The Effectiveness of Low-Level Light/Laser Therapy on Hair Loss

Pietro Gentile, MD, PhD,[1,*,i] and Simone Garcovich, MD[2]

Abstract

Background: A systematic review on low-level light/laser therapy (LLLT) in male pattern hair loss (MPHL) and female pattern hair loss (FPHL) has been performed.

Objectives: Compare the reported effectiveness of LLLT in MPHL and FPHL with any control, through randomized controlled trials (RCTs) analysis.

Methods: The protocol was developed in accordance with the Preferred Reporting for Items for Systematic Reviews and Meta-Analyses-Protocols guidelines. A multistep search of the PubMed, MEDLINE, Embase, PreMEDLINE, Ebase, Clinicaltrials.gov, Scopus database, and Cochrane databases has been performed to identify articles on MPHL and/or FPHL treatment with LLLT.

Results: Of the 298 articles initially identified, 136 articles focusing on MPHL and FPHL were selected and, consequently, only 36 articles focused exclusively on LLLT. Of this amount, 23 articles were clinical trials while 13 articles were systematic reviews. Systematic reviews were excluded, and only seven articles were analyzed as RCTs.

Conclusions: All the articles selected and analyzed reported a positive effect of LLLT for MPHL and/or FPHL treatment without side effects.

Introduction

Androgenetic alopecia (AGA) is one of the most important and frequent hair loss (HL) causes affecting mean 80% of white men and 40% of women, determining, respectively, a male pattern hair loss (MPHL) and a female pattern hair loss (FPHL).[1–4] In AGA, lymphocytes and mast cells have been seen around the miniaturizing follicle detailed in the stem cell-rich lump zone.[1–4] Miniaturization of the follicles is characterized by a diminishment of anagen phase, with an improvement in the amount of resting hair follicles, telogen, containing microscopic hairs in a hairless scalp.[5–7]

In the HL scalp, number of hair follicle stem cells stay unaltered, though the number of more actively proliferating progenitor cells particularly diminishes.[8]

A scientific-clinical need exists for the development of biotechnologies to improve the hair regrowth (H-RG) in MPHL and FPHL. Number of articles evaluating the effectiveness of low-level light/laser therapy (LLLT) in MPHL and/or FPHL has exponentially increased during the past decade (2011–2021).

Recently, LLLT has been introduced in combined use with other procedures as platelet-rich plasma (PRP) and micro-needling technique (MN-T) during randomized controlled trials (RCTs)[9] to further increase hair re-growth (H-RG) through regenerative therapies and noninvasive procedures.

Noninvasive strategies may be based on a regenerative approach, involving stem cells and PRP or on development of biomedical device, involving LLLT. Interesting results related to the use of human follicle stem cells to be used in patients affected by AGA have been reported.[10] The PRP technique may represent a valid regenerative strategy to improve H-RG, thanks to its capacity to release several growth factors,[11–13] promoting the survival of dermal papilla cells during the hair cycle through

[1]Department of Surgical Science, Medical School, "Tor Vergata" University, Rome, Italy.
[2]Institute of Dermatology, F. Policlinico Gemelli IRCSS, Università Cattolica del Sacro Cuore, Rome, Italy.
[i]ORCID ID (https://orcid.org/0000-0003-3123-3977).

*Address correspondence to: Pietro Gentile, MD, PhD, Department of Surgical Science, Medical School, "Tor Vergata" University, Via Montpellier 1, Rome 00173, Italy, Email: pietrogentile2004@libero.it

the Bcl-2 protein's activation (antiapoptotic regulator) and Akt signaling.[14] In contrast, current treatments for MPHL and FPHL approved by the U.S. Federal Drug Administration (FDA) are oral finasteride and topical minoxidil® in various forms, including solution and foam.[13]

The first research on "photo-bio-stimulation" or LLLT has been performed in 1967 on mice by using the ruby laser.[14] The purposed mechanism of LLLT in H-RG is the stimulation of mitochondria located in hair bulge stem cells. Cytochrome c-oxidase (CCO) in the membrane of mitochondria is the target chromophore of red light that leads to mitochondrial respiration. Reactive oxygen species and adenosine triphosphate then stimulate cellular proliferation, migration, and oxygenation, which consequently promote hair growth.[15] In 2007, the first cleared LLLT device was introduced for MPHL by the U.S. FDA.[16] Up to present, LLLT technology, based on laser diode (LD) and on light emitting diode (LED), has been adapted by different manufacturers to create LLLT devices, nevertheless, only some of the LLLT products are cleared by the FDA, with few articles published to support the efficacies.

