Original Article

Use of Helmet with Combined Low-Level Laser Therapy, Light- Emitting Diodes, and Magnetic Field Technologies for Hair Growth Treatments of Male Androgenic Alopecia in Adult Patients

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Short title: Combined Technologies for AGA

Abstract

Background: androgenetic alopecia affects up to 50% of men and women.
Aim: This study aimed to evaluate the use of a treatment combining low-level laser therapy, light-emitting diodes and magnetic field technologies for the improvement of hair loss associated with male AGA in the scalp area.
Methods: the study included healthy men aged 25-45 who had self-perceived thinning hair and reported active hair loss within the previous 12 months. Men who had received physical or chemical aesthetic treatments for hair loss were excluded. All patients received 12 treatment sessions (one per week) with Miltahead®, a noninvasive therapeutic helmet combining these three technologies, and were re-evaluated six months after the last treatment session.
Results: a total of 10 men with a median age of 35.4 years (SD 5.4; range of 28-44 years) were enrolled and completed the study. At 6 months of treatment, terminal hair density had a mean increase of 40.0% (SD 25.1), hair density of 30.2% (SD 14.7), quantity of hairs of 30.2% (SD 14.7), cumulative hair thickness of 37.8% (SD 24.3), number of follicular units of 24.7% (SD 15.3), follicular unit density of 24.8% (SD 15.4), and vellus hair density had a decrease of 3.3% (SD 83.1). The treatment was safe, and no adverse effects were reported.
Conclusions: the combined use of these three technologies for AGA treatment in men provided excellent results for hair growth compared with other studies. However, additional research is needed.

Keywords

Androgenic alopecia, low-level laser therapy, light-emitting diodes phototherapy, magnetic fields, hair growth.

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Introduction

Androgenetic alopecia (AGA) is a polygenic disorder involving both maternal and paternal genes, with variable penetrance and familial predisposition determined by genetic and environmental factors[1]. It is characterized by an excessive response to androgens and affects up to 50% of men and women, with a distinctive distribution by gender[2].In males, hair loss is most prominent in the vertex and the frontotemporal regions[3]. The prevalence in 50-year-old Caucasian males is of 50%, reaching around 80% in 70-year-old male[4]. Its molecular pathophysiology consists of dysregulation of signaling pathways and inappropriate immune and inflammatory responses[5].

There are two FDA-approved drugs for the treatment of AGA: topical minoxidil and finasteride, both requiring four to six months before noticing an improvement, and which must be used indefinitely to maintain a response. New techniques have made hair transplant more effective, cosmetically pleasing, and natural- looking; however, patients need to have more than 40 follicular units/cm2 to cover the bald area[6]. Both Red light and laser at 660 nm have also demonstrated efficacy for hair loss, and the use of low-level laser therapy (LLLT), as well as of phototherapy with light-emitting diodes (LEDs),[9] has been intensified to promote hair growth in AGA[7,8].

For years, LED phototherapy has been presented as an effective and safe tool for the treatment of skin, mucous and scalp conditions in which there is an inflammatory component, being used successfully in the treatment of acne[10], vaginal atrophy[11], facial aging[12,13], and also in disorders related to hair growth[14,15]. The innovative combination of LLLT, LEDs, and magnetic field technologies for the treatment of AGA is of recent development. Synergy of emissions, including visible spectrum, infrared, soft laser, and magnetic field, helps to densify the hair by activating the cellular metabolism of hair follicles and improving the quality and density of the existing hair.

This study aimed to evaluate the use of combined LLT, LED, and magnetic field technologies for the improvement of hair loss associated with male AGA in the scalp area.

Methods

Study Design

The study was conducted in the Elite Laser Clinic and Clínica MC360 as a proof-of-concept, open-label, prospective trial. A treatment period of three months from the first treatment of the first patient to completion of the last treatment of the last patient was estimated. The participation period for each subject was nine months, including the screening/baseline/first treatment visit up to the 12th treatment visit and a follow-up visit at six months. The complete treatment course included 12 treatment sessions conducted once per week for 12 weeks. Patients were re-evaluated six months after the last treatment session. The study was conducted following the principles outlined in the current revised version of the Declaration of Helsinki, Good Clinical Practice (GCP) and in compliance with all applicable laws and regulatory requirements relevant to the use of devices in Spain. All patients signed an informed consent form to participate in the study before starting any procedure.

