# *Low-level laser therapy and narrative review of other treatment modalities in androgenetic alopecia*

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REVIEW ARTICLE

# Low-level laser therapy and narrative review of other treatment modalities in androgenetic alopecia

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**Abstract**
Androgenetic alopecia (AGA), also termed as androgenic alopecia or common baldness, is a condition where there is androgen mediated conversion of susceptible terminal hair into vellus hair. Although it is reported more commonly in males, it also affects females but the incidence is relatively unknown. AGA tremendously affects the psychology of the patient due to its chronicity of treatment and cosmetic implications. There are numerous treatment options available for AGA but the choice of treatment has to often be tailored according to the patient's needs, affordability, and compliance. This review focusses on the various treatment options available, with special emphasis on the role of low-level laser therapy (LLLT) in the management of AGA. The literature research considered published journal articles (clinical trials or scientific reviews). Studies were identified by searching electronic databases (MEDLINE and PubMed) and reference lists of respective articles. Only articles available in English were considered for this review.

**Keywords** Androgenetic alopecia · Treatment · Low-level laser therapy

## Introduction

Androgenetic alopecia (AGA) is the most common type of progressive hair loss. It is inherited as a polygenetic condition with varying severity, age of onset, and pattern of hair loss. The prevalence of AGA depends on age and race. Although data is scarce, it is generally regarded that around 30% of Caucasian men have AGA by the age of 30 years, up to 50% by 50 years, and 70% by 70 years [1]. Chinese, Japanese, and African American people are less affected than Caucasians [2]. In AGA, there is androgen mediated progressive miniaturization of the hair follicle leading to vellus

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transformation of terminal hair. This is due to an alteration in hair cycle dynamics: anagen/growing phase duration gradually decreases and that of the telogen phase increases. This causes the hair to become thinner and shorter, eventually leading to baldness [3]. The grade of hair loss is assessed by the Hamilton-Norwood scale. The areas of the scalp which are affected preferentially are the temples, mid frontal scalp, and the vertex, whereas the occipital region is spared. This typical pattern is because the hair follicles in the frontal and vertex regions have elevated expression of androgen receptors (ARs), whereas the occipital and temporal regions contain androgen-insensitive hair follicles [4]. There are various treatment options available for AGA but currently the only US-FDA approved drugs are oral finasteride and topical minoxidil. Other common treatment options include are platelet-rich plasma therapy (PRP) and hair transplantation [5]. Low-level laser therapy (LLLT) is a relatively new mode of treatment for AGA. It acts by stimulating the telogen hair to reenter anagen phase as well as prolong the duration of anagen phase [6]. Since studies on the effectiveness of LLLT are scarce, this review was focused to bring to light this new and promising treatment option for AGA.

## Treatment options

### Anti-androgens

Finasteride acts by inhibiting the type-II 5-alfa reductase enzyme, which is responsible for the conversion of testosterone to dihydrotestosterone (DHT). DHT is responsible for causing AGA by binding to receptors in the susceptible hair follicles [7]. Finasteride has been found to increase the thickness and length of hair, increase the rate of hair growth as well as the duration of anagen phase [8]. Finasteride is given at a dose of 1 mg every day for at least 6–9 months [9]. Adverse effects are uncommon with the 1 mg dose used for AGA and is usually reversible on discontinuation, but in some cases maybe persistent (i.e., > 3 months) [10]. These include erectile dysfunction, low libido, and gynaecomastia [11]. Although the benefits of finasteride far outweigh the side effects, it is not an acceptable treatment modality for many patients. Hence, a topical formulation was made in order to circumvent these adverse effects. A study conducted to compare the therapeutic effects of topical and oral finasteride found no statistically significant difference between the two groups [12]. Lower total sperm count in patients starting finasteride treatment already with pre-existing oligospermia was reported in a study of Drobins and her colleague [13]. However, more studies are required to evaluate its efficacy and side effect profile.

Dutasteride inhibits both type-I and type-II 5-alfa reductase. It has been proved to be safe and efficacious in a Japanese study where it was given to 110 patients at a dose of 0.5 mg for 52 weeks [14].

