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Hair Growth Booster Effects of Micro-Needling with Low-Level Led Therapy and Growth Factors on Subjects Treated with Finasteride®

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Abstract: A procedure based on Microneedling (MND) with Low-Level Led Therapy (LLLT) and Growth Factors (GFs) could be a booster for hair re-growth (HRG) in patients assuming Finasteride®. The study examined the clinical outcomes of a multicentric, observational, retrospective, case-series investigation in which MND with LLLT and GFs was applied to patients suffering from androgenic alopecia (AGA) who were prescribed Finasteride®. Twenty-one patients were initially enrolled, of which seventeen males were classified in stage II–VI by the Norwood–Hamilton scale, and four females were classified in stage II–III by the Ludwig scale. One male patient was excluded after screening (exclusion and inclusion criteria evaluation). Twenty patients were analyzed, of which ten patients' hair growth has stalled after taking Finasteride®, and ten patients did not achieve good results from Finasteride®. HRG assessment was evaluated with photography, physician's, and patient's global assessment scale, in addition to standardized phototrichograms during a short follow-up: T0—baseline, T1—20 weeks (wks). A statistically significant improvement in HRG ($p = 0.0822$) and an increase in hair density of 19 ± 2 hairs/cm^2 at T1 after 20 wks (20 wks vs. 0 wks) in the targeted area over baseline (74 ± 2 hairs/cm^2 at T1 versus 55 ± 2 hairs/cm^2 at baseline) were reported and described as encouraging results. The effectiveness of MND with LLLT and GFs use was demonstrated in patients whose hair growth stalled after taking Finasteride® and in patients who did not achieve good results from Finasteride®.

Keywords: hair growth; hair growth finasteride; low-level LED therapy; microneedling in hair growth; finasteride and micro-needling; regenerative plastic surgery; plastic surgery

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1. Introduction

The first step to approach hair diseases is to collect the anamnesis from the patient and perform a careful physical and instrumental examination via trichograms. Several kinds of alopecia and hair loss (HL) have been described but androgenetic alopecia (AGA) is the most frequent, shooting eighty percent of men and forty percent of women, producing both a male pattern of hair loss (MPHL) and a female pattern hair loss (FPHL) [1–4]. In the last years, the scientific advancement in the alopecia field aimed to develop new procedures to improve hair re-growth (HRG) in subjects suffering from HL and from AGA. The amount of studies that analyzed the impact of autologous procedures such as Human Follicle Stem Cells (HFSCs), Platelet-Rich Plasma (PRP), and home-hand-made procedures such as microneedling (MND) with low-level LED Therapy (LLLT) and growth factors (GFs) in AGA has interestingly increased [1–9]. PRP effectiveness in patients suffering from AGA (mild to moderate) has been displayed [1–5] as the encouraging effect of HFSCs [6,7], while recently, the home-hand-made procedures based on the MND with LLLT and GFs have been tested [8,9].

Several biomolecular mechanisms have been postulated to explain the usefulness of these strategies in HRG. The activation of mitochondria found in the stem cells of the hair bulge is the biomolecular mechanism trough it LLLT acts with the aim stimulate HRG. Cytochrome c-oxidase (CCO), which is located in the membrane of mitochondria, is the target chromophore of red light that initiates mitochondrial respiration. The stimulation of cellular migration, proliferation, and oxygenation by reactive oxygen species (ROS) and adenosine triphosphate (ATP) subsequently stimulate hair development [10]. Commonly, the purpose of using PRP, HFSCs, and LLLT is to stimulate human dermal papilla cells proliferation through the stimulation of the ERK pathway and Wnt/-catenin signaling [1–9,11].

Numerous treatments have been used to treat AGA, but only oral Finasteride® (a selective 5-alpha-reductase inhibitor), topical Minoxidil® in 2% and 5% solutions or foams, and low-level LED/light/laser therapy have received FDA approval to treat MPHL [12,13]. The FDA has also given approval to Minoxidil® 5% foam for FPHL. Finasteride® is demonstrated as useful in treating MPHL, but it has mostly failed to treat FPHL [14]. Additionally, Finasteride® may determine anomalies in the external genitalia of male fetuses and for this reason is unsuitable for use by premenopausal women [15]. In contrast, daily administration of Finasteride®1 mg has been demonstrated to improve hair density (HD) by increasing anagen phase transition in MPHL hair follicles and stimulating a 70% decrease in serum dihydrotestosterone (DHT) levels [16,17]. HD-significant improvements may require up to one year of taking Finasteride® and male users may experience libido reduction, which may persist after the medication is discontinued [18]. Additionally, the results obtained may be, in some cases, stagnating or ineffective.

LLLT may represent a potentially effective treatment for both MPHL and FPHL, either as monotherapy or concomitant therapy with MND and GFs as previously reported [8,9]. Combination treatments of LLLT, MND, and GFs with Finasteride®, may act synergistically to enhance hair growth, and this new concept represents the hypothesis introduced by the presented work.

This research aimed to describe the potential booster impact of LLLT with MND and GFs on HRG in patients suffering from AGA whose hair growth has stalled after taking Finasteride® and those that did not achieve good results.

