

Microneedling as a monotherapy in treatment of male androgenetic alopecia

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Introduction

Androgenetic alopecia (AGA) is the result of progressive, patterned hair loss that occurs when genetically predisposed individuals are exposed to androgens. The psychosocial impact of AGA may negatively affect patient's quality of life and can lead to personal social and job-related problems⁽¹⁾. Also; AGA can cause indirect physical harm to some patients, such as sunburn as a result of hair loss and exposure to ultraviolet light⁽²⁾. Moreover; AGA is reportedly associated with increased incidence of myocardial infarction, hypertension and hypercholesterolemia⁽³⁾.

Drug therapies for AGA approved by the FDA are limited to topical minoxidil and oral FIN with efficacy varies between 40% and 60%⁽⁴⁾. Multiple factors are implicated in the pathogenesis of AGA which involves not only DHT but also inflammation, genes, signalling pathway, stimulatory pathways like Wnt/B catenin, and growth factors⁽⁵⁾. The existing conventional therapies (i.e. FIN and minoxidil) fail to target all of them⁽⁶⁾.

Microneedling (MN) is a relatively new minimally invasive procedure involving controlled puncturing of the skin by rolling with miniature fine needles⁽⁷⁾. It showed efficacy in some dermatological conditions including post-acne scars⁽⁸⁾, other scars⁽⁹⁾, pigmentary disorders⁽¹⁰⁾, and as a method of drug delivery⁽¹¹⁾.

The demand for new treatment techniques for AGA is growing, various procedures like mesotherapy, MN, platelet rich plasma, low laser light therapy, and stem-cell therapy are under active investigation⁽¹²⁾. MN creates multiple microchannels and increases transdermal penetration of drugs, facilitating higher concentration in dermis⁽¹³⁾.

Scalp needling also stimulates blood flow around blood starved hair follicles and gently exfoliates dead skin cells⁽¹⁴⁾. Scalp MN also induces hair regrowth by the following: release of growth factors through platelet activation and skin wound regeneration mechanism, activation of hair follicle stem cells in the hair bulge area under wound healing conditions which is caused by MN, and overexpression of hair growth-related genes, vascular endothelial growth factors, β catenin, Wnt3a, and Wnt10 b as documented in animal studies⁽⁶⁾.

The use of MN in combination with minoxidil showed promising results in treatment of AGA⁽⁶⁾. Furthermore; the addition of MN to minoxidil and oral FIN improved AGA in patients who were resistant to minoxidil and oral FIN⁽¹⁵⁾. To the best of our knowledge; the use of MN as monotherapy hasn't been previously reported. This study was designed to evaluate the efficacy and safety of MN as a monotherapy in treatment of male AGA.

Patients and methods:

After approval of this study by Ethical and Research committees at Faculty of Medicine, Sohag University; 15 male patients complaining of progressive hair loss diagnosed as AGA were included. All patients assigned informed written consent.

Exclusion criteria

Exclusion criteria included patients with other forms of alopecia including telogen effluvium, alopecia areata, those with dermatological or systemic illness known to cause diffuse hair loss (as thyroid disorders or anemia), and patients received minoxidil, any hair growth promoters in the past six months or those underwent surgical hair transplantation.

Patients on hormonal, androgenic or anti androgenic medications cytotoxic, and inhibitors of CYP3A4 (ketoconazole, verapamil, diltiazem, cimetidine, ciprofloxacin), and those on anticoagulant medications (aspirin, warfarin and heparin) or have skin disease with Koebner's phenomenon were also excluded.

Methods:All patients were subjected to:

I- Initial evaluation

Personal history was reported including the age, occupation, marital status, smoking, and residency. History of hair loss was discussed with all patients including onset, course and duration of hair loss, site of hair loss, and use of hair care cosmetics (dyeing, bleaching, and straightening). History of other skin diseases, systemic diseases or any medications was documented. Family history of a similar condition was reported. Full general examination was done searching for any signs of anemia. Scalp examination was performed as regards any signs of inflammation, scales, erythema or scarring.

II- Evaluation of hair loss:

II.1- Pull test:After instructing the patient not to wash hair for 24 hours; grasping a small clump about 60 hairs in the index, middle and thumb was done, with pulling hairs gently but with firm pressure. The shed hairs were counted and positive test was reported as more than 6 hairs shed⁽¹⁶⁾.

II.2- Grading of AGA according to Norwood-Hamilton scale⁽¹⁷⁾.

II.3- Digital photography: The patients were photo documented before and after six months of treatment. A picture of the fronto-parietal region was obtained in each patient. Before the photograph was taken the patient's hair was combed in a consistent manner for each patient so that the balding area could be optimally viewed.

II.4- Trichoscopy: An epiluminescence digital microscope (compareview A/V; Version 1.5.09) was used in this study. Trichoscope has five magnification lenses of different magnification powers which are x15, x30, x 50, x150 and x200 folds. A magnification of (x 50) was used to detect the density of the hair follicles, vellus and

terminal hairs; while magnification of (x 200) was used to evaluate the caliber of the hair shaft.