There are some natural compounds, which have been found to contain anti-androgen activity. Saw palmetto, an extract of *Serenoa repens* that is a plant of the Arecaceae family, inhibits 5-alfa reductase enzyme. Studies have shown its efficacy in mild to moderate alopecia [15]. Given at a dose of 320 mg/day, it mainly improves alopecia in the vertex region. Compared to oral finasteride, side effects were mild, most commonly abdominal discomfort [16].

To avoid the risk of side effects of systemic anti-androgen drugs, certain topical drugs were formulated that block the androgen receptor (AR) selectively in the scalp hair follicles. One such drug that has been recently developed is Fluridil [17]. It has been found to increase the anagen/telogen ratio, without causing any adverse effects like sexual dysfunction or alteration in the serum biochemistry values [18].

### Minoxidil

Minoxidil solution is US-FDA approved for the treatment of AGA. It is converted to its active form by the enzyme sulfite transferase [19]. This active form, i.e., minoxidil sulfate acts on the ATP sensitive potassium channels on the arterial smooth muscle cells and hence leads to a vasodilatory effect. It also induces angiogenesis. Due to these changes, the duration of the anagen of the miniaturized hair follicle is prolonged [20].

Studies have shown a decrease in hair shedding after using minoxidil and few patients even had regrowth. It is available as 2%, 5% and 10%. The most effective regimen is 5% solution, 1 ml twice daily. In the first few months, patients may notice increased shedding; this is due to loss of telogen hair. Four to six months are required to see significant results; maximum effect takes around 1 year [21]. Side effects are usually minor and include itching and scaling due to allergic/irritant contact dermatitis. This is due to the propylene glycol content of the liquid formulation used as a vehicle. This can be reduced by using a foam preparation which is alcohol free. However, studies have shown lesser efficacy of foam formulation compared to liquid, possibly due to lesser absorption [22]. Other side effects include hypertrichosis of forehead due to dripping of the solution and early telogen effluvium [23]. The effects of minoxidil wear out once it is discontinued, hence patient compliance is the major limiting factor [24]. Also, efficacy of minoxidil as a monotherapy varies in different patients. A study done by Chitalia et al. demonstrated the low response to minoxidil in individuals with low sulfotransferase activity [25]. Pre-treatment measurement of sulfonyltransferase is hence a useful tool to determine its efficacy in patients [26].

## Platelet-rich plasma therapy

Platelet-rich plasma (PRP) therapy is a process by which patients' blood is withdrawn and centrifuged to separate plasma rich in platelets. This is injected into the scalp, following which the activated platelets release growth factors and cytokines. These growth factors stimulate the stem cells in the hair bulge leading to neovascularization and folliculogenesis [27].

Studies regarding the use of PRP in AGA have shown conflicting results. Trichographic hair count measurement is the accepted standard by US-FDA to assess improvement [28]. Two randomized double-blinded placebo-controlled studies showed improvement in total hair count as well density after 3 monthly injections of PRP [29]. However, a study, which was done by Puig et al. in patients with female AGA, showed no statistically significant difference in hair count when compared to placebo [30]. Another study done by Ayatollahi et al., where 5 patients of AGA received 5 sessions of 2–4 ml PRP, 2 weeks apart were followed up and evaluated 3 months after the last injection. These results showed a decreased anagen/telogen ratio and no difference in hair count/density compared to baseline [31]. Lack of standardization of PRP preparation process, i.e., platelet concentration, method of preparation, and presence of granulocytes could be the factors contributing to the lack of improvement in the above two studies [32].

To date, most studies have shown positive results. Improvement is most commonly reported after 3rd month. The most common side effect was pain at the time of injection. Of note, patients with mild grades of AGA (Norwood-Hamilton stage II–IV) showed better improvement to PRP treatment [32].