2. Methods

2.1. Study Overview

A multicentric (Italy and Korea), retrospective case-series observational study was conducted following internationally consented ethics in clinical research and the guidelines reported in the Declaration of Helsinki [19]. A high-quality assessment has been performed based on the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist [20]. All subjects enrolled, signed, and understood detailed informed consent before any treatment, about the applied protocol, including the benefits, risks, and alternative strategies. This paper has been the object of a research contract between the author P.G. and the "Tor Vergata" University, approved by Rectoral Decree (R.D) n. #1467/2017, continued in associate professor contract R.D #13489/2021 released on March 16, 2021, by the University "Tor Vergata", Rome, Italy.

2.2. Data Analysis

The collected data were independently analyzed in Korea, by Dr. Ki Mun-Sang (K.M-S) (NB clinic representative director, NB Hair Implant Center, Ansan, Republic of Korea), while in Italy by Prof Pietro Gentile (P.G.), (Associate Professor of Plastic Surgery, University "Tor Vergata", Rome, Italy).

Information on patients (age, sex, race, HL degree), interventions (identification of targeted area (TA) and use of topical drugs, Minoxidil®, Finasteride®, PRP, retinoids), outcomes (hairs parameters as hair density (HD), hair count (HC), and hair thickness (HT)), session frequency (days/week), treatment duration, and related follow-up (20 weeks (wks)) were gathered by the two authors, screened, and finally identified as eligible data,

according to the inclusion and exclusion criteria evaluation. Any disagreements on the harvested data were settled by a consensus among K.M.-S. and P.G.

2.3. Endpoint Definition

The differences in HD between the baseline (T0), and LLLT with MND and GFs treatments, in patients whose hair growth stalled after taking Finasteride® and in patients who did not achieve good results from Finasteride®, at 20 wks (T1), evaluated with instrumental trichoscopy, was the primary outcome. The *p*-value indicated LLLT with MND and GFs as being an effective treatment option when compared to the baseline.

Clinical effects, as secondary outcomes, were analyzed through objective- and subjective evaluation. The objective evaluation was carried out by the physicians, while subjective evaluation was carried out by the subjects.

The physicians' evaluation regarded clinical, and global picture analysis, applying a scale of 6 degrees (excellent, good, discreet, enough, poor, inadequate).

The subject self-evaluation was carried out by applying the same 6 degrees previously reported. The factors/variables that have been also considered during outcomes analysis were itchings, slight redness, slight numbness of the treated part, and headache.

In terms of outcomes, the type of measurement was described (photo-trichograms, hair analysis software, and physician hair analysis), as well as the primary endpoints (HC, HD, HT, vellus count and density, anagen percentage, telogen percentage, and physician global assessment), and the secondary endpoints (subject satisfaction and their global assessment).

2.4. Protocol Based on Hairgen Booster® Application

Hairgen Booster® (DTS MG Co., Ltd., Seoul, Korea, #B108-147) (Figure 1) permitted the scalp injection of GFs contained in a 1 vial of hair solution (HR3 Matrix Hair Solution Alpha®-DTS MG Co., Ltd., Seoul, Korea, #B108-147) via MND stamp (HR3 Matrix Hair Stamp®-DTS MG Co., Ltd., Seoul, Korea, #B108-147) twice weekly for 20 wks (T1) for a total of 40 applications. The device has been applied directly by the patients using their own hands and seeing themselves in the mirror.

Figure 1. Hairgen Booster® (DTS MG Co., Ltd., Seoul, Korea, #B108-147) with HR3 Matrix Hair Solution Alpha® (DTS MG Co., Ltd., Seoul, Korea, #B108-147) and HR3 Matrix Hair Stamp® (DTS MG Co., Ltd., Seoul, Korea, #B108-147).

The device permitted contextually, the LLLT emission and sterile infiltration (0.22 µm) by MND stamp of a solution (HR3 Matrix Hair Solution Alpha®-Repilosome-EPH1) containing several GFs represented by human growth hormone (GH), Epidermal Growth Factors (EGF), Vasoactive Intestinal Peptide (VIP), and several polypeptides (sh-Polypeptide-7, sh-Oligopeptide-1, sh-Polypeptide-71), Glycerin, Lecithin, Polysorbate 60, Sodium Citrate, Citric Acid, Phenoxyethanol, Water.

The device emits red and blue lights. The red light with a wavelength of 640 nm, improving cell metabolism, blood circulation, and nutrition supply to capillaries. The blue light with a wavelength of 423 nm diminishes the sebaceous glands and the fat of the scalp, additionally activating the keratin (highly resistant fibrous proteins) present in the hair shaft, stimulating its cellular micro-environment influencing the robustness of hairs [9].

2.5. Patients Assessment

This multicentric case series has been performed involving 21 patients affected by MPHL and FPHL, treated since March 2020, aged 21–73 years, of which 17 males were classified in stage II-VI by the Norwood–Hamilton scale, and 4 females were classified in stage II-III by the Ludwig scale. 1 male patient, that contextually performed PRP injection, was excluded after screening (exclusion and inclusion criteria evaluation).