Subjects

This study included males aged between 18 and 55 with AGA. Additional inclusion criteria were: 1) healthy men aged 25-45 who had self-perceived thinning hair and reported active hair loss within the previous 12 months (however, the diagnosis of AGA was confirmed by the investigator to ensure that the patient met the inclusion criteria.); 2) presentation of male pattern hair loss/androgenic alopecia in the temples, and the vertex and mid-frontal scalp (Norwood[2-4]); 3) and willingness to correct their condition and ability to comply with all requirements of the protocol. Exclusion criteria were to have received physical or chemical aesthetic treatments in the target area within six months before study enrollment, and to have taken or plan to take topical or systemic medications for the treatment of hair loss and/or hair volume.

Interventions

Consecutive men diagnosed with AGA were invited to participate and, after confirming their eligibility and signing the corresponding informed consent, they were included in the study. Patients underwent a treatment of 12 sessions with Miltahead® (Milta Technologie, Mudaison, France), a non-invasive therapeutic helmet that combines LLLT, LEDs and magnetic field technologies (*Figure 1*). Technical characteristics of the device were: 1) Nano-Pulsed Cold Laser (NPCL) Laser Emission in Coherent Infrared Light at 905 nanometers, 2) non-coherent emission pulsed by trichromatic diodes RGB CMS (400 to 650 nm), 3) non-coherent continuous pulsed infrared emitting by monochromatic diode at 905 nanometers, 4) constant circular magnetic field (70 milliTesla) equivalent to the Earth's magnetic field, and 5) potentiation of light radiation thanks to the magnetic field. Each session lasted between 20 and 25 minutes.

Figure 1 *- Miltahead® device (Milta Technologie, Mudaison, France).*

Before the first treatment, the target area was shaved, and the baseline assessment was performed. To homogenize the study area, the zone to treat was measured from the birth of the right ear to that of the left ear, placing the tape measure as a headband, and marking the intermediate point as a reference.After this first measurement, on this point was placed a template and with the help of a hook, a lock of hair was extracted that was subsequently shaved. The length of the shaved hair was not be more than 0.3mm (this information was verified with the TRICOSCALE®). A second measurement was performed from the shaved point towards the occipital area to know the exact point that was to be shaved 30 days later. The photos were taken 48 hours after this procedure. In case of gray or blond hair, the area was dyed with a drop of beard dye and a drop of hydrogen peroxide for 12-15 minutes. After that, the area was cleaned with hydrogen peroxide to ensure that the scalp had no traces of dye left before taking pictures. The first photo was taken as MACRO, and after marking the exact point where it was taken, the next photo was taken as MICRO at 20%.

Efficacy Outcomes

The primary efficacy outcome was quantitative hair growth, measured as terminal hair density in the treated area. A quantitative evaluation was conducted per total treated area and per group of hair follicles corresponding to the treated area.