This systematic review aims to compare the reported effectiveness of LLLT with any control for MPHL and FPHL through RCTs analysis evaluating different designs and light/laser source technology.

Methods

Search strategy and literature screening

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews (PRISMA) and meta-analysis.[17]

The research was conducted by the two investigators in accordance with the PRISMA guidelines and the Cochrane handbook.[18] A multistep search of the PubMed, MED-LINE, Embase, PreMEDLINE, Ebase, Clinicaltrials.gov, Scopus, and Cochrane databases was performed to identify studies, published before April 1, 2021, on MPHL and FPHL treatment with LLLT searching without a language or publishing-time restriction.

In total, 298 articles using the keyword "low level laser therapy hair," 31 articles using the keyword "low level led therapy hair," and 136 articles using the keyword "low level laser therapy hair loss" were found.

The articles related to "low level laser therapy hair loss" ($n=136$) and "low level led therapy hair" ($n=31$) were contained in the total amount initially resulted ($n=298$).

Study assessment

This systematic review aimed to assess the selected articles on predetermined criteria according to the patients, intervention, comparator, outcomes, and study design (PICOS) approach,[19] comparing local application of LLLT with any control for MPHL and FPHL. Study assessment was based on inclusion and exclusion criteria (Table 1).

This systemic review, performed on the PICOS approach, is considered an evidence-based medicine (EBM) 1a level study according the Oxford Centre for Evidence-Based Medicine, March 2009.[20]

Study selection

Original articles including RCTs of LLLT in patients affected by MPHL and/or FPHL were all eligible for inclusion. Identification of titles and abstracts of studies was performed by the two investigators. If the information provided in the abstracts was not sufficient to access the eligibility, a full-text evaluation was conducted. The

Table 1. Study assessment based on inclusion and exclusion criteria

Inclusion criteria	
P-Patients	Age 18–79 years, males who showed AGA in stages I–VII according to the NW classification scale, females who showed AGA in stages I–III according to the LW classification scale, and both genders with phototypes I–IV according to FPT classification
I-Intervention	Scalp application of LLLT
C-Comparator	Any type of control, internal, external, and different product
O-Outcomes	Hair density, hair count, hair thickness, hair color improvement, HL reduction
S-Study design	Randomized placebo-controlled trial/randomized, double-blind, placebo- and active-controlled, half-head study/double-blind, placebo-controlled pilot study/blinded randomized clinical trial
Exclusion criteria	
P-Patients	Other types of alopecia, alopecia areata, cicatricial alopecia, lichen planopilaris, use of pharmacological therapeutics targeting MPHL and/or FPHL as finasteride, similar drugs, and/or antiandrogens in the earlier year, use of topical medicines for AGA as lotions as minoxidil®—excepted if finasteride and/or minoxidil was tested as control in LLLT studies—in the earlier year
I-Intervention	Combined use of LLLT with PRP and/or MN-T, combined use of LLLT with other products including finasteride and/or minoxidil
C-Comparator	Not applied
O-Outcomes	Not applied
S-Study design	Expert opinion, comments, letter to editor, single case report, unpublished investigations, conference reports and lack of raw data, preclinical model (animal studies), in vitro studies, articles identified as bias—not correct match with the key word used—group of study <10 patients, shorter follow-up than 3 months, review, and systematic review. No limitations were applied on ethnicity or method of LLLT application

AGA, androgenetic alopecia; FPT, Fitzpatrick; HL, hair loss; LLLT, low-level light/laser therapy; LW, Ludwig; MN-T, microneedling technique; NW, Norwood–Hamilton; PRP, platelet-rich plasma.

two authors also evaluated the quality of the included studies independently. Any disagreement was resolved through discussion.