20 patients were finally analyzed of which 10 patients (8 males-4 Caucasian/4 Asians and 2 females-1 Caucasian/1 Asian) whose hair growth has stalled after taking Finasteride® (Figures 2A and 3A), and 10 patients (8 males-4 Caucasian/4 Asians and 2 females-1 Caucasian/1 Asian) did not achieve good results from Finasteride® (Figure 4A).

Table 1. Characteristics of subjects suffering from MPHL and FPHL taking Finasteride®.

Paitents	Sex	Hamilton-Norwood Degree	Ludwig Degree	Targeted Area	Age	Race	Situation
1	Male	IV	-	Frontal, temporal, parietal, vertex	69	Caucasian	Hair growth stalled
2	Male	II	-	Frontal, temporal,	21	Asian	No good results
3	Male	VI	-	Frontal, temporal, parietal, vertex	73	Caucasian	Hair growth stalled
4	Male	III	-	Frontal, temporal, parietal	29	Asian	No good results
5	Male	IV	-	Frontal, temporal, parietal, vertex	68	Caucasian	Hair growth stalled
6	Male	III-vertex	-	Frontal, temporal, parietal, vertex	46	Asian	No good results
7	Male	III-vertex	-	Frontal, temporal, parietal, vertex	44	Caucasian	Hair growth stalled
8	Male	VI	-	Frontal, temporal, parietal, vertex	46	Asian	Hair growth stalled
9	Male	IV	-	Frontal, temporal, parietal, vertex	41	Caucasian	No good results
10	Male	III-vertex	-	Frontal, temporal, parietal, vertex	31	Asian	Hair growth stalled
11	Male	V	-	Frontal, temporal, parietal, vertex	50	Caucasian	No good results
12	Male	III	-	Frontal, temporal, parietal	34	Asian	Hair growth stalled
13	Male	IV	-	Frontal, temporal, parietal, vertex	59	Caucasian	No good results
14	Male	II	-	Frontal, temporal	39	Asian	Hair growth stalled
15	Male	V	-	Frontal, temporal, parietal, vertex	62	Caucasian	No good results

Table 1. *Cont.*

Paitents	Sex	Hamilton-Norwood Degree	Ludwig Degree	Targeted Area	Age	Race	Situation
16	Male	V	-	Frontal, temporal, parietal, vertex	62	Caucasian	Hair growth stalled
17	Female	-	II	Frontal, parietal, temporal	58	Caucasian	No good results
18	Female	-	III	Frontal, parietal, temporal, vertex	49	Asian	No good results
19	Female	-	II	Frontal, parietal, temporal	69	Caucasian	Hair growth stalled
20	Female	-	III	Frontal, parietal, temporal, vertex	50	Asian	Hair growth stalled

