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ORIGINAL CONTRIBUTION

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Effective combination therapy with high concentration of Minoxidil and Carboxygas in resistant Androgenetic alopecia: Report of nine cases

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Abstract

Background: Androgenetic alopecia (AGA) is widely characterized as the main reason of hair loss which most of the time it has been reported in adults regarding dermatological consultation. Also, it is broadly believed that the progressive miniaturization of hair follicles could be usually different at the age of onset.

Aims: Over the last decade, detecting and understanding newer genetic basis in AGA lead to provide better therapeutic approaches. We have highlighted on an evidence-based method to treat AGA whose incidence is increasing significantly in our country.

Patients/Methods: In this study, 9 adults with AGA including 5 women and 4 men, age range of 25-55 years, were treated with a combination of minoxidil (20%) by micro-needling and carboxytherapy mediated by needling. All cases had a normal physical development. Hair numbers (density) and diameter were calculated using trichograms before and after treatment. Hair growth was assessed by the pull test as well.

Results: Our results showed that combination of high concentration of minoxidil and carboxygas extremely can increase the level of hair growth.

Conclusion: Our treatment effects on the terminal follicles using needling make sticky follicles become progressively smaller as a result of mechanical forces.

KEYWORDS

Androgenetic alopecia, carboxytherapy, minoxidil, needling

1 | INTRODUCTION

Androgenetic alopecia is genetically induced by androgens following excess male hormones called dihydrotestosterone (DHT). It is also termed pattern baldness that affects mainly men but also involves women.[1] In the past, the pathogenesis of androgenetic alopecia (AGA) was not evidently found and people only had one choice to apply cosmetics and just live with it.[1] By the time, recent advances revealed new areas of AGA in terms of genetics, molecular basis, and pathophysiology resulting in effective treatment modalities. It is important to note that in addition to one's genetic background, there are lots of other reasons causing AGA including food, stress autoimmune response, allergies, inflammation, poor diet, chemotherapy, hormonal imbalance, or direct physical tension on the hair follicles.[2] Accordingly, the significance of understanding and treating this situation is extensively growing, as it is different for each individual. As usual, hair loss is an undesirable event at any age, as almost for everyone it absolutely matters how looking good. Therefore, an accurate and timely diagnosis

is essential for a successful treatment. Over the last decade, different approaches were studied for hair loss treatment.[3,4] However, in the face of the range of available treatments, alopecia is a complex situation and no single treatment provides a perfect solution. In this report, we attempt to present a novel combination therapeutic approach (high concentration of minoxidil and carboxygas) to provide a prompt increase in the rate of hair growth in the topic of AGA with emphasis on getting the advantage of needling tactic. All the patients reported here showed remarkable improvements not only regarding hair regrowth in a short time but also lasting for a long term.

2 | METHODS

2.1 | Patients and treatment

The study was performed in Jordan Clinic, Tehran University of Medical Sciences, Tehran, Iran. In this study, 9 adults with AGA including 5 women and 4 men, age range of 25-55 years, were treated with carboxytherapy mediated by needling (gauge 27) and immediately after that with minoxidil (20%) by micro-needling in the same area. In all patients, a strong family history of AGA was observed.

The onset of AGA is not probable to be observed in patients without abnormal androgen levels. Additionally, endocrine assessment and a follow-up were completed per case. Patients received treatment one time monthly for a total of 4 sessions. While treating the scalp with carboxytherapy is not mostly painful, and in an anesthesia is not essential, the patient may describe a crackling or creeping sensation during the procedure.

Hair numbers (density) and diameter were counted by trichograms before and after treatment (Figures 1, 2). The pull test was performed as well (Figure 3). Pictures were obtained before and 3 months after the treatment to assure the authenticity of the results. Informed consent was gained from all patients prior to admission in the study.

2.2 | Trichograms

The joining of a line extending cranially from the lateral angle of an eye (right or left) and a line joining both ears coronally was marked with tattoo on the scalp, and the circle 2 cm in diameter centered on this mark was shaved. PowerShot 450 digital camera (Canon, Tokyo, Japan) was used for the TrichoScope image recording. The number of hairs within a circle of 11 mm in diameter (area, 95 mm^2) placed on the tattoo was counted and documented as data. Trichograms were made before treatment and at 1 and 3 months after the final treatment.