In total, 298 articles focused on LLLT for hair treatment were initially identified and selected using Prisma Flow (Fig. 1). A total of 162 articles were excluded. Of this amount, 87 were duplicates and/or not adequate, whereas 75 articles were not correctly matched with the topic. In total, 136 articles focusing on MPHL and FPHL were selected and, consequently, only 36 articles focusing exclusively on LLLT in EBM level 1a studies (RCTs and systematic reviews) were analyzed. Of this amount, 23 articles were clinical trials (including RCTs, case series, cohort, and case–control studies), whereas 13 articles were systematic reviews. Systematic reviews were excluded, and only seven articles were analyzed as RCTs.

These seven studies were evaluated and summarized by their study characteristics and study outcomes (Table 2).

Data extraction

Data regarding study design, type of intervention, and outcomes were extracted by the two authors and screened for eligible studies for duplication according to titles, abstracts, and full texts. Any disagreement on the extracted data has been settled by a consensus among P.G. and S.G. Informations on interventions (year, sample size, number and type of treatment arms, participant characteristics, comparative arm regimens) and device properties (summary of general LLLT protocol), were gathered by the

first author (P.G.). Data on design of device, type and number of light/laser source, wavelength, irradiation parameter, irradiation time, session frequency (days/week) and treatment duration (weeks), retail cost, and special features were also collected. The quality of the included investigations was independently assessed using the Cochrane Collaboration's Risk of Bias Assessment tool for RCTs[18] while using the Newcastle–Ottawa Scale to evaluate the individual nonrandomized studies.[21] In terms of outcome, the type of measurement was described (unit area trichograms, phototrichograms, global photography, direct hair count, hair analysis software, and blinded or nonblinded investigator hair analysis), as well as the primary endpoints (hair count/density, hair thickness/shaft diameter, vellus hair count/density, terminal hair count/density, anagen percentage, telogen percentage, tensile strength, and investigator global assessment), and the secondary endpoints (patient satisfaction and subject global assessment).

Endpoint definition

The standardized mean differences (SMDs) of hair density (HD) between the LLLT and sham groups were the primary outcome.[22,23] The positive SMD value indicated LLLT as being a more favorable treatment option when compared with sham. The model of random effects was employed to pool individual SMDs. All analyses were performed using Stata/MP 16 software (StataCorp LP, College Station, TX). Between-trial heterogeneity was
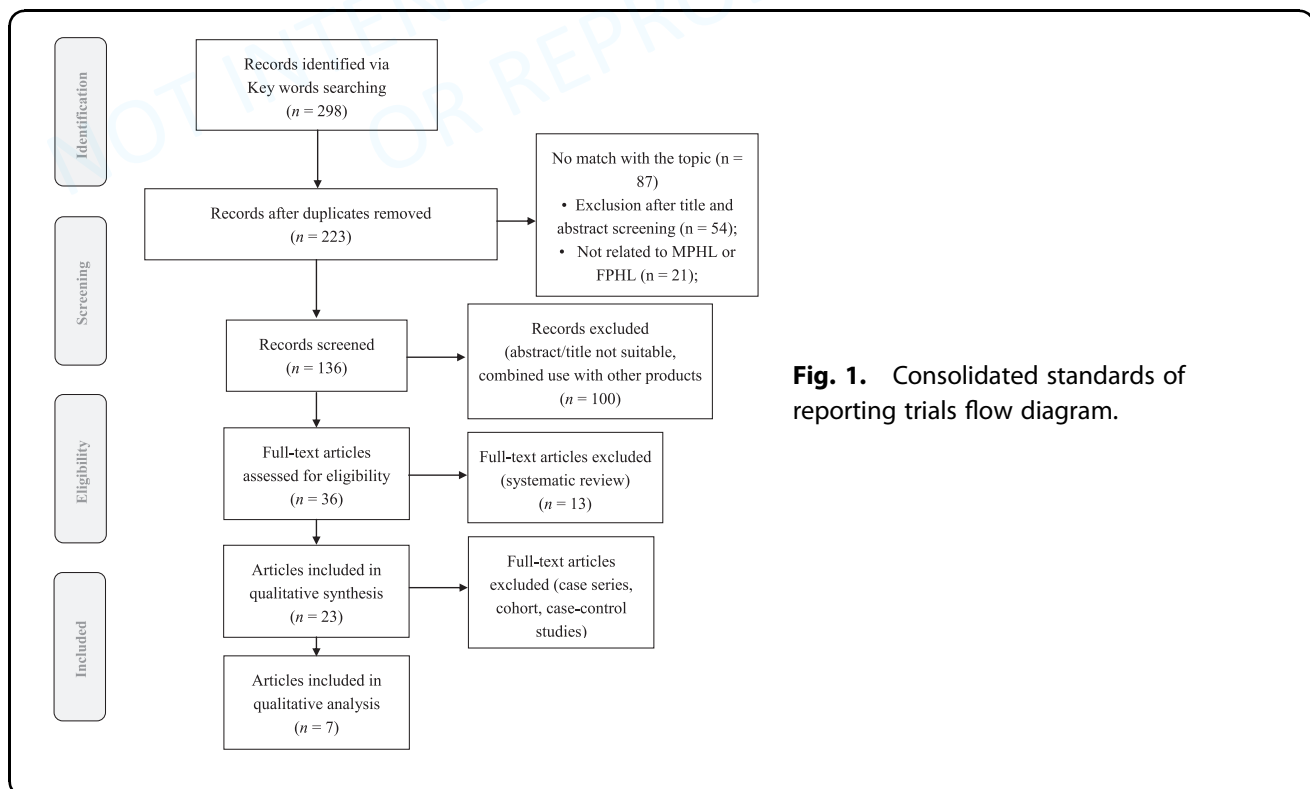

