



Photobiomodulation therapy and 5% minoxidil in female pattern hair loss: a case series focusing on hair growth phases over a shorter timeframe

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Abstract

Purpose Female pattern hair loss (FPHL) is a major concern for women experiencing hair thinning. While minoxidil 5% (MIN) is a medically approved treatment and photobiomodulation therapy (PBMt) has shown effectiveness in stimulating hair growth, treatments typically last 24 weeks. This study aimed to evaluate the effects of combining PBMt with topical MIN for treating FPHL within a shorter 12.5-week timeframe, focusing on hair growth phases.

Methods Nine women aged 30 to 50 years with FPHL participated. They applied MIN twice daily to the scalp throughout the treatment period. In the clinic, hair was sectioned, and one side of the scalp was randomly assigned to receive 25 sessions of red laser (100 mW, 4 J/point), delivered at 15 evenly spaced points. Treatments were administered twice a week, while the opposite side received sham irradiation. Standardized photographs, a quality of life (QoL) questionnaire, and phototrichograms were used to evaluate the outcomes.

Results Both the MIN and PBMt+MIN groups showed significant improvements in QoL scores and hair density. Additionally, both groups experienced increased hair density and a higher percentage of hairs in the anagen phase. Remarkably, the PBMt+MIN group exhibited a significantly greater reduction in telogen-phase hairs.

Conclusion These findings suggest that PBMt may enhance MIN therapy for FPHL, particularly in reducing telogen-phase hair counts within a shorter treatment period.

Clinical trial number Not applicable.

Keywords Female androgenetic alopecia · Hair growth · Phototrichoscopy · Quality of life · Red laser

Introduction

Female pattern hair loss (FPHL) is a common condition in women, characterized by progressive thinning of hair on the frontal and vertex scalp, with sparing of the frontal hair-line and potential involvement of the temporal areas [1]. Its unclear etiology, with no confirmed link to androgens, complicates treatment. FPHL profoundly affects psychological health, exacerbating stress and further hair loss [2].

Although common, FPHL can be challenging to treat due to its chronic nature and the interaction between genetic and environmental factors. Current treatments for FPHL include pharmacological options like topical 5% minoxidil (MIN) and light-based approaches such as photobiomodulation therapy (PBMt). Mechanisms behind MIN involve vasodilation, anti-inflammatory effects, activation of the

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Wnt/ β -catenin signaling pathway, and potential antiandrogenic properties [3]. PBMt, using lasers or LEDs, stimulates cellular activity without generating heat, increasing ATP production in mitochondria, reducing oxidative stress, improving blood flow, and enhancing follicular metabolism [4]. However, research on combining MIN and PBMt in FPHL remains scarce [5, 6]. In the few available studies, participants used helmet-type devices emitting red light (~650 nm) every other day for 25 min over 4 months [5], or for 30 min over a 6-month period [6].

In this study, our primary goal was to investigate the combined effects of PBMt and MIN over a shortened 12.5-week treatment period, introducing a novel focus on whether clinically meaningful responses could be achieved in half the duration typically reported in the literature. Clinical outcomes were monitored through quality-of-life (QoL) assessments and standardized photographs. Moreover, in a pioneering approach, we assessed changes in hair-growth phases (anagen and telogen) by phototrichoscopy, providing a deeper understanding of early biological responses.

Methods

This study was approved by the Ethics Committee of the Federal University of São Paulo (UNIFESP) under number 4.697.146. Nine women aged 30–50 years with Sinclair grades 2–4 FPHL [7] were enrolled after dermatological evaluation and informed consent. Exclusion criteria included recent treatments for FPHL, photosensitivity, use of photosensitive medications, hormonal therapies, and antiandrogenic or anabolic drugs. Before participant enrollment, to increase the validity of the intervention analysis and avoid potential selection bias, a computer program was used to generate a sequence of random numbers to allocate which side (left or right) would receive the intervention and which would serve as the control.

At the first visit, all participants were instructed to apply 1 mL of MIN (U.sk Under Skin, Luxbiotech Farmacêutica LTDA, Brazil) twice daily, with a 12-h interval, to a clean, dry scalp until the end of treatment. For application, they were guided to part their hair using a comb, starting from the central line (aligned with the tip of the nose as a reference to the vertex), apply a spray of MIN to the exposed scalp, and gently massage with their fingertips for optimal absorption. Participants were also advised to refrain from cutting their hair, using chemical products, or undergoing any other hair loss treatments.