The frontal area of the scalp of each patient underwent trichoscopic evaluation, before and six months after treatment (frontal area was defined as approximately 2 cm from the frontal hairline and 2 cm from the midline⁽¹⁸⁾). Trichoscopic images were taken at the same specific area in the frontal area of each patient.

III- Treatment procedues:Microneedling was done using dermapen.

Dermapen is auto-stamp motorized meso machine; it is a pen like instrument with a handle, a disposable needle cartridge, having 12 needles arranged in rows, and a power button to turn the machine on and off. It has guides to adjust needle length (turning the guide clockwise, the needle length will be longer ranging from (0.25 mm to 2 mm maximum).

Topical anesthesia with 4% lidocaine cream was carried out 30 minutes before the procedure to the frontal area of the scalp of each patient, after this period, the cream was removed with saline, and the antiseptis of the entire area to be treated was subsequently performed with alcoholic chlorhexidine. Then the area had been completely dried.

The affected area of the scalp was stretched and MN was carried out in vertical and horizontal directions for about four to five times, until mild erythema was noted. The used needle length was 1.25 mm.

Treatment schedule: 13 sessions were done for each patient according to the following schedule:

- ✓ Once every week for eight weeks (week 0, 1, 2, 3, 4, 5, 6, 7).
- ✓ Once every two weeks for one month (week 9, 11).
- ✓ Once every month for three months (week 15, 19, 23).

IV- Treatment assessment: Assessment was done monthly and one week after the last session (24th week) depending on:

IV.1) Grading scale: according to Norwood-Hamilton grading scale.

IV.2) Photographic assessment: Digital photos of the affected region were obtained from patients before starting treatment (baseline) and at the end of treatment .

IV.3) Phototrichoscope: All patients underwent trichoscopic evaluation. Hair images were taken at 50x and 200x fold magnifications at the same affected area in the scalp of each patient before and after six

months of treatment with (measurements of the hair density, hair thickness and terminal/vellus hair ratio).

IV.4) Patient's self-assessment (Hair growth questionnaire): Patients assessed their scalp hair at the end of the study using a validated hair growth questionnaire containing four questions on treatment efficacy and three questions on satisfaction with appearance ⁽¹⁹⁾ (Figure I).

Check appropriate box below

1. Since the start of the study, I can see my bald spot getting smaller

Strongly agree	1	Disagree	4
Agree	2	Strongly disagree	5
No opinion either way	3		

2. Because of the treatment I have received since the start of the study, the appearance of my hair is

A lot better	1	A little worse	5
Somewhat better	2	Somewhat worse	6
A little better	3	A lot worse	7
Same	4		

3. Since the start of the study, how would you describe the growth of your hair?

Greatly increased	1	Slightly decreased	5
Moderately increased	2	Moderately decreased	6
Slightly increased	3	Greatly decreased	7
No change	4		

4. Since the start of the study, how effective do you think the treatment has been in slowing down your hair loss?

Very effective	1	Not very effective	3
Somewhat effective	2	Not effective at all	4

5. Compared to the start of the study, which statement best describes your satisfaction with the appearance of:

	I am very satisfied	I am satisfied	I am neutral	I am dissatisfied	I am very dissatisfied
a) the hair line at the front of your head ?	1	2	3	4	5
b) the hair on top of your head ?	1	2	3	4	5
c) your hair overall ?	1	2	3	4	5

Figure I: Patient self-assessment questionnaire concerning changes in their scalp hair after treatment ⁽¹⁹⁾.

IV.5) Investigator assessment: The hair density in the fronto-parietal region was compared to that observed before treatment using a 7-point rating scale: greatly decreased (-3), moderately decreased (-2), slightly decreased (-1), no change (0), slightly increased (+1), moderately increased (+2), and greatly increased (+3)⁽²⁰⁾.

IV.6) Safety and tolerability assessment: Any side effects reported by the patient or noticed by the investigator was recorded.

Statistical analysis:

- ✓ Data was analyzed using STATA intercooled version 12.1.
- ✓ Numerical data were presented as mean and standard deviation (SD) values, for parametric numerical data, while Median and range for non-parametric numerical data.
- ✓ For parametric data: Paired t-test was used to assess the statistical significance of the difference between two means measured twice.

✓ For non-parametric data: Wilcoxon signed rank test was used assess the statistical significance of the difference of non-parametric variables measured twice

Results

The study included 15 male patients diagnosed as having AGA. The mean age \pm SD of the patients was 25.73 ± 4.27 years, with 10 (66.67%) of them from rural areas. Family history of AGA was positive in 8 (53.33%) of the patients. Most of the patients 13 (86.67%) showed gradual onset of hair loss and progressive course was reported in all patients with mean disease duration \pm SD was 4.33 ± 2.23 years. The highest prevalence of hair loss was in the frontal and vertex regions (53.33%). Only 2 patients (13.33%) had positive pull test and scales were found in 3 patients (20%).

