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High-Intensity Focused Ultrasound Application to the Scalp to Improve Androgenetic Alopecia in an Adult Woman

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Abstract

Androgenetic alopecia (AGA) is an ordinary type of hair loss that affects both men and women. Diverse treatment modalities have been developed and performed to improve AGA, and recently, energy-based devices (EBDs), including low-level laser therapy (LLLT) and fractional radiofrequency (FRF), also joined the ranks of AGA treatment. High-intensity focused ultrasound (HIFU) is one of the noninvasive EBDs and can apply a focal stimulation to the target region, putatively inducing different bioreactions in tissues and cells like LLLT and FRF. However, regarding HIFU treatment for hair loss or AGA, the authors' understanding is significantly limited. Accordingly, this case study was conducted to examine the possibility of HIFU-driven AGA treatment. HIFU was irradiated to the affected areas on the scalp (250–300 shots per session) along with hair gel (10–16 mL per session) in a female AGA patient, and a total of 6 sessions were carried out for 24 weeks. The visual observation revealed that the overall hair condition of the patient had much improved at the seventh visit (> 90%) compared with baseline. Notably, the quantitative assessment demonstrated that the hair density increased up to 115 hairs/cm^2 at the sixth visit, and the hair loss area (1.3 cm diameter) gradually declined and then completely disappeared at the seventh visit. Regarding safety, there were no adverse events and almost no pain during the study period. Therefore, these results indicate that HIFU is highly effective and safe in AGA treatment, implying that HIFU can be another option for AGA. Further studies are currently warranted to elucidate detailed mechanisms of how HIFU improves AGA or other types of hair loss.

Key Words: Androgenetic alopecia, hair follicle, hair loss, hair regrowth, HIFU, stem cell

Hair loss is a prevalent condition that occurs in both men and women, having a marked impact on their psycho-social aspects. A cross-sectional survey revealed that more than half of the 75 patients often or sometimes felt embarrassed and reported a negative influence on their self-esteem.[1] A systematic analysis demonstrated that hair loss, specifically androgenetic alopecia (AGA), is associated with moderate impairment of health-related quality of life and emotions.[2]

AGA is a common type of hair loss and is characterized by a progressive decrease in the anagen phase, resulting in hair miniaturization and loss. Notably, it was found that the cause of AGA is strongly associated with hormonal and genetic factors, and the prevalence of AGA varies depending on age, sex, and region.[3,4] For females, AGA affects ~5.6% to 12% of women in Korea and China.[5,6] In white women, it affects ~14% to up to 56% of the population in the postmenopausal period.[7] These studies indicate that hair loss or AGA is a crucial personal and social burden and exerts great influence even on women.

Meanwhile, with growing attention to less-invasive or non-invasive treatments for hair loss, energy-based devices (EBDs) are currently highlighted. Specifically, low-level laser therapy (LLLT) is a popular treatment modality for AGA. Clinical trials have been conducted for more than 10 years, verifying the efficacy and safety of LLLT for AGA treatment.[8] More recently, a fractional radiofrequency (FRF) device has dived into this field, showing less hair shedding, fuller hair, and faster hair growth in AGA patients (18 females, 7 males).[9] The exact mechanisms of the 2 modalities have not yet been elucidated, but they provide important clues that photo-biomodulation or thermal energy is much useful to stimulate hair structures and cellular signal pathways that are involved in hair regrowth.[8–10] In this regard, high-intensity focused ultrasound (HIFU) can be another treatment option for

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This study was conducted in compliance with the principles set forth in the Declaration of Helsinki.

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AGA. HIFU is a representative noninvasive method that can apply focal stimulation or deliver thermal energy to the target area inside the skin by adjusting the focal depth. Using HIFU, we can target more precisely critical regions associated with hair regrowth.[11] However, in terms of hair loss restoration, HIFU technology has rarely received public attention. Accordingly, the present study reports one case of HIFU-induced hair regrowth in a female AGA patient.

CASE PRESENTATION

A 44-year-old woman presented to the dermatology clinic with hair loss. At admission, the height and weight of the patient were 159.2 cm and 55 kg (BMI < 22 kg/m^2, normal), respectively. The patient had never previously received any treatment related to hair loss, did not smoke, and did not have any underlying diseases. After diagnosis, the patient was found to have AGA due to the hair loss pattern shown in the crown and frontal areas on the scalp[7] (Figs. 1A and 2A). According to the basic and specific (BASP) classification, this patient belonged to the LF1 type.[12] Importantly, to avoid potential risks associated with HIFU, typically including erythema, swelling, and tingling, the patient was fully guided and consulted regarding adverse events of HIFU and alternative modalities for AGA.