In the clinic, a low-level GaAl laser device was used, emitting continuous red light (660 nm), with a power of 100 mW, a laser tip area of 7 mm², (MMOptics, Brazil), in spot mode, with 2 cm between points and energy per point of

4 J. A total of 15 points were irradiated, 5 points per line, with an exposure time of 40 s per point, totaling 10 min per patient on one side according to randomization. For application, the hair was parted using a comb to expose the scalp while minimizing hair interference with irradiation, starting from the midline with the tip of the nose as a reference. This procedure was performed on the 3 scalp lines, spaced 2 cm apart (Fig. 1). A sham laser irradiation was performed on the control side, ensuring that participants were blinded to which side received the actual intervention. The sessions were conducted twice a week, with a minimum interval of 48 h between sessions, totaling 25 sessions over 12.5 weeks.

The QoL questionnaire for FPHL was freely completed by participants before and after treatment. The questionnaire consists of 16 questions, each scored from 0 to 6, where lower scores indicate minimal impact and higher scores reflect greater QoL impairment [8]. Participants evaluated their social interactions and overall well-being.

Standardized photographs were taken using a 12-mega-pixel Asus Zenfone Max Shot camera, ensuring consistent positioning, chair placement, and lighting. Hair was parted along the midline, using the nasal dorsum as a reference. Participants were positioned with their left hand closed between the chin and collarbone. Photos were analyzed using a seven-point rating scale (+ 3 = greatly increased density, + 2 =

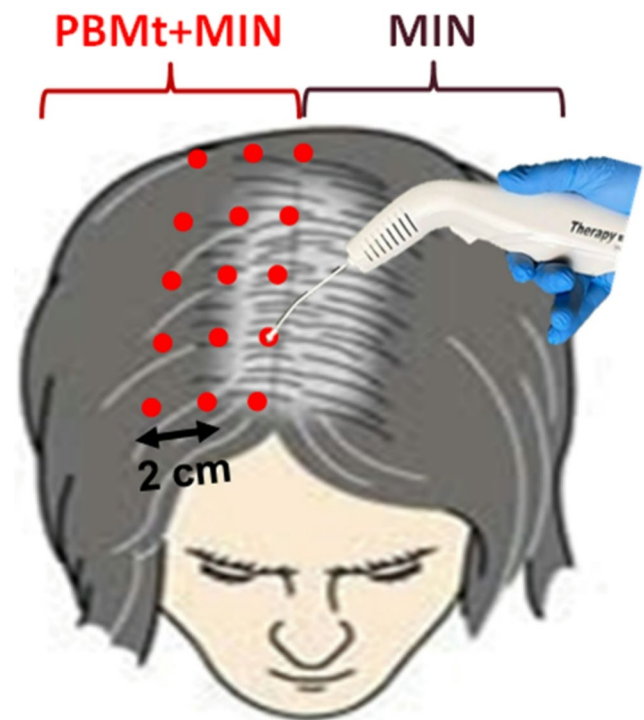


Fig. 1 A representative image of PBMt application ($\lambda=660$ nm, 100 mW) applied to half of the scalp at 15 points, spaced 2 cm apart. Each point received 4 J of energy for 40 s, totaling 10 min per session over 12.5 weeks

increased density, +1 = slightly increased density, 0 = no change, -1 = slightly reduced density, -2 = reduced density, -3 = greatly reduced density) [9]. These photos were taken pre-treatment, monthly during treatment, and one-month post-treatment. Pre- and post-treatment photos were evaluated by two independent blinded observers and by study participants, using the Sinclair scale as reference.

Phototrichograms were obtained using the Photo Finder imaging system (TrichoScan[®], Tricholog GmbH & Datinf GmbH, Germany). A target region was identified 15 cm from the glabella and 5 cm from the midline on both the right and left sides of the central parting, near the vertex. The area, measuring 2 cm², was selected using a fine-toothed comb and a tiara adapted with a measuring tape. Subsequently, using a curved scissor and a Philips HP6390/52 eyebrow trimmer and shaper, the selected scalp area was trimmed and shaved. The scalp area was then marked with the tip of a 26 g hypodermic needle, dipped in electric ink brand fire red tattoo ink. The phototrichogram procedure involved taking two photos of the selected area with 10x magnification. The first photo was taken immediately after shaving and marking the area with a mini tattoo.