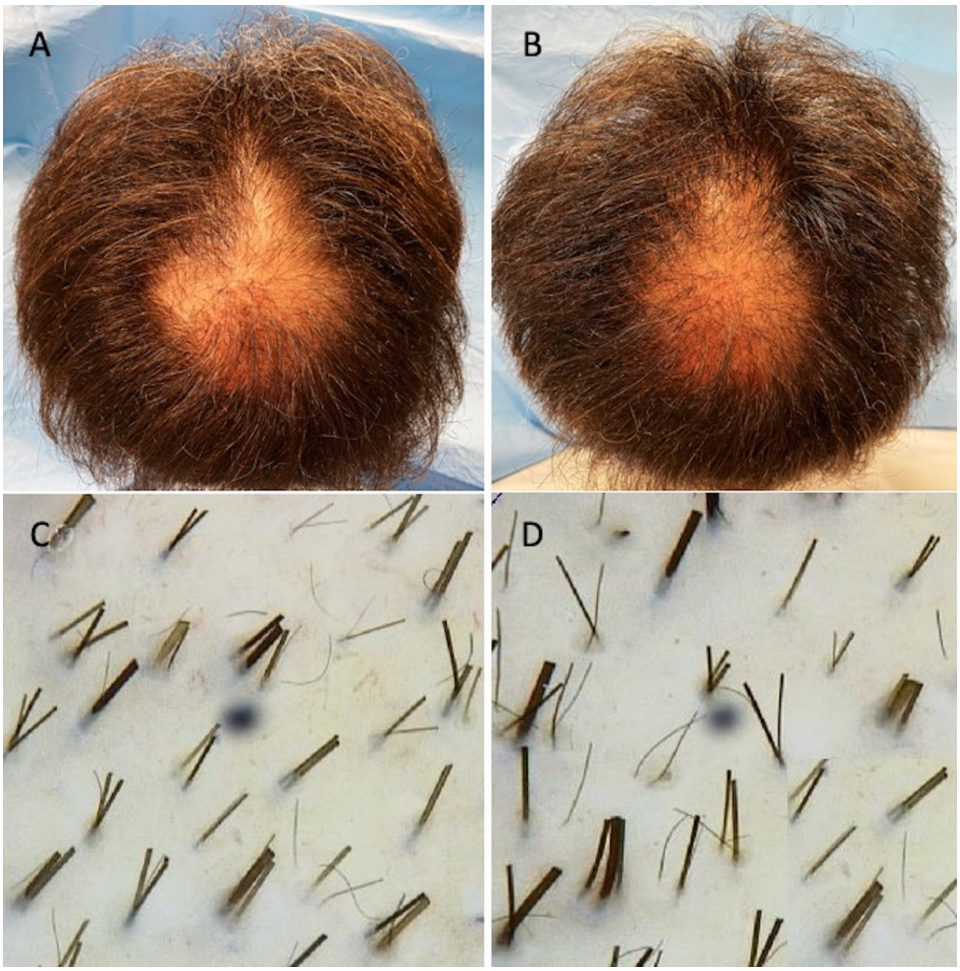

Figure 2. Caucasian 44-year-old male patient affected by MPHL of III-vertex degrees according to Norwood Hamilton scale (indicated as patient 7 in Table 1), whose hair growth has stalled after taking Finasteride® treated with Hairgen Booster® protocol. (**A**) Pre-operative view of the scalp, with HL localized in the frontal, temporal, parietal and especially vertex area; (**B**) post-operative view at T1 20 wks after treatment with detail of HRG in vertex area. (**C**) Trichoscan digital image analysis was performed by Fotofinder at T0 in an area demarcated by semipermanent tattoo (blue di metilene), where the pre-operative HD in the TA was 180.5 ± 5 hairs/cm^2 and proportions of telogen and anagen hairs were 38.8% and 61.2%, respectively; (**D**) at T1 20 wks post-operation, HD was 199 ± 5 hairs/cm^2, and proportions of telogen and anagen hairs were 54.6% and 45.4%, respectively.

