HIGH SCHOOL EDITION
Journal of Student Research

Volume 12 Issue 4 (2023)

Beyond Traditional Treatments: Exploring Cutting-Edge Approaches for Androgenetic Alopecia

Kavya Garg[1] and Dr. Steve Casper[2#]

[1]Monta Vista High School
[2]Keck Graduate Institute
[#]Advisor

ABSTRACT

Androgenetic Alopecia is a genetically predetermined disorder resulting in hair loss from an excessive sensitivity to androgens. Several treatment options have been investigated for androgenetic alopecia, yet only topical minoxidil and finasteride have received approval from the US Food and Drug Administration. This review article examines and evaluates the efficacy of new, cutting-edge techniques for treating AGA, including Low-Level Laser Therapy, Platelet Rich Plasma Therapy, Micro needling, and Topical Growth Factors and Peptides. Several essential factors are stimulated by minoxidil, including vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), and insulin-like growth factor (IGF)-1. IGF-1 also plays a significant role in regulating follicular differentiation, which makes it a vital regulator of hair follicle development and function. Low-level laser therapy (LLLT) uses low-intensity light at red or near-infrared wavelengths to induce changes in cellular activity, which improves blood circulation, reduces inflammation, and boosts cellular energy, ultimately leading to improved hair follicle density and diameter. Platelet-rich plasma therapy (PRP) is used in dermatology for acne scar treatment, lipid transplantation, wound healing, and hair regeneration. It involves a centrifugation process that increases the platelet concentration and reduces the red blood cell ratio. Micro needling is a minimally invasive procedure that stimulates the production of collagen, growth factors, and neovascularization, which promotes tissue rejuvenation. It is most utilized for individuals who are unable to achieve successful results using medical therapy. These approaches have shown positive outcomes in terms of hair regrowth, improved hair density, increased hair shaft thickness, and patient satisfaction.

Introduction

Androgenetic alopecia, impacting both males and females, is a genetically predetermined disorder resulting from excessive sensitivity to androgens, affecting up over 50% of adult females and 70% of males (Gupta, Goyal, & Mahendra, 2019). AGA exhibits a distinct pattern of hair loss in both males and females. In males, the vertex and frontotemporal regions are primarily affected, while females generally suffer from diffuse hair loss at the crown and top of the head (Ho, Sood, & Zito, 2022). In addition to alopecia, there are other factors that can contribute to hair loss. Other causes include Telogen effluvium, or stress-induced hair loss, and hair loss caused by medical treatments. An individual suffering from telogen effluvium may experience temporary hair loss following a change in their body such as physical or emotional stress (Cleveland Clinic, 2022). Several studies have highlighted the potential psychosocial ramifications of AGA, including depression, decreased self-esteem, and reduced enjoyment of social interactions (Gupta, Goyal, & Mahendra, 2019). Additionally, individuals with AGA who experience continuous disease progression may also encounter a decline in their overall quality of life (Gupta, Goyal, & Mahendra, 2019).

Over the past years, several treatment options have been investigated, yet only topical minoxidil and finasteride have received approval from the US Food and Drug Administration (Garza et al., 2020). Minoxidil, a medication used for promoting hair growth, induces the production of the vascular endothelial growth factor (VEGF), leading to an increase of blood vessel formation and hair growth (Nakamura et al., 2018). While topicals like Minoxidil and

Finasteride are among the most used treatments for AGA, the primary challenge lies in effectively addressing individuals who do not respond to these topicals, particularly Minoxidil, despite its high benefit-to-risk ratio (Gupta et al., 2021). Another drawback is the need for long-term use, which may pose challenges in terms of patient adherence. Certain side effects can arise, such as hypertrichosis near the application site of minoxidil, and potential risks of birth defects, decreased libido, and prolonged impotence associated with the use of finasteride in males (Cervantes, 2018). Refer to Table 1 for a list of possible side effects associated with all FDA-approved treatments for androgenetic alopecia (AGA).