This initial photo served as a baseline, allowing the software to scan follicle patterns to locate the exact point on the scalp after 48 h. Images obtained on the first visit and after 48 h were analyzed using Fotofinder Trichoscale AI[®] software. The software provided quantitative data on hair count, density, and the distribution of hair across different growth phases, based on the estimation that anagen hair grows approximately 0.3 mm per day [10]. This procedure was repeated one month after the last laser application, comparing pre- and post-treatment conditions. In this case, the evaluators were not blinded because the software automatically provides the hair counts and quantitative parameters, leaving no subjective criteria that could bias the assessment. Data were analyzed using the Wilcoxon signed-rank test to verify statistical differences, which were considered significant at $p < 0.05$.

Results

Although the initial power analysis indicated a required sample size of 20 participants, nine met the inclusion criteria and were enrolled, and five completed the study (average age: 37 years). Three participants discontinued due to medical leave, scheduling conflicts, and workplace changes, and one was excluded due to adverse effects from MIN (scalp itching and flaking). Before treatment, participants reported significant QoL concerns, particularly regarding hair appearance and fear of ongoing hair loss. Post-treatment, concerns about appearance decreased by 80%, while fear of

persistent hair loss decreased by 40%, suggesting that visible improvements were achieved, yet some anxiety about the condition persisted.

Pre-treatment evaluations by both participants and independent evaluators rated hair loss between -3 and -1, indicating substantial hair thinning. One-month post-treatment, ratings improved significantly, with scores ranging from 2 to 3 (Fig. 2). The Kappa coefficient, measuring inter-evaluator reliability, indicated moderate agreement pre-treatment (0.46) and substantial agreement post-treatment (0.69), reflecting improved consistency in evaluations.

Hair counts remained stable before and after treatment, averaging approximately 185 hairs in both groups. Hair density also showed no significant changes, with both groups maintaining an average of 200 hairs/cm² (Fig. 3a). Four months post-treatment, the number of hairs in the anagen phase increased for both groups (146 to 159 for MIN and 132 to 154 for PBMt+MIN), but the differences between treatments were not statistically significant. Notably, PBMt+MIN significantly reduced the number of hairs in the telogen phase (from 50 to 36), compared to MIN alone (from 41 to 31) (Fig. 3b).

Discussion

Previous studies have reported that combining PBMt with MIN improves patient satisfaction [5], while also enhancing hair diameter and density, and reducing scalp oil secretion [6]. In both studies, participants used helmet-type devices emitting red light (~650 nm) every other day for 25 min over 4 months [5], and 30 min during 6 months [6]. Helmet-type devices, which often combine light-emitting diodes (LEDs) and lasers, are widely used due to their convenience for home use and ability to cover the entire scalp. However, these lasers and LEDs typically have low optical power, around 5 mW. Moreover, hair strands can scatter light and interfere with its penetration into the scalp [11].

This study demonstrates that PBMt, when used in combination with MIN, improves QoL and helps reduce hair loss in women with FPHL. Importantly, our results were observed after 3 months of treatment with two clinic visits per week. These findings may be attributed to the use of a red laser-based device, which delivered a higher power density, allowing more energy to reach deeper tissue layers with just 40 s of irradiation per point across 15 evenly spaced points on the scalp, while minimizing interference from hair strands.

Additionally, those studies did not report on the different phases of hair growth [5, 6]. In this study, we aimed to address that gap and found that, although no significant differences in hair density or count were observed