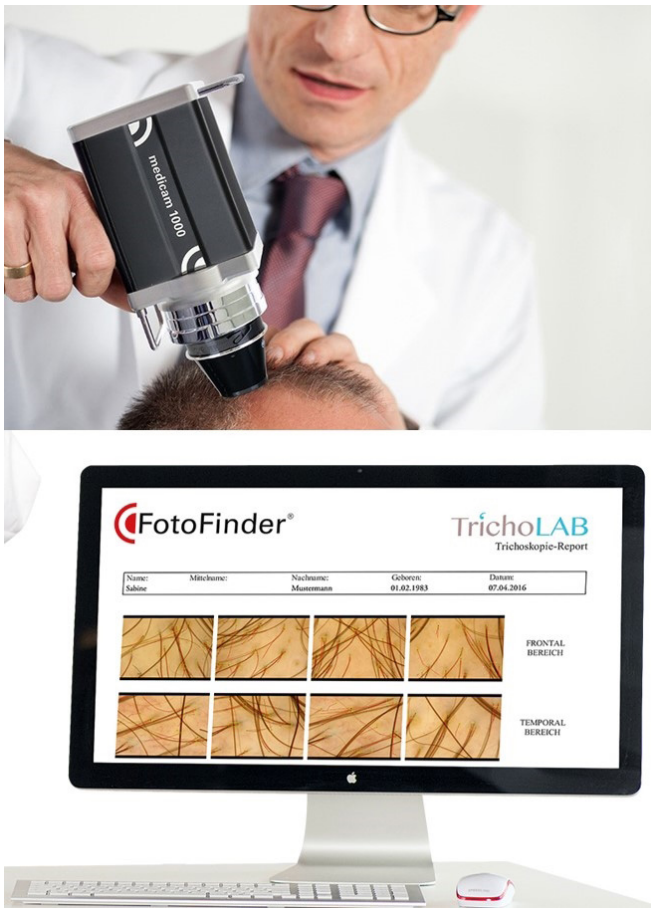

Figure 2 *- Quantitative hair growth by dermatoscopic imaging (FotoFinder Trichoscale Pro System; FotoFinder Systems GmbH, Bad Birnbach, Germany).*

Quantitative hair growth in the treated area was assessed by dermatoscopic imaging (FotoFinder Trichoscale Pro System; FotoFinder Systems GmbH, Bad Birnbach, Germany) at baseline and at the follow-up visit (six months after the last treatment session) (*Figure 2*).
Other outcome measures assessed in the treated area before and after treatment were: 1) number of hair, 2) hair density (number of hairs per cm2), 3) vellus hair density (number of hair per cm2), 4) cumulative hair thickness (mm per cm2), 5) number of follicular units, and 6) follicular units density (number of follicles per cm2) (*Figure 3*).
Treatment safety was assessed by recording all procedure complications and any adverse events that may have occurred during treatment and until the follow-up visit.

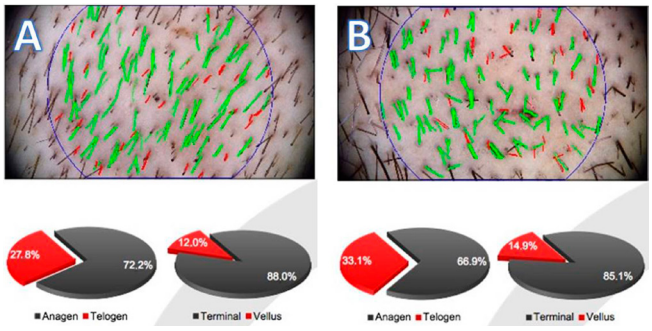

Figure 3 *- Visualization of clinical measurements with Trichoscale Pro System in a study patient before (A) and after 6 months of treatment (B).*

Statistical Analysis

Statistical analysis was limited to the description of study variables, and no hypothesis tests were performed. Quantitative variables were described as the mean and standard deviation (SD), whereas categorical variables were described as frequency and/or percentage. Efficacy outcomes were assessed as the change of the corresponding variable from time 0 (i.e., baseline) to 6 months (i.e., follow-up visit).

Results

Subject Characteristics

A total of 10 males with a median age of 35.4 years (SD 5.4; range of 28-44 years) were enrolled in the study site. All of them completed the study.

Efficacy Outcomes

Table 1 summarizes changes in terminal hair density (primary outcome) from baseline to six months of treatment. Terminal hair density of all patients had a mean increase of 40.0% (SD 25.1) (*Table 1*) (*Figure 4*).
Secondary effectiveness endpoints included subjects' assessment of overall hair growth (Table 1). For all hair parameters, the differences between values at baseline and after six months were calculated. After six months, hair density (*Figure 5*) had a mean increase of 30.2% (SD 14.7), quantity of hair of 30.2% (SD 14.7), cumulative hair thickness (*Figure 2*) of 37.8% (SD 24.3), number of follicular units of 24.7% (SD 15.3), follicular units density of 24.8% (SD 15.4), and vellus hair density had a decrease