This review article examines and evaluates the efficacy of new, cutting-edge techniques, aside from the standard treatments including Low-Level Laser Therapy, Platelet Rich Plasma Therapy, Micro needling, and Topical Growth Factors and Peptides. Introduction to such novel therapeutic approaches can transform the lives of individuals affected by AGA who aren't able to use standard treatments like Minoxidil and Finasteride. The goal of this review article is to provide healthcare professionals and patients with an overview of the latest developments in AGA treatment through an analysis of relevant studies and clinical trials.

Table 1. FDA- Approved Treatments for AGA

Drug name	Possible Side Effects
Topical Minoxidil	irritant and allergic contact dermatitis, pruritus, scalp irritation, and facial hypertrichosis
Topical Finasteride	skin erythema and contact dermatitis, as well as increased liver enzymes, nocturnal enuresis, testicular pain, headaches, presyncope, decreased libido, erectile dysfunction, ejaculatory dysfunction, and oropharyngeal pain
Oral Finasteride	orthostatic hypotension, erectile dysfunction, ejaculatory dysfunction, decreased libido, depression

Methods

A literature search was done on Google Scholar, PubMed, and clinicaltrials.gov covering the period from May 2017 to the present, with no language, publication year, or publication status restrictions. Additionally, reference lists of identified studies were examined to identify additional relevant research. The keywords used to gather relevant literature includes Alopecia treatment strategies, non-pharmacological interventions for alopecia, experimental treatments for androgenetic alopecia, comparative analysis of alopecia treatments, efficacy of new alopecia therapies, and alternative hair loss treatments. Finally, unrelated studies were excluded based on the title review, and the remaining studies' abstracts and full texts were assessed to ensure relevance to the research objectives.

Novel Therapeutic Approaches for Androgenetic Alopecia

Topical Growth Factors and Peptides

Several essential factors have been shown to be stimulated by minoxidil, including vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), and insulin-like growth factor (IGF)-1 (Nakamura et al., 2018). These factors play a crucial role in increasing vascularization, suggesting that its stimulation and enhancement of the production of VEGF, FGF, and IGF-1 could be a potential therapeutic approach for treating AGA (Nakamura et al., 2018).

Insulin-like growth factor (IGF-1) has also been found to have a significant effect on various parts of hair follicle biology, including follicular proliferation, tissue remodeling, and the hair growth cycle (Trueb, 2018). It also plays a large role in regulating follicular differentiation, which makes it a vital regulator of hair follicle development and function (Trueb, 2018). At present, there are available transdermal products that incorporate IGF-1 through the use of a derma roller. These products often combine IGF-1 with other growth factors like basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF), copper peptide, vitamins B3, B6, and B5, and amino acids such as arginine and lysine (Trueb, 2018). However, it is important to note their effectiveness has not been validated through clinical studies published in peer-reviewed scientific journals (Trueb, 2018).

In a study conducted by Nakamura et al. (2018), human follicle dermal papilla cells (HFDPCs) were used to investigate the efficacy of the water-soluble peptide derived from egg yolk. Using enzyme-linked immunosorbent assays (ELISAs), researchers measured levels of vascular endothelial growth factor (VEGF). The results showed the peptide fraction effectively stimulating HFDPCs in vitro, leading to an increase in VEGF production. Although the study did not discuss the side effects, cost, or accessibility, the findings suggest that the peptide, known as HGP, holds promise as an effective hair growth agent for treating AGA. A further investigation of its potential benefits and limitations is needed in clinical settings.

Low-Level Laser Therapy

Low-level laser therapy (LLLT) has emerged as a novel approach for treating AGA. LLLT typically uses low-intensity light at red or near-infrared wavelengths to induce changes in cellular activity, known as photo biomodulation or photo bio stimulation, through non-thermal effects (Suchonwait, Chalermroj, & Khunkhet, 2019). This technique enhances blood circulation, reduces inflammation, and boosts cellular energy in the form of adenosine triphosphatase (ATP), ultimately leading to improved hair follicle density and diameter (Delaney & Zhang, 2017). Furthermore, prior studies have indicated that low-level laser treatment could be a viable and effective choice for addressing pattern hair loss in both males and females (Darwin et al.,2018; Suchonwanit et al., 2019).

