Review Article

Role of Low-Level Light Therapy (LLLT) in Androgenetic Alopecia

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Abstract

Androgenetic alopecia (AGA) is the commonest type of alopecia affecting over half of men and women. Only two drugs have been approved so far (minoxidil and finasteride), and hair transplant is the other treatment alternative. Low-level laser therapy (LLLT) has been claimed to be a new safe devise-based modality for stimulating hair growth in men and women in AGA. Searches of PubMed and Google Scholar were carried out using keywords alopecia, hair loss, and LLLT. Fifteen studies were found to be strongly relevant and were analyzed. Studies have shown that LLLT stimulated hair growth in both men and women. Studies with largest randomized controlled trials demonstrated statistically significant hair regrowth by terminal hair count in both males and females. One study also showed that LLLT and minoxidil had similar efficacy in hair growth and that combination therapy was even more effective. LLLT represents a non-invasive, safe, and potentially effective treatment option for patients with AGA who do not respond or are not tolerant to standard treatment of AGA. Moreover, combining LLLT with topical minoxidil solution and oral finasteride may act synergistic to enhance hair regrowth. However, the level of evidence of the studies is still low and hence more controlled large studies are needed.

Keywords: Alopecia, androgenic alopecia, hair loss, low-level laser therapy

Introduction

Low-intensity light is called low-level laser therapy (LLLT) which stimulates cellular activity in tissues. It is associated with a range of wavelengths from red through to infrared laser light that promotes tissue repair and regeneration. The overall effect of LLLT on body is called photobiomodulation.[1] The "optical window" for biological tissue is approximately 650–1200 nm. The tissue penetration is maximum at these wavelengths, and thus red or near-infrared light (600–950 nm) is utilized in LLLT.[2,3] LLLT has been reported to stimulate hair growth in men and women in androgenetic alopecia (AGA) and was approved by the US FDA in 2007. It is assumed to stimulate anagen phase re-entry in telogen hair follicles (HFs), prolong the duration of anagen phase, and increase rates of proliferation in active anagen HFs. In addition, it also helps to promote reparative regeneration, which occurs during wound healing, and physiological regeneration, which occurs during the hair cycle, which relies heavily on cell proliferation. These laser actions may normalize physiological regeneration of scalp HFs affected in various hair loss disorders such as male and female AGA, alopecia areata (AA), and chemotherapy-induced hair loss.

History

Laser phototherapy relies on exposure of biological tissues to coherent, collimated, monochromatic light,[4] to induce a variety of positive therapeutic benefits. In 1963, Goldman *et al.*[5] were the first to use laser in dermatology, thus heralding an era of great technological development and innovative therapies. In 1967, Mester *et al.*[6] incidentally discovered the ability of lasers to induce hair growth using low intensity light in the red through to infrared wavelengths while treating cancer in mice with shaved backs. Hypertrichosis has been recognized to be

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a possible side effect of laser hair removal treatment as a result of suboptimal fluences that are too low to induce thermolysis, but high enough to promote follicular growth. Stimulation of proliferation was thus found to be one of the mechanisms underlying the pro-regenerative effect and a potential role for laser phototherapy.[7-9]

Objective of this review

Despite its early discovery (1967), usage and evidence for the efficacy of LLLT have been limited. However, of late, there has been much publicity for the device in the internet as a non-drug modality for hair loss—this is partly due to the apprehension with side effects of established drug therapies such as finasteride. Several trichology clinics offer treatment at exorbitant rates and hence the practicing dermatologist needs to be aware of the modality. The review was conducted to meet this need.

Materials and Methods

A literature search was conducted through PubMed, Embase, *Journal of American Academy of Dermatology,* and also from Google Scholar for clinical trials using LLLT to treat AGA using keywords such as androgenetic alopecia, hair loss, LLLT. The research largely focussed on reports or journals documenting LLLT use for hair loss associated with AGA. From the literature review study, it yielded a total of 163 studies. Of these, 15 studies were strongly relevant based on their title and also the data. Five studies using a comb device have been published and four helmet/cap studies published, with two and three of these being randomized controlled trials (RCTs), respectively. As there are few articles on LLLT and AGA, most of which have been written recently, no limitations for publication year were included in the literature search.