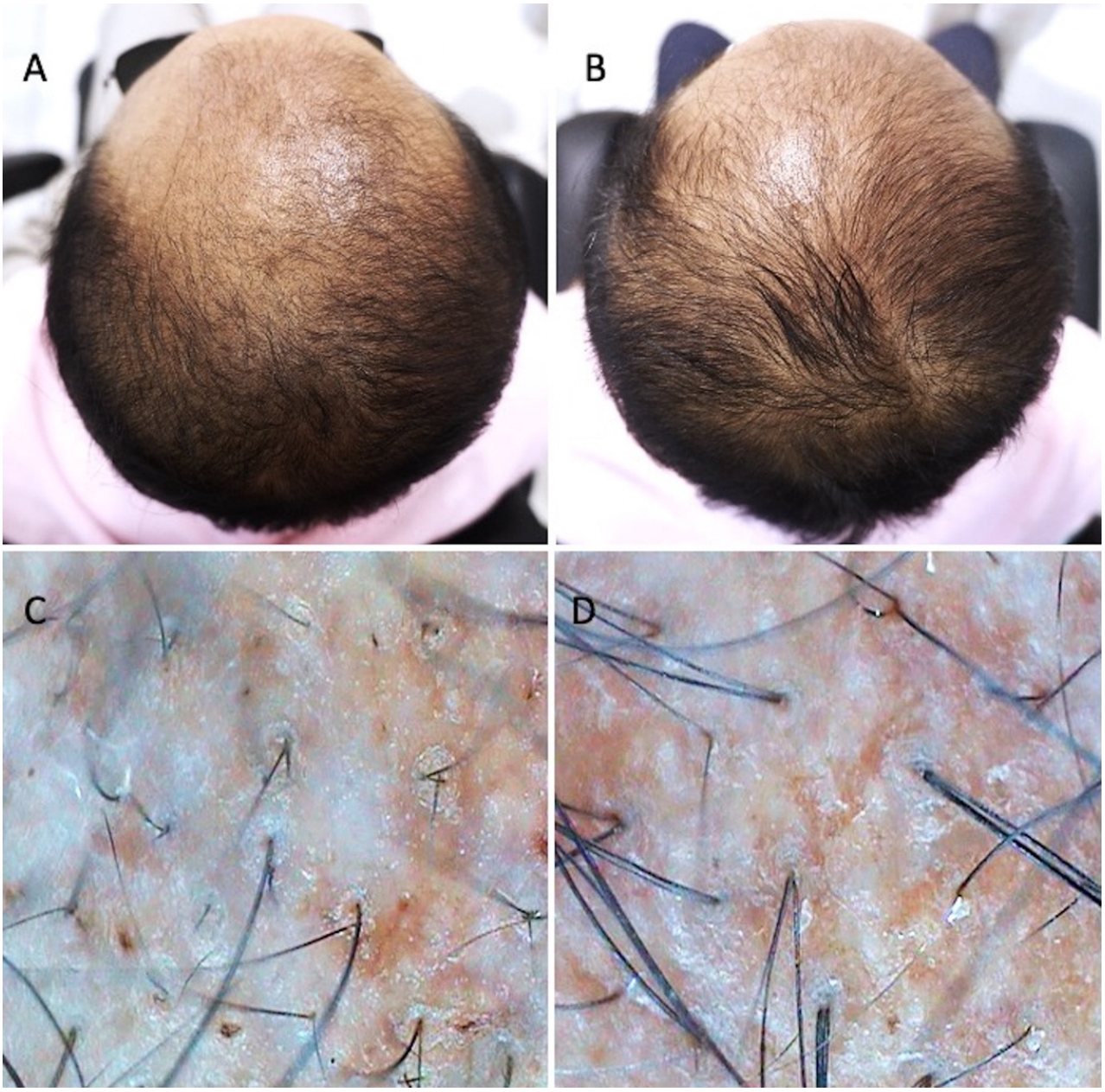

Figure 3. Asian 46-year-old male patient affected by MPHL of VI degrees according to Norwood Hamilton scale (indicated as patient 8 in Table 1), whose hair growth has stalled after taking Finasteride®, treated with Hairgen Booster® protocol. (**A**) Pre-operative view of the scalp, with HL localized in the frontal, temporal, parietal, and vertex area; (**B**) post-operative view at T1 20 wks after treatment with detail of HRG in parietal and vertex area. (**C**) Trichoscan digital image analysis was performed by Fotofinder at T0, where the pre-operative HD in the TA was 17.5 ± 5 hairs/cm^2 and proportions of telogen and anagen hairs were 60.9% and 39.1%, respectively; (**D**) At T1 20 wks post-operation, HD was 36.5 ± 5 hairs/cm^2, and proportions of telogen and anagen hairs were 51.0% and 49.0%, respectively.

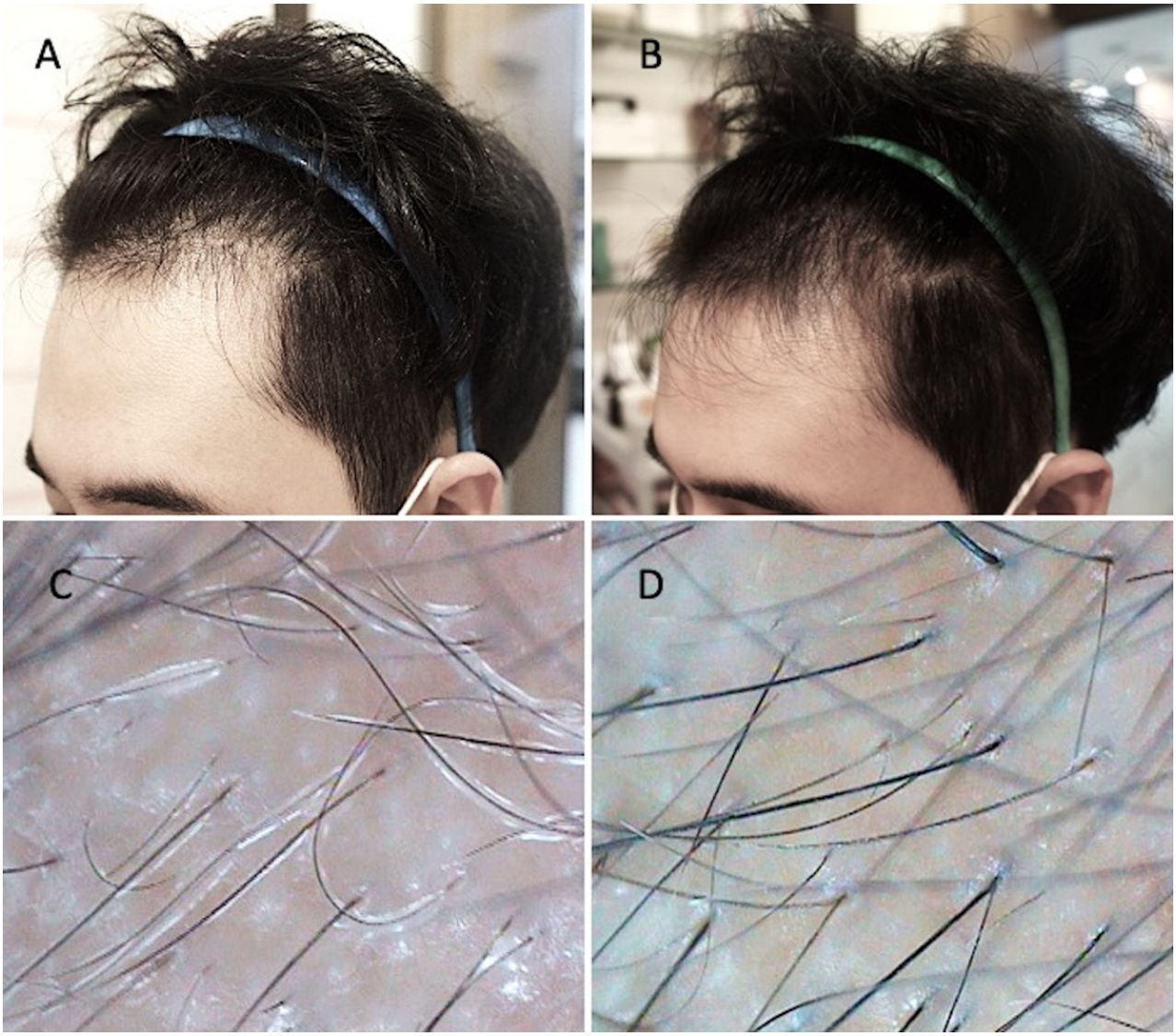

Figure 4. Asian 21-year-old male patient affected by MPHL of II degrees according to Norwood Hamilton scale (indicated as patient 2 in Table 1); did not achieve good results from Finasteride®, treated with Hairgen Booster® protocol. (**A**) Pre-operative view of the scalp, with hair loss localized in the frontal, and especially temporal area; (**B**) post-operative view at T1 20 wks after treatment with detail of HRG in the parietal and temporal area. (**C**) Trichoscan digital image analysis was performed by Fotofinder at T0, where the pre-operative HD in the TA was 40.5 ± 5 hairs/cm^2 and proportions of telogen and anagen hairs were 59.3% and 40.7%, respectively; (**D**) at T1 20 wks post-operation, HD was 59.5 ± 5 hairs/cm^2, and proportions of telogen and anagen hairs were 44.4% and 55.6%, respectively.