2.3 | Statistical analysis

Data are informed as mean ± SD. Statistical analysis was prepared in Prism 8.0 (GraphPad Software Inc, 2007, San Diego, Calif., USA) and Microsoft Excel 2013. Differences between the groups were computed by one-way ANOVA and Student's *t* test. *P*-value less than .05 was considered statistically significant for all tests.

3 | RESULTS

3.1 | Increasing number of hair (hair density)

Numbers of hairs were accurately counted using trichograms in the same area of the same patient before and after treatment (Figures 1). The hair density significantly increased after treatment in the patients (both male (n = 4) and female (n = 5)) (Figure 2A): 249 ± 3 and 178 ± 5 vs 110 ± 3 for 1 and 3 months after treatment vs before treatment in female patients and 217 ± 3 and 145 ± 5 vs 90 ± 3 for 1 and 3 months after treatment vs before treatment in male patients. Also, the results showed that hair density in women significantly more increased in compare to men (Figure 2B).

3.2 | Combination therapy increases hair diameter

As shown in Figure 3, A, the hair diameter increased significantly in all patients after treatment (1 and especially 3 months after the treatment) (91.9 ± 2.3 μ and 77 ± 2.1 μ vs. 53.2 ± 2.5 μ for 1 and 3 months after treatment vs before treatment in female patients and 74.5 ± 2.1 μ and 57.5 ± 1.7 μ vs. 46.5 ± 2 μ for 1 and 3 months after treatment vs before treatment in male patients) (Figure 3B). Significant variation was observed between males and females (Figure 3, B).

3.3 | Combination therapy and pull test

The results of the pull test displayed a significant reduction in the number of extracted hair following combination therapy. We could notice that the hair became stronger at 1 and 3 months after treatment (Figure 4A). Indeed, the values of the pull test in the control group ranged between 4 and 6; however, after treatment they were markedly decreased (0.80 ± 0.1 and 1.2 ± 0.3 vs. 4.2 ± 0.4 after treatment vs before treatment in female patients and 0.90 ± 0.1 and 1.4 ± 0.3 vs. 5.1 ± 0.4 after treatment vs before treatment in male patients). In addition, the results showed no significant differences between female and male patients (Figure 4B).

4 | DISCUSSION

In AGA, increased levels of DHT or susceptibility to the effects of DHT, cause to a shortened anagen phase of the hair cycle, miniaturization of the hair follicle, and final hair loss. There are many recognized treatments for hair loss, from topical uses (such as minoxidil), oral medications (such as cyproterone acetate, finasteride, spironolactone), to

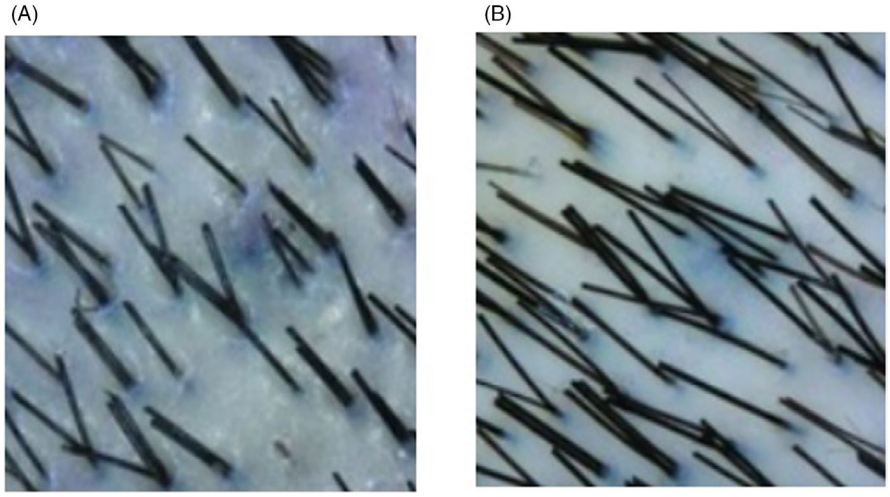

FIGURE 1 TrichoScope images of a 28-year-old male patient. A, Before treatment. B, 3 months after the treatment