Fig. 1. Consolidated standards of reporting trials flow diagram.

Table 2. The study design and results of the included studies

Authors	MPHL or FPHL grade	Protocol and genders (M/F)	Average age (mean ± SD)	Device	LLLT wavelength
Friedman and Schnoor[26]	LW: I-2, II-2, FPT: I–IV	LLLT (0/19) Sham (0/21)	LLLT 48.4 ± 5.3 Sham 47.1 ± 11.6	Dome laser device (helmet type)	650 nm
Lanzafame et al.[27]	LW: I-2, I-3, I-4, II-1, II-2 FPT: I–IV	LLLT (0/24) Sham (0/18)	LLLT 46.3 ± 9.2 Sham 51 ± 7.1	TOPHAT655 (helmet type)	655 ± 5 nm
Leavitt et al.[28]	NW: IIa–V, FPT: I–IV	LLLT (71/0) Sham (39/0)	47.9 ± 8.7	HairMax LaserComb	655 nm (±5%)
Lanzafame et al.[29]	NW: IIa–V FPT: I–IV	LLLT (22/0) Sham (18/0)	18–48	TOPHAT655 (helmet type)	655 ± 5 nm
Kim et al.[30]	NW: III–VII, LW: I–III	LLLT (15) Sham (14)	LLLT 43.9 ± 12.2 Sham 44.5 ± 11.4	Ooze 3R LLLT device (helmet type)	630, 650, 660 nm
Jimenez et al.[31]	NW: IIa–V LW: I-4, II-1, II-2, frontal, FPT: I–IV	LLLT (0/42) Sham (0/21)	LLLT 49.3 ± 9.1 Sham 49.8 ± 7.3	HairMax LaserComb (comb-type) 9-beam	655 ± 5%
		LLLT (0/39) Sham (0/18)	LLLT 48.7 ± 10.2 Sham 49.1 ± 8.3	HairMax LaserComb (comb-type) 12-beam	635 nm (±5%)/ 655 nm (±5%)
		LLLT (24/0) Sham (14/0)	LLLT 47.8 ± 9.0 Sham 40.9 ± 9.5	HairMax LaserComb (comb-type) 9-beam	655 nm (±5%)
		LLLT (19/42) Sham (21/0)	LLLT 47.9 ± 9.6 Sham 45.9 ± 10.4	HairMax LaserComb (comb-type) 9-beam, 12-beam	635 nm (±5%)/ 655 nm (±5%)
Mai-Yi Fan et al.[32]	NW: IIa–V, LW: I-4, II-1, II-2, FPT: I–IV	LLLT (61/13) Sham (61/13)	LLLT 37.1 ± 8.1 Sham 37.1 ± 8.1	iRestore ID-520 (helmet type)	650 ± 10 nm/ 660 ± 5 nm