HRG assessment was evaluated with photography, physician's, and subject's global assessment scale, in addition to standardized phototrichograms during a follow-up: T0—baseline Figures 2C, 3C and 4C), T1—20 wks (Figures 2D, 3D and 4D).

Subject characteristics were reported in Table 1.

2.6. Exclusion Criteria

Exclusion criteria have been distinguished into two categories, local and general. General exclusion criteria included chronic dermatologic conditions such as psoriasis, eczema, infection of the scalp, a history of keloid development or poor wound healing, a history of thyroid dysfunction, and/or autoimmune disorders. Local exclusion criteria

included an MPHL, over VI degrees, and an FPHL, over III degrees, the use of autologous regenerative strategies for AGA (PRP and/or HFSCs) within the earlier year.

2.7. The Risk Mitigation Measures

Risk Evaluation and Mitigation Strategies (REMSs) with Elements to Assure Safe Use (ETASU) were applied for the procedures performed based on hand-home-made devices called Hairgen Booster®, performed in two different countries (Italy and Korea), with significant safety risk reduction. The identical protocols were used for all patients, exclusion and inclusion criteria were established, and CE-marked medical device were used to represent ETASU features. Before the clinical applications, all dangers were established. The most prevalent risks were ineffective outcomes. The majority of REMSs needed education of healthcare professionals and actual patient evaluation. To give patients secure access to the treatments was the main justification behind ETASU. The authors evaluated the individual characteristics of REMSs with ETASU by searching the FDA website (http://www.accessdata.fda.gov/scripts/cder/rems/index.cfm, accessed on 1 March 2020) and specifically identifying them in:

- Informed consent for all subjects, including the risks (represented only by ineffective results) and side effects of the treatments;
- Procedure training for subjects;
- A strategy for communicating negative impacts or side effects (represented only by itching, slight redness, slight numbness of the treated part, headache);
- The requirement of CE markings for used devices;
- Need to involve subjects via inclusion and exclusion criteria.

2.8. Trichoscopy Evaluation of the Targeted Area

A skilled medical professional used Fotofinder video-epiluminescence microscopy (Foto Finder Systems; http://www.fotofinder.de, accessed on 1 March 2020) in conjunction with Trichoscan digital image analysis (Tricholog GmbH and Datinf GmbH; http://trichoscan.com, accessed on 1 March 2020) to collect phototrichograms (Figure 2C,D, Figure 3C,D and Figure 4C,D) from all scalps. Two TAs of HL were established for the trichogram in both the treatment and control half-heads of all patients.

2.9. Statistical Analysis

The standard deviation (SD) plus or minus the mean was used to represent HD. One-way repeated measures analysis of variance was used to compare HD between the various time points, and the Sidak test was used for post hoc analysis. All tests were two-tailed, and $p < 0.5$ was considered statistically significant. An online p-value calculator (https://www.graphpad.com/quickcalcs/ttest2/, accessed on 29 July 2022) was used for all analyses.

3. Results

3.1. Trichoscopy Analysis

Encouraging results were observed using computerized trichograms, by an HD increase of 19 ± 2 hairs/cm^2 at T1 after 20 wks (20 wks vs. 0 wks) in the TA compared with baseline (74 ± 2 hairs/cm^2 at T1 versus 55 ± 2 hairs/cm^2 at baseline), with a statistically significant difference in HRG ($p = 0.0822$), while the control area (CA) did not display a decrease of hairs/cm^2 (control vs. treatment: $p < 0.0001$). All the details in terms of HD are reported in Table 2. No statistically significant differences in vellus HD among the baseline and T1 were reported. No statistically significant differences in HD improvement among Caucasians and Asians at T1 were observed. No statistically significant differences in HT improvement and anagen/telogen ratio among the baseline and T1 were observed.

Table 2. Trichoscopy evaluation in terms of HD (hairs/cm^2) improvement.