Hair cycle

HF undergo repetitive regenerative cycles, and each of these cycles consists of three stages: anagen (rapid growth, active stage), catagen (apoptosis-driven regression, physiological involution stage), and telogen (resting stage).[10] Bulge stem cells are mainly present in the region of the outer root sheath which is located just below the sebaceous gland, coinciding with the point of anchorage of the arrector pili muscles. The most important cells in the HF are those in the dermal papilla (DP). These cells produce signals to control sequential cycling of the follicular epithelium.[11] It is thought that epithelial stem cells, which reside in the bulge area of the HFs, can respond to the signals from the DP. These stem cells give rise to progenitor cells, which then become transiently amplifying cells that migrate downward into the deep dermis. These cells differentiate into matrix cells that actually produce the hair shaft and the sheath. Several growth factor families are involved in HF cycling, namely, fibroblast growth factor, EGF, hepatocyte growth factor, IGF-I, and TGF-β.[11] Signal transducer and activator of transcription 3 (stat3) is the most important transcription factor involved in spontaneous HF cycling.[12]

LLLT appears to stimulate anagen re-entry of telogen HF, prolong the duration of anagen phase, and increase the rate of proliferation in active anagen follicles.[13-15] The modulation of hair cycle reveals an increase of hair density and diameter as well as a decrease of hair shedding, resulting in the clinical improvement of alopecias.

AGA is one of the most common types of hair loss that affects males and females. AGA refers to hair loss in genetically susceptible individuals caused by effects of androgens such as testosterone and its derivative dihydrotestosterone (DHT). In AGA, there is a marked reduction in the proliferative activity in the HF epithelium, which leads to morphological miniaturization of terminal scalp hairs into vellus-like hairs.[16] The etiological basis of AGA is clearly in abnormal androgen signaling, disruption of epithelial progenitor cell activation, and TA cell proliferation, which forms an essential pathophysiological component of this condition.[16]

As of today, the most common methods used for treating AGA are topical minoxidil, finasteride, and surgical hair transplantation. The role of LLLT in AGA suggests that the fraction of all the HFs in the anagen phase is increased. This may be due to the ability of LLLT to stimulate the mitochondria in the bulge stem cells.

Proposed mechanism of action of LLLT

The mechanism of action of LLLT in the treatment of hair loss is not fully known, although there are several theories. It is feasible to suggest that the hair growth stimulatory effect of laser phototherapy is mediated through either a direct or an indirect increase in the proliferative activity within the HF epithelial matrix. LLLT may accelerate keratinocyte and fibroblast mitosis by generating reactive oxygen species (ROS) and antioxidants.[17] The proposed cellular chromosphere responsible for the effect of visible light is *cytochrome c oxidase* (*COX*) with absorption peaks in the near infrared and mitochondria the likely site for the initial effects.

The hypothesized *mechanisms of action* of LLLT are:

i) increased adenosine triphosphate (ATP) production;
ii) modulation of ROS;
iii) induction of transcription factors such as nuclear factor kappa B and hypoxia-inducible factor-1.

These transcription factors enhance gene transcription and protein synthesis, contributing to cell proliferation and migration. The most widely accepted mechanism is that LLLT displaces nitric oxide from COX allowing an influx of oxygen to bond to COX and progress forward in the respiratory process to ATP production and ROS signaling. These effects further lead to increased cellular

proliferation, modulation in levels of cytokines, growth factors, and inflammatory mediators, and increased tissue oxygenation.[18-20] Several studies have shown that LLLT can decrease inflammation, which may then activate hair growth. Specifically, trials of LLLT have shown decreased inflammatory prostaglandin E-2 and an increase in anti-inflammatory cytokines.[21]

The speculated mechanism for LLLT and hair growth promoting effects is the direct stimulation of HF stem cells in the bulge region, thereby inducing differentiation and proliferation via increasing the level of heat shock proteins (HSPs), such as HSP27.[13,22] Increasing evidence also suggests that the transition to anagen phase might be a result of combination effects between (1) direct stimulation on cell proliferation of outer root sheath keratinocytes (ORSKs) and dermal papilla cells (DPCs) and (2) the release of paracrine growth factors from DPCs, which in turn stimulate proliferation of ORSKs. The ORSK proliferation is upregulated by activating the extracellular signal-regulated kinase (ERK) pathway, whereas the DPC proliferation is stimulated via the Wnt/β-catenin and ERK pathways. Several potential paracrine mediators from the DP induced by LLLT are suggested: hepatocyte growth factor, leptin, vascular endothelial growth factor, fibroblast growth factor 7, lymphoid enhancer-binding factor 1, noggin, Wnt10a, andWnt10b.[14,18,23-25]

