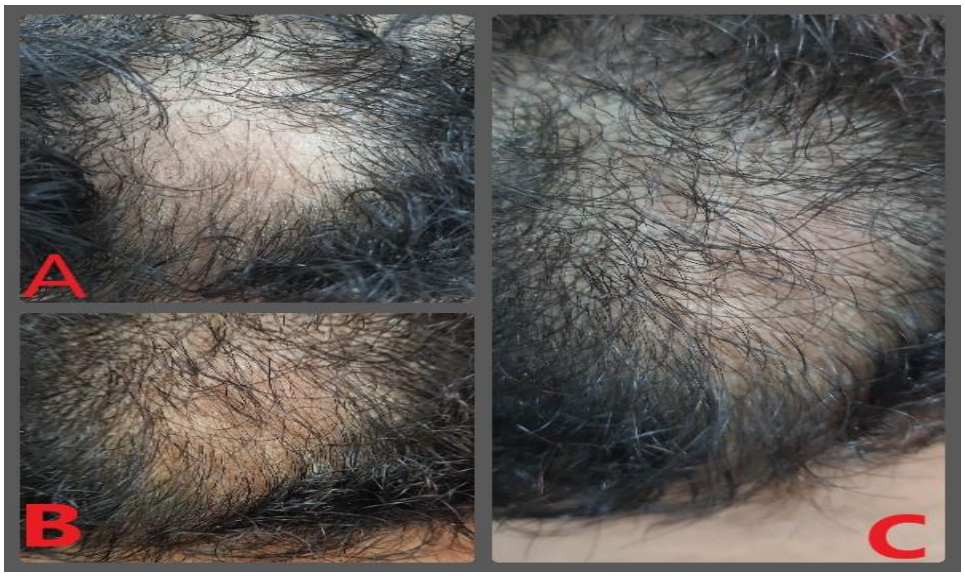

Photo (4) From Group II A: Alopecia areata before treatment, B: During treatment with Combined Microneedling with Minoxidil 5 % at 6th week, C: after therapy showing complete response.

4. Discussion:

Alopecia areata is an organ-specific T cell mediated autoimmune disease targeting hair follicles. Peribulbar lymphocytic infiltration impairing the normal hair cycle is the main pathophysiologic mechanism responsible for the disease process.perifollicular inflammatory infiltrate spares the bulge region of the follicle where follicular epithelial stem cells reside. Thus, in contrast to cicatricial alopecia, the inflammation does not interfere with the hair follicle integrity.[9]

The objective assessment of treatment efficacy of alopecia areata is very difficult and spontaneous remission is unpredictable, but if the affected area is patched, the hair may regrow spontaneously in many cases. None of the existing therapeutic options are curative or preventive.[10]

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Micro-needling is popularly used in the treatment of acne scars; recently it is also used in treatment androgenic alopecia The proposed mechanism of action is the stimulation of dermal papillae and stem cells. It causes release of platelet-derived growth factor, epidermal growth factors are increased through platelet activation and skin wound regeneration mechanism.(11)

Topical minoxidil solution, has been approved by Food and Drug Administration and Health Canada for the treatment of alopecia areata. Evidence for the effectiveness of using 3% minoxidil, twice daily, was shown in several studies. A dose response effect exists, with the 5% solution being more effective than the 2% solution.(12)

Treatment of alopecia areata is challenging as there are many therapies available which can induce hair growth but there is no proven therapy that alters the course of the disease and sustains remission. Prognosis in extensive and long-standing alopecia's is usually less favorable.(13)

Our study was aiming to assess the efficacy and safety of microneedling with minoxidil solution 5%, versus microneedling alone on hair growth in patients with alopecia.

In this study 86.7% of AA patients in group 1 showed partial response and only 6.7% showed complete response after microneedling alone. While in group 2, 66.7% of patients showed complete response after combined therapy with minoxidil 5%, with a highly statistically significant difference.

In agreement with these results, Chandrashekar and colleagues have used micro-needling with triamcinolone acetonide in the treatment of AA in two patients with patchy AA and have concluded that combination treatment can induce faster re-growth of hairs due to uniform and painless administration of the drug.(14)

As treatmentof hair loss with microneedling is still a relatively new procedure,a best practice has yet to be definitively determined. It is worth mentioning that this lack of standard procedure has a bearing on success of treatment. No side-effects have been reported so far in the literature, and microneedling appears to be quite safe.(15)

The results of the present study coincides with that reported by Malhotra and colleagueswho reported excellent response with Combined therapy of microneedling with minoxidil in 13.3% of patients compared to 6.7% with monotherapy with minoxidil. They also reported that combined therapy is a safe, simple, cost effective promising treatment option for alopecia patients.(16)

Dhurat and colleagues analyzed the results of weekly microneedling sessions used in conjunction with 5% minoxidil solution applied twice a day for 12 weeks. One hundred men with mild-to-moderate AGA, ages 20–35, were randomly assigned to the microneedling group (N = 50) or the control group (N = 50). After 12 weeks of treatment, the microneedling group showed significantly higher hair count (91.4 hairs per cm2) than the control group (22.2 hairs per cm2) (P = 0.039).(17)

In a 2016 study of 40 female patients with, hair growth following microneedling combined with 5% minoxidil monotherapy was studied. Hair growth was assessed at 12 and 28 weeks after treatment initiation. There was a significant increase in hair count and density following therapy by 48% experienced hair regrowth(18). While in our study 66.7% were completely responded. This difference in response may be due to decreased number of patients and duration of treatment in our study.

During our study, we found that all cases in Group I & II had no side effects. There were no statistical significance differences between the studied groups in side effects of treatment.

5. Conclusion:

This study demonstrated that use of microneedling and use of minoxidil 5% solution for the treatment of alopecia areata give best result with superiority of microneedling with minoxidil 5% solution over microneedling alone.

6. ConflictofInterest: Noconflictofinterest.

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