FPHL, female pattern hair loss; LD, laser diode; LED, light emitting diode; MPHL, male pattern hair loss; N/A, not available; Tx, treatment minute(s).

determined by using I^2 tests. The two-tailed p-value, I^2 values >50%, and p-value <0.05 were considered as significant heterogeneity.[24,25] Funnel plots and Egger's test were used to examine potential publication bias.[23,24] Statistical significance was defined as p-values <0.05.

Results
Study subjects

A total of seven RCTs were included in the systematic review. The effectiveness of LLLT devices was compared between patient populations of these RCTs and controls. Two articles performed by Friedman and Schnoor[26] and Lanzafame et al.[27] were strictly related to FPHL treatment with LLLT. On the other side, the articles by Leavitt et al.[28] and Lanzafame et al.[29] were strictly related to MPHL treatment with LLLT. Meanwhile, three RCTs by Kim et al.,[30] Jimenez et al.,[31] and Mai-Yi Fan et al.[32] were conducted in both MPHL and FPHL. Besides, the study by Jimenez et al.[31] had the largest number of participants (128 males and 141 females). On the contrary, the remaining articles had small sample sizes. Finally, the qualitative analysis included 607 patients. LLLT's specifications and protocols adopted in the seven RCTs analyzed are reported in the Supplementary Data S1.

The SMDs of changes in HD

All studies evaluated the changes in HD. There was a statistically significant increase of HD in the LLLT group. The overall SMD of LLLT versus sham regarding the changes in HD was 1.27 (95% confidence interval [CI] 0.96–1.59). Regarding SMD heterogeneity, the I^2 was 64.17%.

Subgroup analysis comparing each gender

The subgroup analysis showed no significant difference between genders. The changes in HD of LLLT versus sham in the male group (SMD 1.40, 95% CI 0.78–2.01) and the female group (SMD 1.36, 95% CI 1.04–1.68) were analyzed.

Regarding SMD heterogeneity, the I^2 was <0.01% in the female group and 74.30% in the male group.

Subgroup analysis comparing LLLT devices and LLLT procedure

The subgroup analysis showed no significant difference between the comb- and helmet-type LLLT devices. The changes in HD of LLLT versus sham in the comb-type group (SMD 1.53, 95% CI 1.11–1.96) and the helmet-type group (SMD 0.97, 95% CI 0.64–1.29) were analyzed. Regarding SMD heterogeneity, the I^2 was <58.99% in the comb-type group and 35.09% in the helmet-type group.