Biphasic dose response has been demonstrated in a variety of *in vitro* studies and animal experiments on LLLT.[19,26] This response follows the Arndt–Schulz rule reference,[27,28] which states that for every substance, small doses stimulate, moderate doses inhibit, and large doses kill. In addition, effects of LLLT appear to depend on irradiance (or power density; W/cm^2) and illumination time rather than fluence (or energy density; J/cm^2).[19] Different irradiances but the same fluence show different results. Insufficient irradiance or too short an illumination time will have no response. Too high irradiance or too long an illumination time will have inhibitory effects. Only an optimal balance between power density and time will produce stimulating effects.

The results of LLLT for AGA suggest that the fraction of all the HFs in the anagen phase is increased. This may be due to the ability of LLLT to stimulate the mitochondria in the bulge stem cells. Stem cells are quiescent cells that have adapted to survive in their hypoxic niche. The low metabolic rate of stem cells accounts for their relative quiescence and increased resistance to stress. Because stem cells must last for such a long time, they have to minimize the number of cell divisions they undergo because each division carries a small risk of DNA damage. One of the most damaging agents to the longevity of cells is oxidative damage to DNA and other biomolecules, caused by the ROS that is an inevitable by-product of aerobic respiration. Therefore, stem cells tend to have an overall anaerobic metabolism characterized by low mitochondrial activity and high expression of glycolytic enzymes.[29]

So the hypothesis is that when LLLT is delivered to the hypoxic stem cell niche, the rudimentary mitochondria in the stem cells are triggered into action, and mitochondrial biogenesis can take place producing even more mitochondria.[30] Increased mitochondrial activity is accompanied by an increasing demand for oxygen, which is not available in the low-oxygen environment of the niche. Therefore, stem cells have to leave their niche in pursuit of the oxygen they need to satisfy their new metabolism involving oxidative phosphorylation. The burst of intracellular ROS that is observed to follow LLLT[31] may also have a role in triggering the differentiation of stem cells.[32] As mentioned above, the stem cells become progenitor cells, transiently amplifying cells and finally matrix cells as the HFs enter the anagen phase.

LLLT has also shown to be of possible use in a variety of medical conditions such as promotion of wound healing, nerve regeneration, joint pain relief, stroke recovery, and the prevention and treatment of mucositis.[33-38] Clinical studies have shown that LLLT is effective as an analgesic and accelerates the healing of injured tissue.[39-41]

Devices available

Initially, lasers were used as hood. But the penetration to scalp was questionable, especially in females with long hair. Later in 2007, Laser HairMax® comb was approved by the FDA for LLLT in hair loss for AGA, initially for men. In 2011, it was approved by the FDA for female pattern hair loss also. Another home therapy device called laser cap was also approved by the FDA. It has an advantage of full scalp coverage and even distribution. Recently, non-laser devices such as light-emitting diode (LED) have also been tried. Clinical data regarding the LED devices remain inadequate.

The various other devices available are Hairmax Laser Comb (Lexington International, Boca Raton, FL, USA), GrivaMax Laser Cap 272 (Richmond County, NY, USA), RedRestore Max Laser Cap 272 (Capillus, Miami, FL, USA), and HairMaxLaserBand (Lexington, USA).

Usage

The most commonly used devices have wavelengths in the range of 650–1200 nm and fluences of 1–10 J/cm^2, with a power density of 3–90 mW/cm^2. The treatment is usually for 15–20 min, three times a week for 6 months.