In a recent study conducted in 2022, the efficacy of an LLLT device called the iHelmet, equipped with 200 laser diodes distributed across seven scalp sections, was evaluated. The study revealed that for 51.9% of individuals with mild AGA and 57.4% with moderate-to-severe AGA, the LLLT helmet treatment was moderately effective. In comparison, 27.7% of individuals with mild AGA and 20.0% with moderate-to-severe AGA showed significant effectiveness. In contrast to previous research studies done on LLLT, this study addressed the concerns of validity by utilizing a large number of patients, considering scalp conditions, and implementing flexible inclusion and exclusion criteria (Qiu et al., 2022). The study's conclusion concludes that the clinical effectiveness of the iHelmet is approximately 80%, thus suggesting its potential as another treatment option for AGA (Qiu et al., 2022).

An additional study conducted by Mai-Yi Fan et al. studied 100 patients with AGA for 24 weeks as part of a self-comparison study. During the study, patients received LLLT on one half of the scalp and sham light treatment on the other, three times a week. The effectiveness of the treatments was measured using various methods including investigators' global assessment (IGA) of hair regrowth, global scalp photography, and phototrichogram. At the end of the treatment period, the scalp area treated with LLLT showed a notable increase in hair coverage compared to the side treated with sham light (14.2% vs. 11.8%) as well as statistically significant improvements in hair thickness, hair count, hair coverage, and IGA. Furthermore, no serious adverse effects related to the treatment were reported (Fan et al., 2019).

Platelet-Rich Plasma Therapy

Platelet-rich plasma therapy (PRP) has evolved from its initial use in dental restoration, maxillofacial surgeries, orthopedics, and sports medicine, to a wider application in the field of dermatology, particularly in acne scar treatment, lipid transplantation, wound healing, and hair regeneration (Oh et al., 2011). PRP treatment involves a centrifugation process that increases the platelet concentration and reduces the red blood cell ratio, which results in a high concentration of platelets (94%) and a low concentration of red blood cells (5%). The abundance of growth factors and cytokines in PRP is what is believed to promote tissue rejuvenation and healing (Dhillon & Maloney, 2012).

In a study conducted by Anitua et al., the effectiveness of plasma rich in growth factors (PRGF) was assessed in 19 individuals with AGA. These participants received 5 injections on the scalp of PRP combined with a platelet-rich growth factor (PRGF) activator to stimulate the release of growth factors and morphogens. After a year of follow-up, all outcome measures showed notable improvements compared to the baseline. Significant improvements were seen in mean hair density, hair diameter, and the ratio of terminal/vellus hair. Histomorphometry analysis further supported the use of PRP, demonstrating positive changes in epidermal thickness, perifollicular neo angiogenesis, and the ratio of terminal to miniaturized hair (Anitua et al., 2017).

Another study was conducted in Italy in 2018 by Starace et al. aimed to evaluate the effectiveness, tolerability, and clinical improvement of PRP in the treatment of specifically women with AGA who had not responded to minoxidil and/or oral antibiotics. After 24 weeks, there was a positive relative change percentage observed for all the hair density parameters. Furthermore, there was a significant increase in mean hair diameter in the frontal area after 12 and 24 weeks (Starace et al., 2019). Overall, the studies conducted by Anitua et al. and Starace et al. demonstrate potential for PRP as a treatment option for patients who are unresponsive to standard medical treatments.

Micro needling

Micro needling (MN) is the treatment option most utilized for individuals who are unable to achieve successful results using medical therapy. This technique is a minimally invasive procedure that stimulates the production of collagen, growth factors, and neovascularization, which promotes tissue rejuvenation (Garza et al., 2020).

In a study conducted by Starace et al. in 2019, a total of 50 patients were enrolled, including 36 females and 14 males with AGA. The participants underwent three sessions of MN with a 4-week interval over a period of 6 months. At the end of the 6-month treatment period, all patients experienced decreased hair loss, improved hair density, and thickened hair shafts. The frontal median density showed an increase of 36.64%, while the vertex median density improved by 35.1%, and the medium hair diameter increased in the frontal and vertex areas by 9.75% and 9.08%, respectively (Starace et al., 2020).