## Adipose-derived stem cells

Adipocytes, in addition to their role in energy storage, also secrete growth factors and cytokines like leptin, platelet derived growth factor (PDGF), and transforming growth factor-alfa (TGF-alfa). This activates follicular stem cells and leads to hair growth [33]. A study was done where patients were injected with adipose-derived stem cells, obtained from liposuction of superficial layer of fat from the abdomen. Serial hair counts after 6 months showed a significant improvement. No side effects were noted [34]. However, clinical trials are required to evaluate their long-term efficacy.

## Hair transplantation

Hair transplant is a process by which hair extracted from a donor area is transplanted into the bald areas of the scalp, i.e., frontal region/vertex. The most common donor site selected is the occipital region of the scalp as it is androgen resistant. When hair in occipital region is inadequate, it can be harvested from sites such as the mustache, beard, and chest [4]. The gold standard of hair transplantation is follicular unit transplantation (FUT) [35]. There are two methods of graft harvesting: strip method and follicular unit extraction (FUE). In the first method, a strip of scalp is harvested from the occipital region, and then, individual follicles are dissected and inserted into slits made at the recipient region. In FUE method, individual hair follicles are dissected using small punches of 0.6–0.8 mm diameter. For the first few days to weeks after transplant, some transplanted hair will be lost due to telogen shedding or graft failure. At least 3 months are required to see results, as this is the time required for the transplanted hair to enter anagen phase [17]. Hair transplantation can be combined with other modes of treatment like oral finasteride, topical minoxidil, and PRP to achieve better results [36, 37].

## Microneedling

Microneedling is a procedure of creating controlled tissue injury using devices like rollers and electric pens of various lengths and diameters. This leads to the activation of genes related to hair growth, release of growth factors like PDGF, and hair bulge stem cell activation [38]. It is most commonly used in combination with PRP or to enhance absorption of topical medications through the microchannels created.

## Fractional radio frequency

One of the latest treatment options for AGA is fractional RF. A study done by Verner and Lotti evaluated the efficacy of fractional RF in stimulating hair growth. The device used was HairLux, Innogen technology Ltd., Yokneem, Israel. A total of ten treatments were given two weeks apart to 25 patients. Hair density increased by 31.6% and hair shaft by 18%. The treatment was found to be well tolerated [39].

## Electrotrichogenesis

Electrotrichogenesis involves the application of pulsed electric field to the scalp to stimulate hair growth. A study was done by Maddin et al. in 73 male patients with AGA grade III(v)and Grade IV and evaluated over 36 weeks. At the end of the study, there was a significant increase in hair count in treatment group compared to placebo [40].

## Carboxytherapy

The utility of $CO_2$ injections have meaningfully supplemented and enhanced the practical relevance of carboxytherapy as a method for the management of multiple disorders. Doghaim and his colleagues evaluated carboxytherapy in alopecia areata and androgenetic alopecia and demonstrated that it is a promising therapy for patchy AA and is an option for

adjuvant therapy of AGA; however, more than 6 sessions are needed for results maintenance [41].

### Low-level laser light therapy (LLLT)

Although the potential of low-level laser therapy was first discovered in the 1960s, it is a relatively new treatment modality for hair loss. Laser therapy works on the principle of photobiomodulation; however, its exact mechanism of action in the treatment of AGA is unknown [42]. Several theories put forth suggest that LLLT generate anti-inflammatory cytokines and anti-oxidants that accelerate keratinocyte and fibroblast mitosis. This eventually leads to stimulation of hair growth [43]. These concepts need to be questioned based upon most recent investigations on the role of white dermal adipose tissue in hair cycling [44].

The first RCT on the role of LLLT in AGA was done by Leavitt et al. in 2009. This led to HairMax LaserComb (Lexington International, Boca Raton, FL) to receive FDA clearance. It was a double-blind, sham device controlled multicenter study in which 110 AGA patients were enrolled to receive either LLLT or sham device for 15 min thrice a week for 26 weeks. Patients in the LLLT group were found to have significantly greater improvement in terminal hair density, hair regrowth, and slowing of hair loss. It was also found to be well tolerated with no significant difference in adverse effects between the two groups [45].