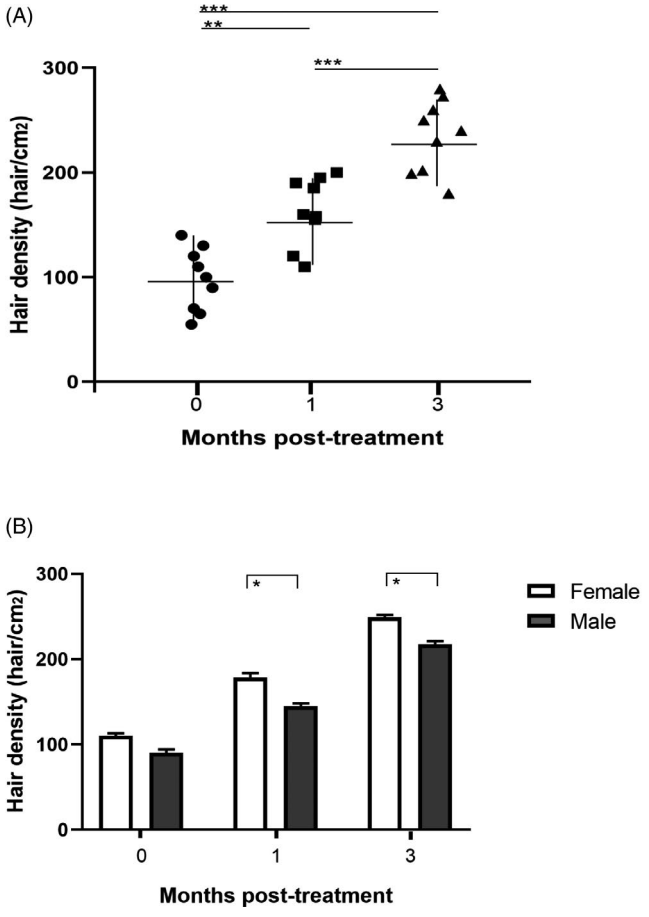

FIGURE 2 Difference between hair density of patients before and 1 or 3 months after the treatment. A, Whole population. B, Variation between males and females. ***$P < .0001$, **$P < .001$, *$P < .05$

injectable cures (such as platelet-rich plasma, stem cell treatments), surgical procedures, and many other molecules and techniques currently undergoing further research. However, in the face of the range of available treatments, alopecia is a complex situation and no single treatment provides a perfect solution.[3,4]

We found that combination therapy with high concentration of minoxidil and carboxygas promotes hair regrowth in androgenic alopecia. Micro-needling was firstly discovered in 1970 to be extensively effective to open the pore of the skin causing the easier drug delivery.[5] The microneedle technology has been used in several health-related fields. Their utilization in drug and vaccine delivery and determination of biomarkers has been reported.[5] Microneedles are applied in therapeutic uses and are manufactured by materials such as polymer (polyglycolic acid (PGA), poly-lactide-co-glycolide acid (PLGA), poly-L-lactic acid (PLA), chitosan), metal (steel, titanium, nickel), silicon, glass, carbohydrates (trehalose, sucrose, mannitol), and ceramic. However, new thicker hair growth at the hairline of the stage II alopecia androgenetica patient was shown after 3 months of last carboxytherapy.[6] Other case studies on male pattern baldness stage IV-A showed the signs of regrowth of hair after carbon dioxide injection during three treatment sessions at 4-week intervals. Also, no side effects were reported.[6] After 3 weeks of carboxytherapy in alopecia areata patient, the regrowth of normal hair was informed.[6] In the other study, the whole scalp of the alopecia totalis patient was injected with carbon dioxide (by a 30-gauge needle) and after two weeks hair regrowth was observed.[6] Another study informed hair regrowth ranging from minimally recognizable hair to an appreciable restoration of pigmented, larger terminal hair in three androgenic alopecia patients after using 5% minoxidil (12 months). Regrowth response related to the serum minoxidil blood levels was also observed in the patients with androgenic alopecia.[7] Another study reported that minoxidil as a direct vasodilator can reduce blood pressure in the resistant hypertension persons with unsuccessful therapy with multidrug regimens. However, it is important to mention that the effects of minoxidil can be restricted by an increase in pulse rate and/or sodium (and water) retention. The largely annoying side effect of minoxidil on hypertrichosis may limit its use, mainly among women, and a specialist of hypertension should most likely become involved in the patient's care. There is, however, a place for minoxidil in resistant hypertension treatment.[8] Finasteride, as usual medication for male pattern hair loss, has been accompanying with persistent sexual side effects. In addition, depression has also been reported