Variables assessed	Baseline (N=10)		Six months of treatment (N=10)		Difference		% of increase	
	Median	SD	Median	SD	Median	SD	Median	SD
Primary efficacy outcome								
Terminal hair density (1/cm2)	78.2	29.1	104.5	27.6	26.4	14.0	40.0	25.1
Secondary efficacy outcome								
Quantity of hair	88.2	36.0	110.7	35.8	22.5	3.0	30.2	14.7
Cumulative hair thickness (mm)	6.0	2.0	8,1	2.4	2.1	1.2	37.8	24.3
Hair density (n/cm2)	97.6	39.9	122.6	39.7	24.9	3.4	30.2	14.7
Vellus hair density (n/cm2)	12.6	12.0	9.7	7.2	-2.8	10.0	-3.3	83.1
Follicular units	63.4	18.4	77.1	16.5	13,7	7.5	24.7	15.3
Follicular unit density (n/cm2)	70.2	20.4	85.4	18.3	15,2	8.4	24.8	15.4

Abbreviations: N, number of patients; SD, standard deviation; n, number; cm, centimeters; mm, millimeters

Table 1 *- Results of variables assessed at baseline and at 6 months of treatment.*

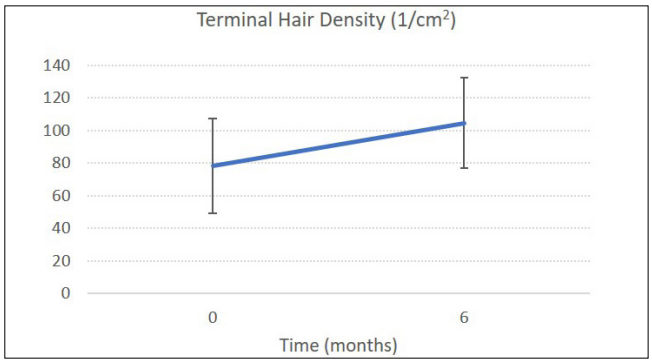

Figure 4 *- Terminal hair density at baseline and at 6 months of treatment (N=10).*

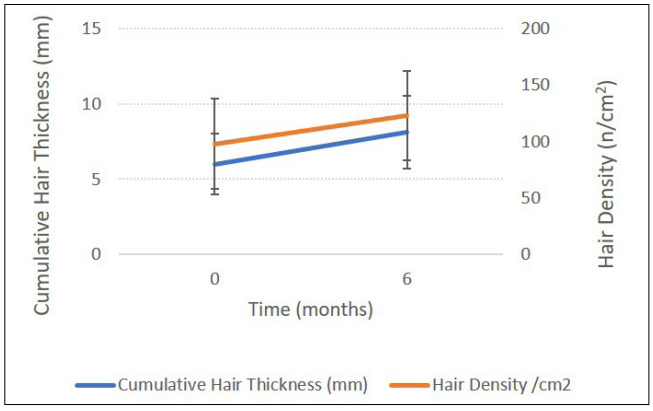

Figure5 *- Cumulative hair thickness and hair density at baseline and at 6 months of treatment (N=10).*

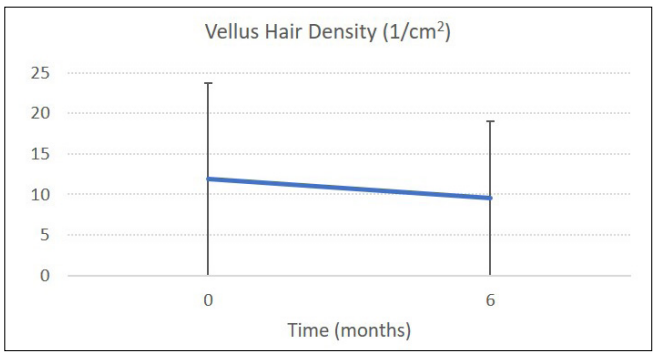

Figure 6 *- Vellus hair density at baseline and at 6 months of treatment (N=10).*

of 3.3% (SD 83.1). Regarding vellus hair density, after six months of treatment it was observed that it had increased in three (30%) patients , it had decreased in six (60%) patients, and there were no changes in one (10%) patient (*Figure 6*).