Patients	Procedure	Hair Density (T0)	Hair Density (T1, 20 wks)
1	Hairgen booster®	41 ± 5	60 ± 5
2	Hairgen booster®	40.5 ± 5	59.5 ± 5
3	Hairgen booster®	51 ± 5	70 ± 5
4	Hairgen booster®	35 ± 5	54 ± 5
5	Hairgen booster®	65 ± 5	84 ± 5
6	Hairgen booster®	83 ± 5	102 ± 5
7	Hairgen booster®	180.5 ± 5	199 ± 5
8	Hairgen booster®	17.5 ± 5	36.5 ± 5
9	Hairgen booster®	40 ± 5	59± 5
10	Hairgen booster®	39 ± 5	58 ± 5
11	Hairgen booster®	50 ± 2	69 ± 2
12	Hairgen booster®	75 ± 5	94 ± 5
13	Hairgen booster®	40 ± 2	59 ± 2
14	Hairgen booster®	65 ± 5	84 ± 5
15	Hairgen booster®	38 ± 5	57 ± 5
16	Hairgen booster®	48 ± 5	67 ± 5
17	Hairgen booster®	71 ± 5	90 ± 5
18	Hairgen booster®	30 ± 5	49 ± 5
19	Hairgen booster®	60 ± 5	79 ± 5
20	Hairgen booster®	32 ± 5	51 ± 5

3.2. Clinical Evaluation

Regarding the investigator evaluation, scores ranged from 2 to 5 (p = 0.101), and 15 patients (75%) (14 males, 8 whose hair growth stalled after taking Finasteride®, 6 did not achieve good results from Finasteride®, and 1 female did not achieve good results from Finasteride®) who underwent the Hairgen booster® protocol (LLLT, MND, and GFs) reported good results in global scalp coverage and HT (Figures 2B, 3B and 4B) versus 5 patients (25%) (2 males did not achieve good results from Finasteride®, and 3 females, 1 of which did not achieve good results from Finasteride® and 2 whose hair growth stalled after taking Finasteride®) with ineffective results.

Regarding the patients-evaluation, scores ranged from 1 to 4 (p = 0.033), and 17 patients (85%) (15 males, 8 whose hair growth stalled after taking Finasteride®, 7 did not achieve good results from Finasteride®, and 2 females did not achieve good results from Finasteride®) who underwent the Hairgen booster® protocol, reported good results in global scalp coverage and HT versus 3 patients (15%) (1 male did not achieve good results from Finasteride® and 2 females whose hair growth stalled after taking Finasteride®) with ineffective results.

The results reported show a trend in male patients to be more satisfied than female patients. Satisfaction grade assessment questionnaire analysis showed that all people would choose to undergo hair bio stimulation with Hairgen Booster®, and they were sufficiently informed about the risks and side effects of this treatment (including the ineffective results and risk of the high possibility to repeat the treatment more times).

4. Discussion

Clinical presentation of AGA in MPHL and FPHL consists of progressive hair miniaturization developing due to the influence of DHT, on a background of genetic susceptibility of the hair follicles, in specific areas of the scalps such as the temporal, frontal, and vertex regions. AGA outcome is a slow progression that, if not cured, causes diffuse hair thinning in the androgen-sensitive regions of the scalp.

According to the latest European Guidelines, effective medical therapies, such as Minoxidil® and Finasteride®, are classified as evidence-based medicine (EBM) of level one. To maintain clinical efficacy, these therapies should be continued for life, but it is well known that they can lose their effectiveness over time.

In the other way, the encouraging results obtained with LLLT in HL, as also confirmed by a recent systematic review [21], pushed several authors and companies to develop new treatments and/or devices, combining two or more procedures. In this way, the combined use of MND with LLLT and GFs in patients suffering from AGA has been recently described as aiming to improve HRG [8,9].

In detail, two studies have been conducted by the author Gentile P. et al. [8,9]. The first study, published in 2020 [8], aimed to report the combined effects of autologous PRP with MND and LLLT in 23 patients affected by AGA (13 males were classified in stage I–V by the Norwood-Hamilton scale, and 10 females were classified in stage I–III by the Ludwig scale) with a follow-up of 12 wks (T1), 23 wks (T2), 44 wks (T3), and 58 wks (T4). In the first work of Gentile et al. [8], interesting results were shown, represented by an HD increase of 81 ± 5 hairs/cm^2 and 57 ± 7 hairs/cm^2 respectively at T1 and T2 compared with baseline (173 ± 5 hairs/cm^2 at T1 and 149 ± 9 hairs/cm^2 at T2 versus 92 ± 2 hairs/cm^2 at baseline) using trichograms. The extreme variability of the PRP products used, and contextually, the absence of standardized protocols of PRP preparation widely shared, and the necessity to perform the procedures in an operatory room of an authorized clinic (the PRP was subjected to the approval of transfusion service in Italy) were the limitations of the study.

In the second study published in the current year 2022, Gentile et al. [9] reported the effects of the combining use of MND, LLLT, and synthetic GFs (without autologous PRP use) in a single hand-homemade application device in 26 patients suffering from several degrees of AGA (I–III vertex according to Norwood Hamilton and I–II by the Ludwig scale) on HRG showing an HD increase of 12 ± 2 hairs/cm^2 at T1 after 16 wks (16 wks vs. 0 wks) in the TA compared with baseline using computerized trichograms, with a statistically significant difference in HRG ($p = 0.0238$), In this case, the absence of PRP use seems to be incisive in the results obtained (57 ± 7 hairs/cm^2 at 23wks versus 12 ± 2 hairs/cm^2 at 16 wks) but on the other hand, the introduction of the hand-home-made device-based MND-LLLT-GFs at the same time made the patient free to perform the treatment at home with great comfort and with promising results.