The patient's hair was photographed with the area 15 cm away from the middle of the eyebrows toward the crown as the center. The photo showed a circular pattern of hair loss with a diameter of 1.3 cm in the crown (a red circle, diameter 1.3 cm) and a frontal hair thinning in the parting area (a red rectangle, length 9 cm; Fig. 1A). The hair density of the patient was measured with a hair analyzer (A-ONE Tab, Bomtech co. ltd.), and the diameter and length of the hair loss areas were measured using Image J program. Next, AGA treatment was conducted using a HIFU device (Ultraformer MPT, Classys Inc.) and 2 cartridges, including Ultra F 2.0 mm (focal depth: 2.0 mm, 5.5 MHz) and Ultra Booster 1.5 mm (focal depth: 1.5 mm, 7 MHz; Classys Inc.), along with hair gel containing multiple ingredients helpful for hair growth and scalp health (GroHair, Classys Inc.). Specifically, HIFU was irradiated to the parting and crown areas where hair loss occurred (Fig. 1A) at an energy level of 0.2 J/cm^2 and the Micro-Pulsed (MP) mode. Notably, Ultra F and Ultra Booster cartridges were used for the parting and crown areas, respectively. Upon the Ultra F cartridge, HIFU energy is irradiated in a straight line, and thus, this cartridge is suitable for straight hair loss. In contrast, the Ultra Booster cartridge is suitable for circular hair loss since HIFU energy is irradiated in a circular shape in this cartridge. The MP mode is an advanced HIFU irradiation technology designed to create continuous and uniform thermal coagulation points (TCPs), allowing the delivery of HIFU energy in a linear pattern by minimizing the gap between TCPs. Importantly, this mode reduces pain and discomfort that may occur during HIFU procedure, improve procedure speed, and cover a larger area. This hair treatment was performed at each visit (once every 4 weeks, a total of 6 times for 24 wk), and photo-taking and hair measurements were carried out before treatment and at each visit (a total of 7 times for 28 wk). A total of 250 to 300 shots (230–250 shots for the parting area, 50–70 shots for the crown) were irradiated for one session. The hair gel was applied to the affected areas appropriately, 10 to 16 mL for one session.

Preferentially, the patient was visually assessed at each visit, finding that the affected areas were almost fully restored at the seventh visit (Figs. 1A and 2C). Based on the visual scoring scale for hair growth (no change = 0 point, improved by $< 30\%$ = 1, improved by 30%–50% = 2, improved by 50%–70% = 3, improved by 70%–90% = 4, improved by $> 90\%$ = 5), the hair growth was achieved in $> 90\%$ of the affected area at the seventh visit (Fig. 2C), corresponding to the maximum score (5 points). In effect, the diameter of the circular hair loss area was reduced at the third (1.1 cm) and seventh visits (0 cm) compared with baseline (1.3 cm). Furthermore, the hair density (hairs/cm^2) of the patient was gradually increased until the fourth visit and showed large differences from the fifth visit (110 hairs/cm^2) compared with baseline (20 hairs/cm^2; Fig. 1B). Regarding safety, pain intensity was rated using Numeric Rating Scale (NRS) immediately after treatment (scoring pain intensity on a 0–10 basis: 0 = no pain, 1–3 = mild pain, 4–6 = moderate pain, and 7–10 = severe pain). The mean NRS score was 0.33 ± 0.21 (almost no pain) in all sessions, which fully recovered within 10 minutes. In addition, the patient did not report any adverse events related to this procedure during the study period. Collectively, these results indicate that this HIFU device has an excellent efficacy and safety profile in treating AGA.

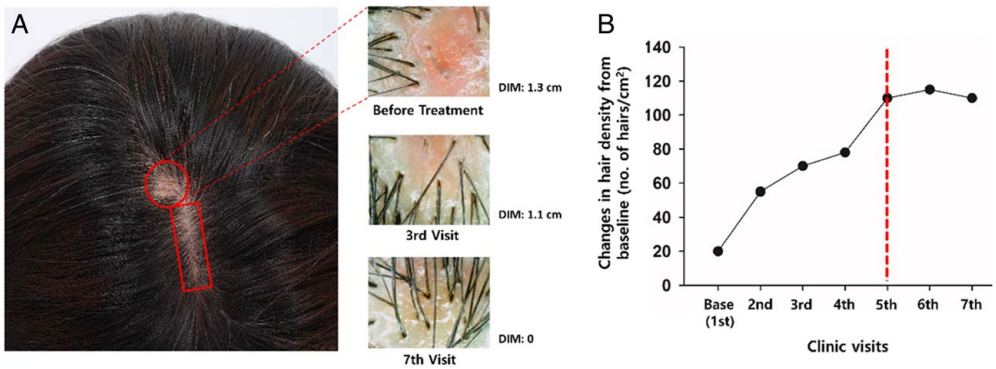

FIGURE 1. Increased hair density after HIFU treatment. There are 2 affected areas on the scalp of the patient, circular (a red circle, 1.3 cm diameter) and straight (a red rectangle, 9 cm length) types. The diameter of the affected area (a red circle) declined at the third visit (1.1 cm) and completely disappeared at the seventh visit (A). The hair analyzer investigation showed that the hair density of the patient dramatically increased from the fifth visit (B). DIM indicates diameter.