Safety Outcomes

The procedure did not require analgesia/anesthesia. Patients did not report pain during the treatment, and no complications or side effects were reported.

Discussion

The results of the study showed a considerable increase in the values of the primary outcome. Mean increase of terminal hair density was 40%, as well as the rest of the variables (23% to 30%), except for vellus hair density, which decreased by 1.7%.

Some studies had investigated a variety of light sources and treatment parameters for the management of alopecia, such as LLLT,[16–21] various wavelengths of LED light[14,15,22,23] and several techniques combined, such as LED-LLLT [9,12,14,15,19,24]. The device used in this study is a technological innovation that combines, in a synergistic way, Nano Pulsed Cold Laser (NPCL) laser emitters, infrared diodes and RGB diodes in a magnetic tunnel. The synergy of these energies (magnetic field, infrared, laser) allows thanks to the scattering of photons up to 13 cm in soft tissues to act directly on the hair bulb to lengthen the hair growth (anagen phase). This effect promotes the stimulation of stem cells, increasing vascularization of hair bulbs and activating the stem cells of the dermal papilla, which improves the oxygenation of the capillary bulb and the metabolism of cells[25–26].

Although the available literature regarding phototherapy-based devices to treat AGA is limited, study results regarding the primary outcome showed a better performance than those reported in previous studies.

Leavitt et al. (2009) conducted a 26-week, randomized, double-blind, sham device- controlled, multicenter trial in which 110 males with Norwood-Hamilton classes IIa–V AGA were randomized for treatment with either the HairMax LaserComb® or the sham device (2:1)[24].

The primary efficacy endpoint was mean terminal hair density. At 26 weeks, this variable had an average percentage of increase of 19.8% in treated patients, 50.5% lower than the result obtained in our study, which was of 40.0%.
Kim et al. (2013) performed a randomized, double-blind, sham device-controlled trial at two research centers that included 40 male and female subjects with AGA treated with a helmet- type 3R LLLT device with a light source consisting of light-emitting diodes (LEDs) emitting wavelengths of 630 nm (3.5 mW, 24 units, L-513ECA) and 660 nm (2.5 mW, 18 units, L- 513LRC) and laser diodes (LDs) with wavelengths of 650 nm (4 mW, 27 units, DL3147– 060). [17] The primary endpoint was change in hair density in the target area between baseline and after 24 weeks of treatment as measured with a phototrichogram. Six months after the last procedure, the average percentage of increase in hair density was of 14.7%, 51.3% lower than the result obtained in our study, which was of 30.2%.
Finally, Suchonwanit et al. (2018) conducted a 24-week, prospective, randomized, double- blind, sham device-controlled clinical trial that included male subjects aged over 18 years with AGA treated with RAMACAP, a combat helmet-shaped device containing single-mode laser diodes, which emit at a wavelength of 660±10 nm.[8] The primary efficacy endpoint was change in hair density and diameter of the target area of the scalp from baseline and at weeks 8, 16, and 24, by photographing the target area with a Folliscope® and measuring it with Folliscope 2.8 software (LeadM Corporation, Seoul, Korea). Six months after treatment, the average percentage of increase in hair density was of 9.1%, 69.9% lower than the result obtained in our study, which was of 30.2%.
Despite the higher increase in terminal hair density observed in this study, our results should be assessed in the context of the limitations of the study design. Thus, unlike other studies mentioned previously[8,17,24],our study was not randomized and did not compare the efficacy of the investigation device with that of a sham device. Furthermore, the low number of patients did not allow to assess any statistical significance using hypothesis tests. We did not perform a split-scalp study since there are published studies that describe that when acting with LLLT in one part of the scalp the benefits on the treated area may affect the untreated area, distorting the results of the study. The treatment was safe, and no adverse effects were reported. All patients could take up their usual activities at the end of each session.

Conclusion

In summary, the combined use of NPCL laser emitters, infrared diodes and RGB diodes in a magnetic tunnel for the treatment of AGA in men provided excellent results for hair growth. However, future randomized, double-blind studies with sham devices and a more significant number of patients will be necessary to confirm these results.

Potential conflicts of interest

The authors declare no conflicts of interests.

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