LLLT for hair regrowth in animal studies

Wikramanayake *et al.*[13] in 2012 used HairMax Laser Comb (which emits nine beams and attached combs help to part the hairs and improve delivery of laser light to scalp), to demonstrate the effects of LLLT on hair growth in the C3H/HeJ mouse model of AA, using 655 nm for 20 s daily three times a week for a total of 6 weeks.[13] In this study [Table 1], hair regrowth was observed in all the laser-treated mice both clinically and on histology, but no difference was observed

Table 1: Summary of the studies that investigated the efficacy of LLLT for hair growth

	Study	Study group	Devices used, parameters	Results and treatment regimen
1.	Wikramanayake *et al.*[13]	C3H/HeJ mice, AA	HairMaxLaserComb® 655 nm, 20 s daily, 3 times/week, for 6 weeks	Improved hair growth both clinically and on histology
2.	Wikramanayake *et al.*	Rat model, chemotherapy-induced alopecia	HairMaxLaserComb® 655 nm, 1 min daily for 10 days.	Improved hair clinically and on histology
3.	Shukla *et al.*[15]	Swiss albino mice	HairMaxLaserComb® 632 nm, 1 and 5 J/cm^2 at 24-h intervals for 5 days	Increase in the no. of hair follicles at 24-h intervals for 5 days treated with 1 J as compared to the group treated with 5 J/cm
4	Kim *et al.*[44]	24 male patients	655 and 780 nm once a day for 10 min for 4 weeks	Increased hair growth in the vertex and occipital region
5.	Satino and Markou[45]	28 male and 7 female patients (AGA)	HairMaxLaserComb® 655 nm, 5–10 min every other day for 6 months	Improvement seen in hair count and VIP HairOScope for tensile strength
6.	Lanzafame *et al.*[47]	44 male patients (AGA)	Helmet (TOPHAT655®) 655 nm, 67.3 J/cm^2, 25 min every other day, for 16 weeks	Improvement seen in hair count compared to placebo
7.	Leavitt *et al.*[46]	110 male patients (AGA)	HairMaxLaserComb® 3 times/week for 15 min, for 26 weeks	Improvement seen compared to sham-treated group
8.	Jimenez *et al.*[50]	128 male and 141 female patients with hair loss	HairMaxLaserComb® 655 nm, 3 times/week for 8–15 min for 26 weeks	Increased terminal hair density with overall improvement on thickness or fullness of hair compared with sham-treated group
9.	Esmat *et al.*[51]	45 female patients with AGA	iGrow® helmet 655 nm laser diode for 25 min every other day	LLLT and combination therapy showed improved hair density by ultrasound and biomicroscopy. Folliscope showed increase in mean hair density in all groups

Table 2: Therapeutic recommendation for LLLT

For males and females

↑S3 guidelines suggest using LLLT as ancillary therapy for AGA with devices that use energy levels shown to be effective in randomized controlled clinical trials
O S3 guidelines cannot make a recommendation for or against treatment for more than 6 months with LLLT for AGA at the present time

in the sham-treated group (control group undergoing similar treatment procedures without administration of the key therapeutic element, such as application of light that has no therapeutic effect).[13] Another study by them in 2013 on the rat model of chemotherapy-induced alopecia (CIA) using HairMax Laser Comb® demonstrated similar results of hair regrowth clinically and on histology.

Shukla *et al.*[15] studied the effect of helium–neon (He–Ne) laser (632 nm, at doses of 1 and 5 J/cm^{2}at 24-h intervals for 5 days) on the HF growth cycle of testosterone-treated and -untreated Swiss albino mice skin. The results showed that the exposure of testosterone-treated mice to the He–Ne laser at a dose of 1 J/cm^2 led to a significant increase in the number of HFs in the anagen phase when compared with the other groups. However, the 5 J/cm^2-treated group showed a significant decrease in the number of anagen hairs and an increase in telogen HFs. This is consistent with the biphasic effect of LLLT wherein low irradiation doses may cause biostimulation and high irradiation doses may cause inhibition. Another interesting observation in this study is that in He–Ne laser (1 J/cm^2)-irradiated skin, some of the anagen follicles appeared from deeper layers of the skin and possessed a different orientation which both represent the late anagen stage in the hair cycle, which in turn suggests that laser irradiation prolongs the anagen phase.[42,43]

LLLT for hair growth in clinical trials

Kim *et al.* in 2007[44] studied the effects of using a portable light source (655 and 780 nm) in AGA patients for 10 min once a day. Hairs in precisely defined circle at the vertex (AGA region) and occipital sites of the scalp in 24 AGA male patients were evaluated using global photography and phototrichogram. After 14 weeks, the response and the degree of satisfaction of patients and physicians were assessed. Increase in hair density on both the vertex (145.1 vs. 137.3/cm^2 pre-treatment, $P < 0.005$) and occiput (163.3 vs. 153.3/cm^2, $P < 0.005$) as well as anagen/telogen ratio (vertex: 84.7 vs. 79.7 pre-treatment and occiput: 91.9 vs. 89.6 pre-treatment) was observed, and 83% of the patients reported to be satisfied with the treatment.[44]