Jimenez et al. conducted another large RCT to determine the effectiveness of HairMax LaserComb. It was a multicenter study involving 141 female and 128 male patients of AGA. Patients were randomly assigned to receive LLLT or sham device as a control. Subjects were evaluated at baseline, 16 and 24 weeks. Improvement in terminal hair density was noted in the study group compared to control, which was statistically significant. Patients also reported reduced hair fall and noticeably thicker hair. No serious adverse effects were noted [43].

In a randomized, double-blinded case-control study done by Faghihi et al., a total of 50 patients were randomly assigned to the study group and control group. All patients received 5% minoxidil solution 2 ml twice daily. In addition, patients of the study group also received 20 min of LLLT twice weekly for 24 weeks (using LDU 8024PN/8024BN with 10–50 MW power and 785-nm wavelength). All patients were assessed by trichogram at baseline; and later at 3, 6, 9, and 12 months. Results showed a significantly increased hair count in study group at months 6 and 9 and increased hair thickness only after 12 months. In addition, there was a statistically significant difference in patient satisfaction in the study group compared to control [6].

Kim et al. were the first to evaluate the effects of LLLT on both male and female pattern hair loss. Forty subjects (14 females and 26 males) were enrolled in this 24 weeks randomized double-blind sham device controlled multicenter study. Patients received either a helmet type home use LLLT or sham device for 18 min daily for 24 weeks. There was a statistically significant difference noted in hair density, hair diameter, and investigators global assessment (IGA) scale at the end of the study. No significant difference in adverse effects was noted [46].

In a study done by Suchonwanit et al., 40 patients, 20 male and 20 female, were randomized to receive either a home-use laser helmet (RAMACAP) or a sham helmet 20 min per session thrice weekly for 24 weeks. There was statistically significant improvement in hair density at weeks 16 and 24 and in hair diameter at week 24 in the test group compared to the control (sham device) [47].

In another study done by Mai-Yi Fan et al., 100 patients of AGA were enrolled in a 24-week double-blinded, self-comparison study. Patients received LLLT on one-half of scalp and sham light treatment on the other half, three times a week. Patients were assessed by investigators' global assessment (IGA) of hair regrowth, global scalp photography, and phototrichogram. A significant improvement in hair thickness, hair count, hair coverage, and IGA was observed in the LLLT-treated area compared to the sham light treated area at week 12,24. There were no serious adverse effects on treatment [48].

In an RCT done by Lanzafame et al., 44 male patients with AGA were randomized into a study and control group. The study group received LLLT using a bicycle helmet type apparatus named "TOPHAT655." This device emitted LLLT at 655 nm wavelength, and each treatment was given for 25 min every alternate day for 16 weeks. After 16 weeks, it was observed that the study group had a 35% improvement in terminal hair count as compared to the sham-treated control group [49].

Lanzafame et al. conducted another similar study to evaluate the efficacy of LLLT at 655 nm for female patients with AGA. Forty-seven patients were randomly assigned to the study and control group. Thirty-seven percent improvement in hair count was found in the study group compared to control [50].

## Conclusion

Although androgenetic alopecia is a condition of only cosmetic concern, it causes a lot of psychological distress and financial burden to the patient. Earlier, AGA used to affect males in mid-thirties or forties, but in the current generation, the onset of balding has been seen in patients as young as 17–18. In addition, patients are more cosmetically concerned and seek quick solutions. All the current options of treatment available have their own limitations. Low-level laser light therapy is a promising new treatment modality for AGA. The RCTs

reviewed in this study highlights these benefits. It has proved to improve hair thickness and density with very few tolerable side effects. In addition, patients were satisfied with the results. There is a need for larger RCTs, especially comparing it to the standard treatment modalities like finasteride and minoxidil. The role of dermal white adipose tissue is critical for further improvement of AGA treatment. Pharmacological and non-pharmacological methods need to be optimized to influence adipocyte differentiation and dedifferentiation in dermal white adipocytes to obtain better and more specific results in AGA.

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Disclaimer** "We confirm that the manuscript has been read and approved by all the authors, that the requirements for authorship as stated earlier in this document have been met and that each author believes that the manuscript represents honest work."

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