Microneedling is also frequently combined with other techniques, as shown in Jha et al.'s study. This study investigated the effectiveness of combining platelet-rich plasma (PRP) with MN and compared the dermoscopic features of individuals with AGA before and after the treatment. The study involved participants between the ages of 18 and 45 with mild to moderate AGA who were administered PRP injections combined with MN. The treatment was conducted over a span of 3 months, with sessions occurring every 3 weeks. Significant hair growth was observed following the initial session of treatment and with over 75% of patients expressing a high level of satisfaction. In individuals with AGA who received PRP treatment, positive changes were noted, including an increase in the number of vellus and total hairs, thicker hair shafts, and a reduction in yellow dots, after completing three sessions. Additionally, in 14 patients, the hair pull test yielded negative results post-treatment.

While studies have concluded that MN is an effective treatment option, its limitations include the invasive nature of the procedure and its associated high cost. Furthermore, surgical alternatives depend on the availability of donor hair for each patient, and the potential for scarring in the donor sites is a large concern, although advancements in techniques such as follicular unit grafting have mitigated this issue (Dhillon et al., 2012). Additionally, common side effects of MN include erythema or pinpoint bleeding, seborrheic dermatitis, itching, infection, granulomatous reactions, and lymph node enlargement (Bao et al., 2020).

Conclusion

This review article provided an overview of the novel therapeutic approaches for androgenetic alopecia (AGA). It discussed various treatments, including platelet-rich plasma (PRP) therapy, micro needling (MN), topical growth factors and peptides, and low-level laser therapy (LLLT). These emerging approaches offer promising alternatives for individuals who have not achieved satisfactory results with conventional treatments like minoxidil and finasteride. The review has also highlighted the effectiveness and potential benefits of these novel approaches. Studies have shown positive outcomes in terms of hair regrowth, improved hair density, increased hair shaft thickness, and patient satisfaction. Additionally, the combination of these therapies like MN and PRP holds promise for enhanced results. However, it is important to take into account the limitations of these approaches, including factors such as invasiveness, high costs, and incomplete results regarding long-term safety. It is also important to note the individual variability in treatment response, as well as the need for individualized approaches, underscoring the complexity of managing AGA. These novel approaches can potentially revolutionize the field of hair loss, offering hope to those dissatisfied with existing treatment options and offering potential cures for AGA.

Acknowledgments

I would like to thank Dr. Steven Casper for his time and valuable feedback on my article.

References

Anitua, E., Pino, A., Martinez, N., Orive, G., & Berridi, D. (2017). The Effect of Plasma Rich in Growth Factors on Pattern Hair Loss: A Pilot Study. Dermatologic Surgery : Official Publication for American Society for Dermatologic Surgery [et Al.], 43(5), 658–670. https://doi.org/10.1097/DSS.0000000000001049

Bao, L., Zong, H., Fang, S., Zheng, L., & Li, Y. (2020). Randomized trial of electrodynamic micro needling combined with 5% minoxidil topical solution for treating androgenetic alopecia in Chinese males and molecular mechanistic study of the involvement of the Wnt/β-catenin signaling pathway. Journal of Dermatological Treatment, 1–11. https://doi.org/10.1080/09546634.2020.1770162

Cervantes, J., Perper, M., Wong, L. L., Eber, A. E., Villasante Fricke, A. C., Wikramanayake, T. C., & Jimenez, J. J. (2018). Effectiveness of Platelet-Rich Plasma for Androgenetic Alopecia: A Review of the Literature. Skin Appendage Disorders, 4(1), 1–11. https://doi.org/10.1159/000477671

Darwin, E., Heyes, A., Hirt, P. A., Wikramanayake, T. C., & Jimenez, J. J. (2018). Low-level laser therapy for the treatment of androgenic alopecia: a review. 33(2), 425–434. https://doi.org/10.1007/s10103-017-2385-5

Delaney, S. W., & Zhang, P. (2017). Systematic review of low-level laser therapy for adult androgenic alopecia. Journal of Cosmetic and Laser Therapy, 20(4), 229–236. https://doi.org/10.1080/14764172.2017.1400170

Gupta, A. K., Talukder, M., Venkataraman, M., & Bamimore, M. A. (2021). Minoxidil: a comprehensive review. Journal of Dermatological Treatment, 1–11. https://doi.org/10.1080/09546634.2021.1945527