LEDs or LDs wavelength/ quantity/power	Power density/fluence	Treatment duration	Treatment frequency	Outcomes (change in hair density)	Side effects
LDs 650 nm/272/5 mW	Total power density: 2.34 mW/cm^2	17	30 min/Tx, every other day	LLLT: 63.7±50.9 Sham: 12.5±13.8	Not reported
LEDs 655±20 nm/30 LDs 655 (±5) nm/21/5 mW	Fluence 67 J/cm^2 for 25-min Tx	16	25 min/Tx, every other day	LLLT: 48.1±17.6 Sham: 11.1±48.33	Not reported
LDs 655 nm/9/≤5 mW	N/A	26	15 min/Tx, 3 Tx/week	LLLT: 17.3±11.9 Sham: −8.9±11.7	Paresthesia: 4 cases Mild urticaria: 4 cases
LEDs 655±20 nm/31 LDs 655±5 nm/20/5 mW	Fluence: 67.3 J/cm^2 for 25-min Tx	16	25 min/Tx, every other day	LLLT: 67.2±33.4 Sham: 32.3±44.2	Not reported
LEDs 630 nm/24/3.5 mW LEDs 660 nm/18/2.5 mW LDs 650 nm/27/4 mW	630-nm LEDs: 60.7 mW/cm^2 660-nm LEDs: 182.8 mW/cm^2 650-nm LDs: 115.4 mW/cm^2 Total power density of device: 92.15 mW/cm^2 Fluence: 47.90 J/cm^2 for 18-min Tx	24	18 min/Tx, daily	LLLT: 17.2±12.1 Sham: −2.1±13.3	Headache: 9 LLLT, 7 sham Dermatologic problem: 5 LLLT, 4 sham
LDs 655 (±5) nm/9	N/A	26	11 min/Tx, 3 Tx/week	LLLT: 20.2±11.2 Sham: 2.8±16.5	Dry skin (5.1%) Pruritus (2.5%) Scalp tenderness (1.3%) Irritation (1.3%) Warm sensation (1.3%)
LDs 635 nm (±5%)/6 LDs 655 nm (±5%)/6	N/A	N/A	18 min/Tx, 3 Tx/week	LLLT: 20.6±11.6 Sham: 3.0±9.3	N/A
LDs 655 nm (±5%)/7	N/A	N/A	15 min/Tx, 3 Tx/week	LLLT: 18.4±13.7 Sham: 3.0±9.3	N/A
LDs 655 nm (±5%)/9 LDs 635 nm (±5%)/6, 655 nm (±5%)/6	N/A	N/A	8 min/Tx, 3 Tx/week	LLLT: 25.7±17.1 Sham: 9.4±12.9	N/A
LEDs 660±5 nm/27/<22 mW/cm^2 LDs 650±10 nm/27/<4.6 mW	N/A	24	30 min/Tx, 3 Tx/week	LLLT: 6.0±12.5 Sham: −2±12.6	Eczema (4%) Pruritus (3%) Acne (1%)

Subgroup analysis comparing LLLT light/laser sources

The subgroup analysis showed a significant difference between LLLT light and laser sources ($p=0.043$). The changes in HD of LLLT versus sham in the LDs alone group (SMD 1.52, 95% CI 1.16–1.88) and the LEDs and LDs combination group (SMD 0.85, 95% CI 0.55–1.16) were analyzed.

Regarding SMD heterogeneity, the I^2 was 51.25% in the LDs group and 20.15% in the LEDs and LDs combination group. The Egger test revealed no significant publication bias for overall SMD ($p=0.708$).

LLLT protocols and specifications

Overall, there were four different devices, including sport cap (20 devices), headband (2 devices), comb (4 devices), and helmet (6 devices) according to the manufacturers. Each device had its number of LLLT sources. Of these, Revian Red[®] (REVIAN, Inc., Durham, NC) was the device with only LED of 620 to 640 nm wavelength. iGrow[®] (Apira Science, Inc., Boca Raton, FL) and iRestore[®] (Freedom Laser Therapy, Inc., Irvine, CA) devices contained both LDs and LEDs. Besides, 28 of the devices contained only LDs, with the number ranging from 7 LDs (HairMax Lasercomb[®] 7; Lexington International LLC., Boca Raton, FL) to 304 LDs (LaserCap

HD+; LaserCap Company, Highland Heights, OH). The median (range) number of LDs used in these devices was 148 (7–304), with power <5 mW. Nevertheless, the median (range) total output of these devices was 740 mW (35–1520 mW), with median (range) wavelength of 650 nm (620–678 nm). The treatment duration time was 30 min (ranging from 90 s to 36 min), depending on the shapes and total power outputs. HairMax[®] LaserBand 82 (Lexington International LLC.) required the least treatment time of 90 s. Meanwhile, LaserCap[®] LCPRO (LaserCap Company) required a maximum treatment duration of 36 min. Most devices were advised to be used about three to four times per week. Only Revian Red was instructed to be used daily.