FIGURE 2. Significant improvements in AGA after HIFU treatment. Consistent with the results of hair density, the overall hair condition improved after treatment. In particular, the visual observation showed that AGA was restored ~by 30% at the third visit (B) and then almost fully improved at the seventh visit (C) compared with before treatment (A).

DISCUSSION

The present case study reported one case of HIFU-induced hair regrowth in a female AGA patient. There were dramatic increases in hair density from the fifth visit (4 wk after the fourth HIFU treatment). The visual observation revealed that the 2 affected areas were almost fully restored at the seventh visit. Importantly, this HIFU treatment also showed an excellent safety profile, finding that there were no adverse events and almost no pain.

AGA has great influence on the hair growth and condition in both men and women. A diversity of modalities have been tried to improve AGA or hair loss, and LLLT and FRF were introduced relatively recently for AGA patients.[13] It is unclear exactly how the 2 modalities improved hair loss, but the following mechanisms have been proposed. It was hypothesized that the bio-stimulatory function of LLLT activates stem cells located in the hair bulge, which play a key role in the regeneration of hair follicles. In addition, LLLT may trigger intracellular signaling pathways, including extracellular signal-regulated kinase (ERK) and Wnt/β-catenin, crucial for hair growth cycle regulation, resulting in the reentry and extension of the anagen phase.[14–16] Similarly, FRF is assumed to upregulate growth factors involved in hair regeneration and elongation.[17] Also, it was reported that FRF can cause minimal micro-wounds in inner skin layers, potentially stimulating Wnt signaling and stem cells, which in turn facilitates tissue repair and hair follicle regeneration.[9]

Given the previous results and speculations, it can be assumed that HIFU also stimulates multiple factors deeply engaged in hair regeneration and hair growth cycle. In the present case study, cartridges with 1.5 mm or 2.0 mm focal depth were used at a low energy level (0.2 J/cm^2). The focal locations are adjacent to the hair bulge where most of hair follicle stem cells reside, accordingly, this HIFU irradiation potentially stimulates the stem cells, and then it might contribute to the increase in hair density (Fig. 1A, B). Second, HIFU can cause minimal micro-wounds to the focal area like the FRF system. Interestingly, the stem cells are also activated in response to wound stimulation. In effect, wounding triggers toll-like receptor 3 (TLR3)—signal transducer and activator of transcription 3 (STAT3), which in turn upregulates fibroblast growth factor 9 (FGF-9) in γδ T cells. And importantly, FGF-9 activates Wnt/β-catenin pathway in both epithelial and mesenchymal cells, which greatly affects hair follicle induction and morphogenesis. The Wnt/β-catenin pathway is one of the most crucial molecular signaling factors in the entire hair regrowth pathway, especially in terms of the wound-induced hair follicle neogenesis (WIHN). Moreover, this pathway drives the expression of sonic hedgehog (SHH) and bone morphogenetic protein 4 (BMP4) in the epithelium, initiating hair follicle formation.[18] Third, HIFU can induce blood-vessel widening by increasing temporarily local temperature around the target area.[19] This thermal effect improves blood flow, which may promote nutrient transport and ultimately hair regrowth. Lastly, this HIFU procedure was conducted combined with hair gel application. The hair gel contains numerous ingredients and nutrients that can improve the condition of scalp and hair. Growing evidence demonstrates that ultrasound-mediated acoustic waves improve transdermal or intradermal drug delivery,[20] suggesting that HIFU may promote drug (hair gel) penetration into the skin. In effect, the 2 cartridges, Ultra F 2.0 mm (5.5 MHz) and Ultra Booster 1.5 mm (7 MHz), vibrate the contacting and surrounding skin tissue 55,000 and 70,000 times per second, respectively, which in turn opens a diffusion pathway where the ingredients of the hair gel can easily penetrate. Thus, it facilitates transdermal hair gel penetration, putatively contributing to hair regrowth. Collectively, it can be speculated that these mechanisms are all involved in the increased hair density and the ameliorated overall hair condition in the patient.