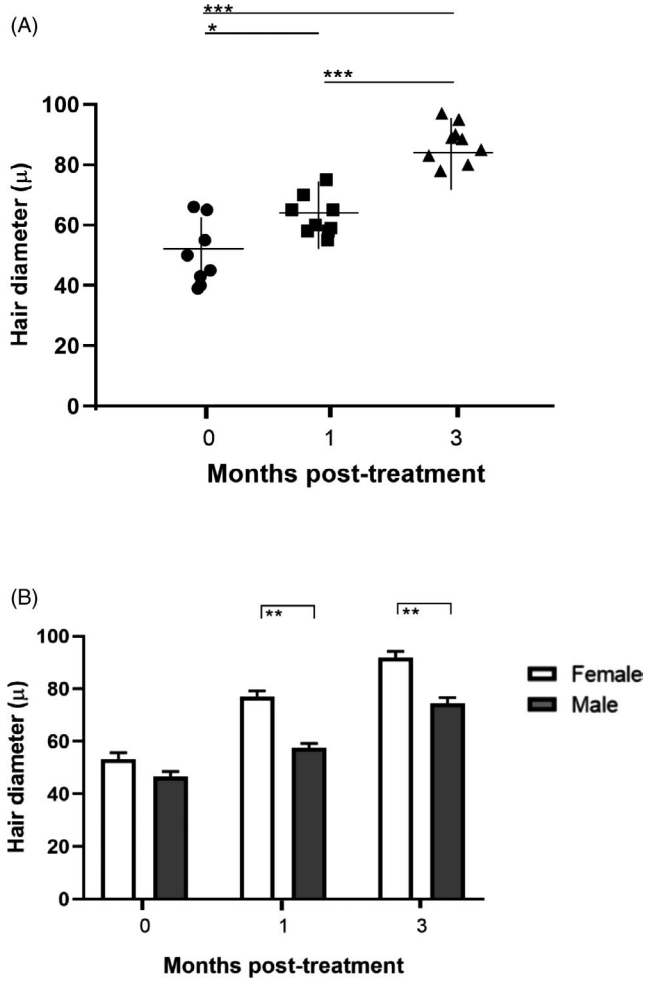

FIGURE 3 Difference between hair diameter of patients before and 1 or 3 mo after the treatment. A, Whole population. B, Variation between males and females. ***$P < .0001$, **$P < .001$, *$P < .05$