LLLT, through the red light, stimulates the CCO in the membrane of mitochondria positioned in hair bulge stem cells, acting on ROS and ATP that stimulate cellular proliferation, migration, and oxygenation, leading to HRG improvement [10]. The first LLLT device for MPHL approved by US FDA was introduced in 2007 [22]. LLLT comprises both Light Emitting Diodes (LED) and Laser Diodes (LD), which showed effectiveness for HL treatment through the red lights and lasers emission at 660 nm. For these reasons, the LLLT use, such as phototherapy with LED [23], has been intensified into the market of devices aiming to stimulate HG in AGA [24,25]. Precedently, LED phototherapy was described as a good and safe procedure for the treatment of acne [26], vaginal atrophy [27], facial aging [28,29], and in HL disorders [30]. Different low-level laser and light sources for the management of alopecia, such as LLLT, [31–36], various wavelengths of LED light [11,37], and several other techniques combined, such as LED-LLLT [38], have been analyzed by many investigators, with the aim to establish the related treatment parameters and the outcomes.

In a 26-week trial, Leavitt et al. [38] randomly assigned 110 AGA patients with MPHL IIa V to receive therapy with the HairMax LaserComb®. At 26 wks, HD had an average increase of 19.8% in the study group patients. Kim et al. [31] performed a 24 wk trial

including 40 AGA patients treated with a helmet-type 3R LLL-T device doted both LEDs emitting wavelengths of 630 nm and 660 nm that LD with wavelengths of 650 nm. At 24 wks, the mean percentage of increase in HD was 14.7%. Finally, Suchonwanit et al. [25] conducted a 24 wk, trial that included male AGA patients treated with RAMACAP®, a combat helmet-shaped device containing single-mode LD, emitting at a wavelength of 660 ± 10 nm [25]. At 24 wks, the mean percentage of increase in HD was 9.1%.

There was a substantial distinction between light and laser sources, though. The shape, light source, number of LEDs and LDs, wavelength, and overall power output of LLLT devices made each protocol different. Additionally, the hand-free devices, such as hats [31] and helmets [30,39,40], which were also demonstrated to be clinically effective, frequently employed a large number of user-friendly diodes, ranging from 40 to 304.

The mean change in HD from baseline to week 24 in Suchonwanit's study [25] was 10.21 ± 3.25 hairs/cm^2 in the laser group against 3.95 ± 1.32 hairs/cm^2 in the sham group. In the laser group, the mean change in hair diameter from baseline to weeks 24 was 6.11 ± 2.15 µm, compared with 3.76 ± 1.24 µm in the sham group. These data appear to be in line with the data published by Gentile et al. [9] (12 ± 2 hairs/cm^2 at 16 wks).

Considering standard treatments including oral Finasteride® and topical Minoxidil® with LLLT, taking 1 mg of Finasteride® in MPHL for 12 months significantly increased total HC by 7.3% at 24 wks [41]. Applying 2% and 5% topical Minoxidil® showed a significant HC increase for 8.84% ($p = 0.013$) and 12.3% ($p < 0.001$) at 48 wks, respectively [42]. The LLLT effectiveness revealed a significant HC increase for 20.9 (12.79%, $p = 0.0249$) vs. 25.7/cm^2 (16.96%, $p = 0.0028$) in the 9- and 12-beam laser comb treated side at 26 wks after treatment, respectively [43]. Hence, the effectiveness of LLLT appeared to be comparable to the conventional HL treatment. Furthermore, the combination treatment of 5% Minoxidil® and LLTT seemed to provide a better response of HD than Minoxidil® or LLLT alone [43].

In every case, the efficacy and safety of LLLT in the treatment of MPHL and FPHL have been demonstrated [43].

In the present research paper, 10 patients whose hair growth stalled after taking Finasteride®, and 10 patients who did not achieve good results from Finasteride® were treated with LLLT with MND and GFs. Encouraging results, in terms of hair growth booster, have been reported confirmed from an HD increase of 19 ± 2 hairs/cm^2 at T1 after 16 wks (16 wks vs. 0 wks) in the TA compared with baseline (70 ± 2 hairs/cm^2 at T1 versus 51 ± 2 hairs/cm^2 at baseline). Therefore, it was proven that the combination of MND with LLLT and GFs can provide a good HRG effect on subjects who did not achieve a good effect from Finasteride® or who were on a stagnant period due to some limitations of Finasteride's DHT production inhibitory effect alone. As known, Finasteride® relieves the capillaries constricted by DHT and supplies a small amount of blood to the hair follicles, but when there is not enough nutrition, passing through a period of stagnation seems to be mandatory, which is the limit of Finasteride® treatment. MND with LLLT and GFs could help many patients overpass the stagnant period. In fact, this treatment provides nutrients to the hair follicles smoothly through angiogenesis and cell regeneration through wound healing, leading to a hair growth effect because the hair becomes thicker, and the density rises according to observation.

5. Conclusions

In conclusion, the effectiveness of MND with LLLT and GFs via Hairgen Booster® protocol use, as a hair growth booster, was demonstrated both in patients whose hair growth stalled after taking Finasteride® and in patients who did not achieve good results. Further research is needed to define standardized protocols, and large-scale trials still need to be conducted to confirm their effectiveness.

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data curation, analysis, and validation protocol. All authors have read and agreed to the published version of the manuscript.

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