Satino and Markou[45] tested the efficacy of LLLT on hair growth and tensile strength on 28 male and 7 female AGA patients. Each patient was given a HairMaxLaserComb® 655 nm, to use at home for 6 months for 5–10 min every other day. Tensile strength was measured by VIP HairOScope removal of three typical terminal hairs from a one-square centimeter area. In terms of hair tensile strength, the results revealed greater improvement in the vertex area for males and temporal area for females; however, both sexes benefited in all areas significantly.[45] In terms of hair count, both sexes and all areas had substantial improvement (for temporal area: 55% in women, 74% in men, in vertex area: 65% in women,

120% in men) with vertex area in males having the best outcome.[45]

Leavitt *et al.*[46] used the Hairmax® comb in a double-blind, sham device-controlled, multicenter, 26-week trial randomized study among 110 male AGA patients. Patients used the device three times a week for 15 min for a total of 26 weeks.[46] Significantly greater increase in mean terminal hair density has been reported when compared with subjects in the sham device group.[46] Significant improvements in overall hair regrowth, slowing of hair loss, thicker feeling hair, better scalp health, and hair shine were demonstrated in terms of patients' subjective assessment at 26 weeks over baseline.[46]

Recently, a double-blind randomized controlled trial by Lanzafame *et al.*[47] using a helmet containing 21.5 mW lasers and 30 LEDs (655.5 nm, 67.3 J/cm^2, 25 min treatment) every other day for 16 weeks reported a 35% increase in hair growth among male AGA patients.

Kim *et al.*[48] conducted a 24-week, randomized, double-blind, sham device-controlled multicenter trial among both male and female AGA patients in order to investigate the efficacy of a helmet-type LLLT device combining 650 nm laser with 630 and 660 nm LEDs (total energy density—92.15 mW/cm^2, 47.90 J/cm^2 for 18 min). Even though mean hair thickness and hair density increased significantly in the treatment group, there was no prominent difference in global appearance between the two groups.[48] Findings from a different study by Avram and Rogers[49] were in accordance with these results in which LLLT increased hair count and shaft diameter; however, blinded global images did not support these observations.

In a largest randomized controlled trial, Jimenez *et al.*[50] demonstrated statistically significant hair regrowth by terminal hair count in all HairMaxLaserComb® devices tested compared with sham controls in both males and females. It was given on the whole scalp for three times a week for 26 weeks. The increase in terminal hair density was independent of the age and sex of the subject and the lasercomb model. Additionally, a higher percentage of lasercomb-treated subjects reported overall improvement of hair loss condition and thickness and fullness of hair in self-assessment when compared with sham-treated subjects.[50]

Esmat *et al.* in 2017[51] studied efficacy and safety of LLLT in comparison to topical minoxidil 5% and to a combination of both therapies in the treatment of 45 patients with female pattern hair loss. They were randomly divided into three equal groups, where group (i) patients were instructed to apply topical minoxidil 5% twice daily, group (ii) patients received LLLT using iGrow® helmet device for 25 min 3 days weekly, and group (iii) patients received a combination of both topical minoxidil 5% twice daily and LLLT for 25 min 3 days weekly for 4 months (study duration). Evaluation was done according to clinical, dermoscopic (folliscopic), and ultrasound biomicroscopic (UBM) parameters. In this study, the combination group (iii) occupied the top position regarding Ludwig classification and patient satisfaction. UBM and dermoscopic findings showed a significant increase in the number of regrowing HFs at 4 months in all groups, whereas only UBM showed such significant increase at 2 months in the combination group (iii). A non-significant increase in the hair diameter was also documented in the three groups.[51]