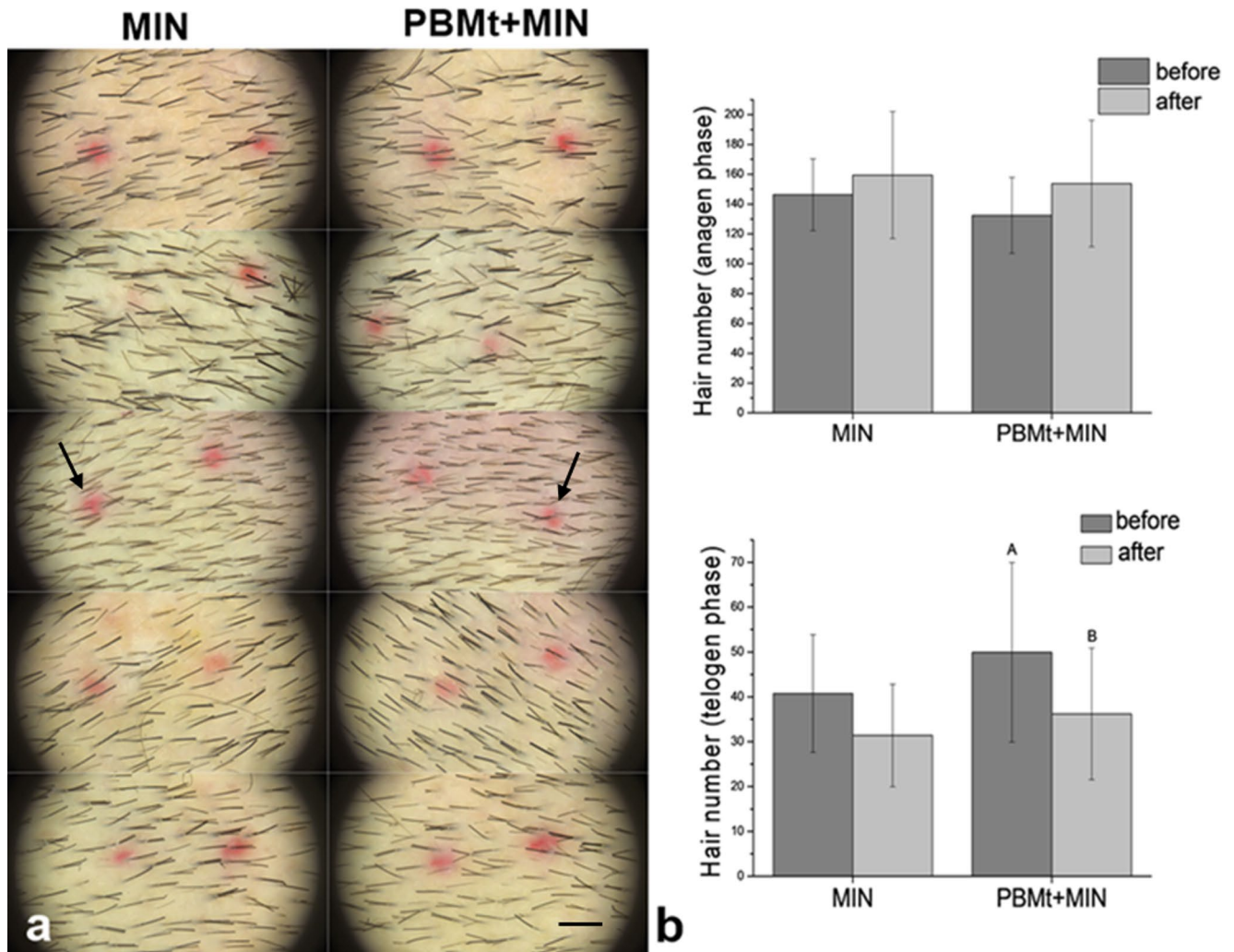


Fig. 3 (a) Phototrichogram images showing red tattoo marks on the scalp used as reference points (arrows). Hair count and density remained similar before and after treatment in both groups. (b) Mean number of hairs (\pm standard deviation) in the anagen and telogen

phases, both assessed 32 days after the final treatment session. Quantitative analysis of hair count assuming anagen hair growth of ~ 0.3 mm/day. Different uppercase letters indicate statistically significant differences between groups. Bar = 1 mm

between the two treatment groups, PBMt + MIN significantly reduced the number of hairs in the telogen phase. This suggests that the treatment promotes the transition of hair follicles out of the resting phase. The shortened telogen phase allowed for earlier detection of changes, whereas improvements in the anagen phase may require a longer observation period.

In conclusion, under the conditions used in this study, the combination of PBMt and MIN may contribute to hair

cycle regulation and reduction of shedding in women with FPHL, even within a shorter treatment period. Although the small sample size represents a limitation that may restrict the generalizability of our findings, the results provide valuable preliminary evidence warranting confirmation in larger, controlled trials. By improving both dermatological and psychosocial outcomes, PBMt may serve as a valuable adjunct to MIN in FPHL management.

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Data availability Data are available from the authors upon reasonable request.

Declarations

Ethics statement This study was approved by the Ethics Committee of the Federal University of São Paulo (UNIFESP) under approval number 4.697.146.

Informed consent All participants were informed about the objectives and procedures of the study and provided their written informed consent before inclusion.

Competing interests The authors declare no competing interests.

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