Discussion

This systematic review included seven RCTs[26–32] in which patients affected by MPHL and/or FPHL who received LLLT treatments demonstrated a significant increase in HD, compared with the sham controls. The outcomes indicated that the LLLT devices could improve HD in both men and women affected by MPHL and FPHL, respectively, with no significant difference between the two genders. Both the helmet-type and the comb-type LLLT devices also yielded effective treatment outcomes. The findings reported in this systematic review

are consistent and extend those from prior reports, being able to be compared with those obtained by PRP injection[3,4] and/or MN-T.[9]

The two main limitations of the analyzed studies were the short-term follow-up (not >26 weeks) and the absence of head-to-head studies with effectiveness comparison. Although the mechanism of action on hair follicles is still under debate, it has been proved that LLLT is a promising option for MPHL and/or FPHL treatment.

However, there was a significant difference between light and laser sources. In this study, 32 home-use LLLT devices cleared by the U.S. FDA were analyzed. Thus, the systemic review purposed to compare the effectiveness of those devices with controls in seven RCTs, that is, one Capillus®,[26] two HairMax,[28,31] two iGrow,[27,29] and two iRestore.[30,32]

Moreover, there were two cohort studies: one prospective cohort study[33] and one retrospective cohort study[34] to support the efficacies of home-use LLLT devices. The subjects in most RCTs had mild-to-moderate pattern HL as MPHL (Norwood–Hamilton scale grade IIa-V) and/or FPHL (Ludwig scale–Savin Baldness Scale I-2, I-3, I-4, II-1, and II-2). The duration of studies ranged from 16 to 26 weeks, with the mean duration of 21.3 weeks. For the assessment, most articles in RCTs showed positive results of an increase in microscopic hair counts. The majority of LLLT treatment group yielded a statistically significant improvement in hair counts compared with the control group. In two noncontrolled trials,[33,34] LLLT also demonstrated an improvement when compared with baseline, with no provided *p*-value. Meanwhile, there was one RCT that also studied the effectiveness of helmet LLLT device in combination with topical minoxidil in FPHL.[35] The application protocol differences of LLLT devices included shape, light source, number of LEDs and LDs, wavelength, and total power output. Owing to no head-to-head study to evaluate those devices, it was unable to determine the clinical benefits over one another. When considering number of diodes, the comb-type LLLT devices used the least number of diodes, ranging from 7 to 12 diodes. Besides, the prices of comb-type LLLT devices were cheaper than other shapes and, also proved for clinical efficacies.[28,31] So, they could be good options for patients with financial limitations. In addition, the hand-free devices including caps,[26] and helmets,[27,29,35] which were well proved for clinical efficacies, usually used a high number of diodes, ranging from 40 to 304 diodes with user-friendly capability. In particular, patients could manage their daily activities during treatment sessions. Among 32 home-use LLLT devices, the majority (87.5%) of them were composed of only LDs, with essential lasers for therapeutic benefits. Following the collimated, coherent, highly monochromatic beam properties, the possibility of high-power densities was then