CONCLUSION

Hair loss has a significant impact on our daily lives and emotions. In this respect, hair loss is closely associated with self-esteem as well as psycho-social burdens in the society. Historically, a great number of struggles and efforts have been dedicated to improving hair loss or AGA. Some of these have performed well, but still have limitations. This case study reports a noninvasive focal stimulation by HIFU for AGA treatment for the first time, showing that the hair density and overall hair condition of the patient much improved with no adverse events and pain. Therefore, it suggests the possibility that HIFU can be introduced as another option for AGA treatment. In addition, this study encourages further research to unveil specific modes of action about HIFU-driven hair loss treatment in animals, and it is hoped that clinical

studies will be conducted in patients with AGA or other types of hair loss.

REFERENCES

[1] Adamowicz R, Załęcki P, Dukiel A, *et al*. Association between androgenetic alopecia and psychosocial disease burden: a cross-sectional survey among polish men. Dermatol Res Pract 2022;2022:1845044.

[2] Huang CH, Fu Y, Chi CC. Health-related quality of life, depression, and self-esteem in patients with androgenetic alopecia: a systematic review and meta-analysis. JAMA Dermatol 2021;157:963–70.

[3] Katzer T, Leite Junior A, Beck R, *et al*. Physiopathology and current treatments of androgenetic alopecia: going beyond androgens and antiandrogens. Dermatol Ther 2019;32:e13059.

[4] Nestor MS, Ablon G, Gade A, *et al*. Treatment options for androgenetic alopecia: efficacy, side effects, compliance, financial considerations, and ethics. J Cosmet Dermatol 2021;20:3759–81.

[5] Wang TL, Zhou C, Shen YW, *et al*. Prevalence of androgenetic alopecia in China: a community-based study in six cities. Br J Dermatol 2010;162:843–7.

[6] Paik JH, Yoon JB, Sim WY, *et al*. The prevalence and types of androgenetic alopecia in Korean men and women. Br J Dermatol 2001;145:95.

[7] Starace M, Orlando G, Alessandrini A, *et al*. Female androgenetic alopecia: an update on diagnosis and management. Am J Clin Dermatol 2020;21:69–84.

[8] Egger A, Resnik SR, Aickara D, *et al*. Examining the safety and efficacy of low-level laser therapy for male and female pattern hair loss: a review of the literature. Skin Appendage Disord 2020;6:259–67.

[9] Verner I, Lotti T. Clinical evaluation of a novel fractional radiofrequency device for hair growth: fractional radiofrequency for hair growth stimulation. Dermatol Ther 2018;31:e12590.

[10] Pillai JK, Mysore V. Role of low-level light therapy (LLLT) in androgenetic alopecia. J Cutan Aesthet Surg 2021;14:385–91.

[11] Bachu VS, Kedda J, Suk I, *et al*. High-intensity focused ultrasound: a review of mechanisms and clinical applications. Ann Biomed Eng 2021;49:1975–91.

[12] Lee WS, Ro BI, Hong SP, *et al*. A new classification of pattern hair loss that is universal for men and women: basic and specific (BASP) classification. J Am Acad Dermatol 2007;57:37–46.

[13] Galadari H, Shivakumar S, Lotti T, *et al*. Low-level laser therapy and narrative review of other treatment modalities in androgenetic alopecia. Lasers Med Sci 2020;35:1239–44.

[14] Faghihi G, Mozafarpoor S, Asilian A, *et al*. The effectiveness of adding low-level light therapy to minoxidil 5% solution in the treatment of patients with androgenetic alopecia. Indian J Dermatol Venereol Leprol 2018;84:547–3.

[15] Gentile P, Garcovich S. Advances in regenerative stem cell therapy in androgenic alopecia and hair loss: wnt pathway, growth-factor, and mesenchymal stem cell signaling impact analysis on cell growth and hair follicle development. Cells [Internet] 2019;8:466.

[16] Liu J, Xiao Q, Xiao J, *et al*. Wnt/β-catenin signalling: function, biological mechanisms, and therapeutic opportunities. Signal Transduct Target Ther 2022;7:3.

[17] Yoon SY, Kim KT, Jo SJ, *et al*. Induction of hair growth by insulin-like growth factor-1 in 1,763 MHz radiofrequency-irradiated hair follicle cells. PLoS ONE 2011;6:e28474.

[18] Vasserot AP, Geyfman M, Poloso NJ. Androgenetic alopecia: combing the hair follicle signaling pathways for new therapeutic targets and more effective treatment options. Expert Opin Ther Targets 2019;23:755–1.

[19] Ashar H, Ranjan A. Immunomodulation and targeted drug delivery with high intensity focused ultrasound (HIFU): principles and mechanisms. Pharmacol Ther 2023;244:108393.

[20] Jeong WY, Kwon M, Choi HE, *et al*. Recent advances in transdermal drug delivery systems: a review. Biomater Res 2021;25:24.