Summary of the studies that investigated the efficacy of LLLT for hair growth

Analysis of results

Studies have shown that LLLT is safe and has some efficacy in the treatment of AGA. At least more than half of the studies showed an improvement in the hair regrowth in the form of increased hair count, increased hair density and tensile strength, and also the prevention of hair loss among the subjects on whom the studies were carried out. While early trials were small and lacked controls, more recent trials have been larger and better designed and had more effective control groups which improve their validity. All studies showed that repeated treatments of LLLT improved AGA over time. In the largest randomized controlled trial, Jimenez *et al.*[50] demonstrated statistically significant hair regrowth by terminal hair count in all patients. HairMaxLaserComb® devices tested, compared with sham controls, in both males and females. Esmat *et al.*[51] demonstrated efficacy of LLLT when used as concomitant therapy to finasteride and minoxidil, thus suggesting that combination treatment can be useful. This study also showed that LLLT and minoxidil had similar efficacy in hair growth and that combination therapy was even more effective.[51]

Studies suggest that patients with male AGA (Hamilton–Norwood III and IV) and female AGA (Ludwig I and II) respond best, since effective photobiostimulation depends on a minimum of hair for effective photobiostimulation, and on a maximum of hair for the laser beam to reach the scalp without absorption or interference from existing hairs. In AA patients, LLLT accelerates the process of hair regrowth.

Evidence level and recommendations for the treatment of AGA in women and in men

The European Dermatology Forum (EDF) initiated a project to develop evidence-based guidelines for the treatment of AGA and based on a systematic literature research the efficacy of the currently available therapeutic options was assessed and therapeutic recommendations were passed in a consensus conference.

According to this evidence-based (S3) guideline [Table 2] for the treatment of AGA in men, two studies assessing the efficacy of LLLT in male patients with AGA with grade

of evidence A2 and C were included in the evaluation, resulting in a level of evidence 2.[45,46]

The two studies assessing the efficacy of LLLT in female patients with AGA met the inclusion criteria of the guideline, with grade of evidence A2 and C and also resulted in a level of evidence 2.[46,52]

In total, three studies concerning LLLT fulfilled the inclusion criteria of the S3 guideline. When used for 16 and 26 weeks under different protocols and with two different devices, LLLT showed an increased hair count (level of evidence 2). However, no long-term follow-up was performed.

Hence according to the evidence-based S3 guideline for the treatment of AGA, further controlled randomized clinical studies are required to establish the efficacy of these devices for hair growth in comparison with established therapies and to evaluate long-term use.

Adil and Godwin in 2016 conducted a systematic and meta-analytical study to assess the efficacy of non-surgical treatments of AGA in comparison to placebo for improving hair density, thickness, and growth (defined by an increased anagen:telogen ratio). This meta-analysis was conducted separately for five groups of studies that tested the following hair loss treatments: low-level laser light therapy in men, 5% minoxidil in men, 2% minoxidil in men, 1 mg finasteride in men, and 2% minoxidil in women. All treatments were superior to placebo (P <0.00001) in the five meta-analyses. The study concluded strongly suggesting that minoxidil, finasteride, and low-level laser light therapy are effective for promoting hair growth in men with AGA and that minoxidil is effective in women with AGA.[53]

LLLT represents a safe and potentially effective treatment option in non-scarring alopecias who do not respond or are not tolerant to standard treatment of hair loss. Combination of LLLT with topical minoxidil and oral finasteride may act synergistically to enhance hair growth. Based on the studies demonstrating LLLT's effects on promoting graft survival, it may be further suggested to have a potential to be used during the immediate period of post-hair transplant surgery to facilitate the healing process and enhance viability and earlier growth of the grafts.

Adverse effects of LLLT

LLLT has demonstrated a remarkably low incidence of adverse effects when it has been used over 50 years for diverse medical conditions and in a variety of anatomical sites. In the specific area of LLLT for hair growth, the only adverse reports in humans were the temporary onset of telogen effluvium developing in the first 1–2 months after commencing LaserComb treatment,[45] but disappearing on continued application. Some other possible considerations are the presence of dysplastic or malignant lesions on the scalp which could be stimulated to grow by proliferative effects of LLLT.[54]

Conclusion

LLLT represents a non-invasive, safe, and potentially effective treatment option for patients with AGA who do not respond or are not tolerant to standard treatment of AGA. Moreover, combining LLLT with topical minoxidil solution and oral finasteride may act synergistic to enhance hair regrowth.[25,48] Due to the known beneficial effect on wound healing, LLLT as an adjunctive therapy in hair transplant surgery may also reduce post-operative healing time and increase graft survival. The scientific basis for such an approach is given, but there is a need for controlled studies with a higher number of patients to establish their position in the management of AGA.

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Conflicts of interest

There are no conflicts of interest.

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