considered preferable.[36] Interestingly, this systematic review revealed a significant difference between light and laser sources. However, the noncoherent light sources, such LEDs, and broad-band lamps, have recently become common with advantages of LEDs, including no laser safety considerations, ease of home use, ability to irradiate a large area of tissue at once, possibility of wearable device, and much lower cost per mW. A range of light energy sources from LEDs to lasers have been used with specific advantages and limitations.[37] Currently, there is an evidence to show the nondependence of photobiomodulation (PBM) on lasers or coherence. However, the monochromatic LED devices could also yield physiological effects.[36] The study of LLLT devices for MPHL and FPHL treatment consisted of 224 red LDs (660 nm, 5 mW) for the treatment group. Whereas the sham devices composed of 224 LEDs (650 + 20 nm) for the control group. Each LD had the optical power at the irradiance of 3.5 mW/cm². Whereas the LEDs had the power of 0.5 mW/diode (10 × lower than LDs). The result of the study yielded an increase in HD and diameter in both groups. The treatment group was significantly superior to the sham devices. The mean change from baseline to week 24 for HD was 10.21 ± 3.25 hairs/cm² in the treatment group versus 3.95 ± 1.32 hairs/cm² in the sham group. The mean change for hair diameter was 6.11 ± 2.15 μm in the laser group versus 3.76 ± 1.24 μm in the sham group. Therefore, the LEDs seemed to have effect on PBM as the LDs. Owing to the very low power of LEDs used in this study (0.5 mW/diode) when compared with the appropriate dose of 2–4 J/cm², the results of LEDs in this study could not be obviously concluded.[38] Nevertheless, some head-to-head studies that compared both light sources showed no difference in their effects.[36] Hence, more high-quality head-to-head comparison studies should be recommended to verify the significant difference between dose responses or physiological effects of LEDs and laser PBM.[35,37] When considering the wavelength, all devices used the light/laser sources with 620–678 nm due to the absorption peak at 660 nm[39] of CCO as the chromophore for LLLT. According to the Arndt–Schulz Law, as reported in the article of Huang et al.,[40] it is widely accepted that if the irradiance or the duration is too short, there is no response. Similarly, if the irradiance or duration is too high, then the response may be instead inhibited. According to Hamblin et al.,[40] the irradiance of 2–4 J/cm² was suspected to be appropriate. When this theory was applied to the LLLT devices, it was usually provided to patients with this therapeutic irradiance. From the published articles to support the effectiveness of devices, it was obvious that the included participants were only mild-to-moderate MPHL and/or FPHL.

However, no study was conducted in severe cases of HL. In a study to compare the effectiveness of standard

treatments including oral finasteride and topical minoxidil with LLLT, the 1 mg of finasteride in MPHL for 12 months could significantly increase total hair counts for 7.3% and 8.99% at 6 and 12 months, respectively ($p < 0.001$).[41] Whereas the 2% and 5% topical minoxidil demonstrated a significant increase of nonvellus hair counts for 8.84% ($p = 0.013$) and 12.3% ($p < 0.001$) at 48 weeks, respectively.[42] The LLLT effectiveness revealed a significant increase of terminal hair counts for 20.9/cm^2 (12.79%, $p = 0.0249$) versus 25.7/cm^2 (16.96%, $p = 0.0028$) in the 9- and 12-beam laser comb-treated side at 26 weeks after treatment, respectively.[31] Hence, the effectiveness of LLLT appeared to be comparable with the conventional HL treatment. Moreover, the comparable effectiveness was also observed in treatment of FPHL for 4 months. Furthermore, the combination treatment of 5% minoxidil and LLLT seemed to provide better response of HD than minoxidil or LLLT alone.[35] This systematic review demonstrated a relative effectiveness and safety for LLLT in the treatment of MPHL and/or FPHL from the analysis for RCTs, offering another new effective treatment method for HL. In the author's opinion, the need for large scale RCTs and more extensive systematic review appears necessary to confirm the effectiveness of LLLT currently suffering considerable applicative protocols heterogeneity. Heterogeneity is mainly because of the different treatment regimens, represented by the LEDs or LDs number, devices shape, and kind (cap, comb, hairband, and helmet), wavelength and power adopted, and duration times. For the mentioned reasons, currently a widely shared protocol of LLLT application is lacking.

Conclusions

In conclusion, this systematic review showed the effectiveness of LLLT in only mild-to-moderate MPHL and/or FPHL through haircount and HD evaluation. Given the current treatments differ in methodology and applicative protocols, further studies are needed to define standardized protocols, and large-scale randomized trials still need to be conducted to confirm its effectiveness.

Authors' Contributions

P.G. designed the studies, performed the procedures, analyzed the results, wrote the article, wrote editing review, dealt with methodology and validation, performed the data analysis, conducted the study as leader, performed formal analysis and investigation, writing—original draft preparation, writing—review and editing, and visualized the study; S.G. validated the study; and P.G. and S.G. conceptualized the study, and methodology, software, resources, data curation, supervision, project administration, and funding acquisition were taken care of P.G. and S.G.

Author Disclosure Statement

No competing financial interests exist.

Supplementary Material

Supplementary Data S1

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