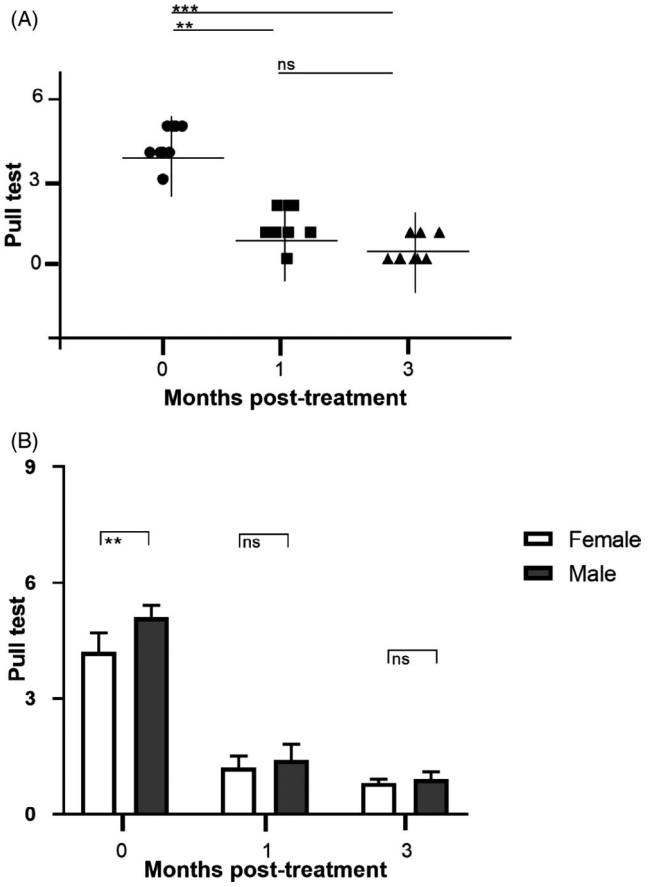

FIGURE 4 Pull test results' comparison before and after 1 and 3 mo after the treatment. A, Whole population. B, Variation between males and females. ***$P < .0001$, **$P < .001$, ns: nonsignificant

when finasteride 1 mg is used as the drug.[2] Androgenetic alopecia in both women and men has affected by topical 2% and 5% minoxidil a vasodilator medication. The 5% minoxidil was more effective (a 40% greater response rate) than the 2% when used twice a day for 1 year.[9] However, the mechanism that it increases hair growth is not completely understood. Minoxidil can open a potassium channel, triggering hyperpolarization of cell membranes, and can also act as a vasodilator, so, by opening potassium channels and widening blood vessels, it allows more blood, oxygen, and nutrients to the follicle.[9,10] So, this can cause shedding of follicles in the telogen phase, generally soon to be substituted by new, thicker hairs in a new anagen phase. However, in this method, it is mentioned that applied regularly (once or twice daily) is needed, for hair grown to be sustained. For topical formulations, the most common adverse reactions are limited to allergic contact dermatitis and irritant on the scalp. Additionally, another study addressed an uncommon adverse effect of finasteride (at a dose of 1 mg/day) that was associated in a 38-year-old androgenic alopecia man with painless hematuria and hematospermia during treatment.[10] In contrast, another study concluded that finasteride in a male androgenic alopecia has proved to be reasonably safe and effective in the therapeutic management. However, literature data inform several endocrine imbalances persuading different adverse effects such as mild sexual dysfunction and moderate depressive symptoms.[11] Another case presented that it is important to evaluate more cautiously the necessity of injecting filler into the hair-bearing area for lifting purpose. This procedure may cause foreign body granulomatous reaction, which may result in hair loss at the injection region.[12] Our combination therapy method is based on the relationship between the administration of carboxygas and minoxidil (20%). Following administration of carboxygas using needling technique at the same time, the terminal sticky follicles were mechanically unglued and detached to cause a better local blood circulation. It is necessary to point out those areas under the exposure of better and more carboxygas had a higher rate of hair growth which can confirm that needling also plays a crucial role to provide the availability of carboxygas. However, carboxytherapy is a very safe, well-tolerated, quick, and straightforward in-clinic procedure that can be considered as a standalone treatment or as adjunctive with other therapies to enhance growth results. Consequently, medical therapy for AGA with the use of topical solutions such as minoxidil or the medication of carboxygas can help to spread public

awareness and stimulated the search for other medical approaches to the treatment of AGA resulting in an intense change to organize and transmit the available knowledge about these procedures.

5 | CONCLUSION

While AGA is considered as the most common cause of hair loss, still little is known about its prevalence, clinical features, and response to treatments in the adult and pediatric population. More importantly, an effective and long-term medication should be limited to fewer side effects. In this report, our observation could suggest and confirm that combination therapy using needling is a well-tolerated therapy in androgenic alopecia patients over long periods considering the less possible side effect.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

ETHICAL STATEMENT

The authors state that the patient has given their informed consent for the photographs and details.

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