Gupta, S., Goyal, I., & Mahendra, A. (2019). Quality of life assessment in patients with androgenetic alopecia. International Journal of Trichology, 11(4), 147. https://doi.org/10.4103/ijt.ijt_6_19

Ho, C. H., & Zito, P. M. (2019, May 18). Androgenetic Alopecia. Nih.gov; StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK430924/

Mai-Yi Fan, S., Cheng, Y.-P., Lee, M.-Y., Lin, S.-J., & Chiu, H.-Y. (2018). Efficacy and Safety of a Low-Level Light Therapy for Androgenetic Alopecia: A 24-Week, Randomized, Double-Blind, Self-Comparison, Sham Device-Controlled Trial. Dermatologic Surgery, 44(11), 1411–1420. https://doi.org/10.1097/dss.0000000000001577

Nakamura, T., Yamamura, H., Park, K., Pereira, C., Uchida, Y., Horie, N., Kim, M., & Itami, S. (2018). Naturally Occurring Hair Growth Peptide: Water-Soluble Chicken Egg Yolk Peptides Stimulate Hair
Growth Through Induction of Vascular Endothelial Growth Factor Production. Journal of Medicinal Food, 21(7), 701–708. https://doi.org/10.1089/jmf.2017.4101
Nestor, M. S., Ablon, G., Gade, A., Han, H., & Fischer, D. L. (2021). Treatment options for androgenetic alopecia: Efficacy, side effects, compliance, financial considerations, and ethics. Journal of Cosmetic Dermatology. https://doi.org/10.1111/jocd.14537
Ocampo-Garza, S. S., Fabbrocini, G., Ocampo-Candiani, J., Cinelli, E., & Villani, A. (2020). Micro needling: A novel therapeutic approach for androgenetic alopecia, A Review of Literature. Dermatologic Therapy, 33(6). https://doi.org/10.1111/dth.14267
Oh, D. S., Cheon, Y. W., Jeon, Y. R., & Lew, D. H. (2011). Activated Platelet-Rich Plasma Improves Fat Graft Survival in Nude Mice: A Pilot Study. Dermatologic Surgery, 37(5), 619–625. https://doi.org/10.1111/j.1524-4725.2011.01953.x
Qiu, J., Yi, Y., Jiang, L., Miao, Y., Jia, J., Zou, J., & Hu, Z. (2022). Efficacy assessment for low-level laser therapy in the treatment of androgenetic alopecia: a real-world study on 1383 patients. Lasers in Medical Science, 37(6), 2589–2594. https://doi.org/10.1007/s10103-022-03520-4
Sharma, V., Bhari, N., Patra, S., & Parihar, A. (2019). Platelet-rich plasma therapy for androgenetic alopecia. Indian Journal of Dermatology, 64(5), 417. https://doi.org/10.4103/ijd.ijd_363_17
Starace, M., Alessandrini, A., Brandi, N., & Piraccini, B. M. (2019). Preliminary results of the use of scalp microneedling in different types of alopecia. Journal of Cosmetic Dermatology, 10.1111/jocd.13061. https://doi.org/10.1111/jocd.13061
Starace, M., Alessandrini, A., D'Acunto, C., Melandri, D., Bruni, F., Patrizi, A., & Piraccini, B. M. (2018). Platelet-rich plasma on female androgenetic alopecia: Tested on 10 patients. Journal of Cosmetic Dermatology, 18(1), 59–64. https://doi.org/10.1111/jocd.12550
Suchonwanit, P., Chalermroj, N., & Khunkhet, S. (2018). Low-level laser therapy for the treatment of androgenetic alopecia in Thai men and women: a 24-week, randomized, double-blind, sham device-controlled trial. Lasers in Medical Science, 34(6), 1107–1114. https://doi.org/10.1007/s10103-018-02699-9
"Telogen Effluvium: Symptoms, Causes, Treatment & Regrowth." Cleveland Clinic, my.clevelandclinic.org/health/diseases/24486-telogen-effluvium#:~:text=Telogen%20effluvium%20is%20a%20common.
Trüeb, R. M. (2017). Further Clinical Evidence for the Effect of IGF-1 on Hair Growth and Alopecia. Skin Appendage Disorders, 4(2), 90–95. https://doi.org/10.1159/000479333