There was small decline in hair density but with no significant difference between hair density at the baseline and at 6th month. There was no significant difference between hair caliber at the baseline and at 6th month. There was mild increase in terminal/vellus ratio, with no significant difference between terminal/vellus ratio at the baseline and at 6th month (Table 1).

Table 1: Results of phototrichoscope of the study population (n= 15) before and after treatment.

Variables	At baseline	After treatment	Change	Percent of change	*P value
Hair density:					
Mean \pm SD	189.07 \pm 143.1	180 \pm 130.48	[-9.07] \pm 30.30		
Median (range)	187.5 (6-467)	150 (12-410)	0.5 ([-87]-22)	-4%	0.65
Hair Caliber:					
Mean \pm SD	0.020 \pm 0.016	0.020 \pm 0.013	0.0003 \pm 0.015		
Median (range)	0.018 (0.001-0.05)	0.015 (0.004-0.045)	0.001 ([-0.027]-0.031)	3%	0.69
Terminal/vellus hair ratio:					
Mean \pm SD	2.72 \pm 3.88	2.89 \pm 5.06	0.17 \pm 1.40		
Median (range)	1.75 (0.14-15.4)	1.45 (0.13-20)	-0.005 ([-1.3]-4.6)	4%	0.73

* P value <0.05 was significant.

As regards the investigator assessment; 13/15 (86.67%) of the patients showed no change in hair density, one patient (6.67%) showed slight increase, and the last patient (6.67%) showed slight decrease. Results of the patient self-assessment questionnaire are shown in table 2. The only side effect was pain, which was reported in 10(66.67%) of the patients.

Table 2: Results of the patient self-assessment questionnaire in the study groups (n=15).

Variables	Frequency (Percentage)	Variables	Frequency (Percentage)
1) Bald spot getting smaller:		2) Appearance of hair:	
Agree	0	Somewhat better	0
No opinion either way	1 (6.67%)	A little better	2 (13.33%)
Disagree	7 (46.67%)	Same	10 (66.67%)
Strongly disagree	7 (46.67%)	A little worse	3 (20.00%)
3) Hair growth:		4) Slowing down hair loss:	
Greatly increased	0	Very effective	0
Moderately increased	0	Somewhat effective	0
Slightly increased	6 (40.00%)	Not very effective	2 (13.33%)
No change	7 (46.67%)	Not effective at all	8 (53.33%)
Slightly decreased	2 (13.33%)		5 (33.33%)
5) Satisfaction about hairline at the front of the head:		6) Satisfaction about hair on the top:	
Very satisfied	0	Very satisfied	0
Satisfied	0	Satisfied	0
Neutral	3 (20.00%)	Neutral	0
Dissatisfied	2 (13.33%)	Dissatisfied	10 (66.67%)
Very dissatisfied	10 (66.67%)	Very dissatisfied	5 (33.33%)
7) Hair overall satisfaction:			
Very satisfied	0		
Satisfied	0		
Neutral	0		
Dissatisfied	10 (66.67%)		
Very dissatisfied	5 (33.33%)		

Discussion

The presence of AGA has its negative effects on the patient's quality of life⁽¹⁾. As multiple factors are implicated in the pathogenesis of AGA and the existing conventional therapies (i.e. FIN and minoxidil) fail to target all of them; the demand for new treatment techniques for AGA is growing. MN is one of these techniques that showed promising results in treatment of male AGA^(6,15).

In the current study; there was statistically insignificant decrease in hair density with mean percentage of change (-4%) after treatment. This decrease can be taken as the "normal" hair loss with AGA, so patients go bald despite therapy. On the contrary; increased hair count was previously reported with use of MN in male AGA⁽⁶⁾. Authors found that MN along with minoxidil-treated group was statistically superior to minoxidil alone-treated group in promoting hair growth. Concerning terminal/ vellus ratio; there was 4% mean percentage of change, which was mild and not statistically significant. The minimal improvement noticed might be

attributed to stimulation of hair growth by the trauma which increases the blood supply to the HF, but it was minimal and not clinically or statistically significant

in men. The mean change in hair count after 3 months was significantly greater for the MN group compared to the minoxidil group (91.4 versus 22.2 respectively)⁽⁶⁾. This may be related to the value of MN as drug delivery method rather than mechanical effect. Concerning hair shaft diameter in the present study; there was minimal statistically insignificant increase with mean percentage of change (3%). The increase in the hair shaft diameter goes with the alleged role of trauma of MN in improvement of AGA. These results were consistent with a previous report of mild statistically insignificant increase in mean hair shaft diameter in patients receiving mesotherapy with saline, this goes with the alleged role of trauma of mesotherapy injection in improvement of AGA⁽²¹⁾.

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