The Efficacy of Green Light Emitting Diodes and Microneedle Patches on Androgenetic Alopecia: A Pilot Study

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Abstract

Androgenetic alopecia (AGA) is a hair condition that affects all populations and age groups globally. Hair follicles may shrink as a result of androgen hyperactivity, which can also shorten the anagen phase and lengthen the telogen phase (Blume-Peytavi et al., 2011). Gradual hair loss can have a negative impact on social interactions and seriously lower quality of life.

The standard treatment for AGA is commonly known as minoxidil and finasteride. Due to adverse effects, the standard treatment for AGA at present, which consists of oral finasteride and topical minoxidil, is not always effective (Hirshburg et al., 2016). As a result, novel therapeutic options should be considered Recently, FDA-approved LLLT devices in combination with microneedling have shown to be safe and effective for hair growth in patients with AGA.

The purpose of this study was to investigate the safety and therapeutic efficacy of an LED microneedle patch in encouraging hair growth among individuals with AGA in comparison to topical minoxidil treatment as conventional management. Dermatologists evaluated the clinical examinations in response to the outcomes. Additionally, the outcomes of the study would be assessed to demonstrate the efficacy of green LED in combination with microneedles, which could be beneficial for dermatologists who want more efficient management approaches to AGA patients.

Keywords: *Androgenic Alopecia, Low-level Light Therapy, Red LED, Green LED, Microneedle, Photobiomodulation*

1. Introduction

Androgenetic alopecia (AGA) is the most prevalent hair condition in terms of non-scarring alopecia. The etiology is frequently caused by a genetic disease resulting from an excessive reaction to androgens in an androgen-dependent characteristic (Inui, & Itami, 2013). The terminal hair on the scalp undergoes a vellus development as a result of the gradual miniaturization of AGA (Pathomvanich, et al., 2002). The frequency and severity of AGA tend to increase with age.

Nowadays, topical minoxidil and oral finasteride are the standard treatment options for AGA. However, the limitations of drug properties and side effects decrease the efficacy of management (Hirshburg et al., 2016). Low-level light therapy (LLLT) and microneedling have emerged as the newest technique, known as a "microneedle patch". These innovative, safe device-based modalities can help with hair regrowth and offer an alternative treatment option for AGA (Katzer, Leite Junior, Beck, & da Silva, 2019).

The precise mechanism that underlies LLLT and microneedling to generate biomodulation effects remains unknown (Fertig, Gamret, Cervantes, & Tosti, 2018). Through the promotion of neocollagenesis, neovascularization, and growth factor generation in the treated area, the combination of LLLT and microneedling is an alternative treatment option that can increase hair density and hair shaft diameter (Waghule, 2019).

Previous research has demonstrated that hair growth can be stimulated by visible red LED or near-infrared (NIR) light (Dhurat et al., 2013). This is because LLLT plays a role in the mitochondria undergoing cell metabolism by photodissociation to inhibit nitric oxide (NO) from cytochrome c oxidase (CCO), which increases ATP production and modifies reactive oxygen species (ROS) (Guo et al., 2021). Following a change in the cellular level, cytokines are released for anti-inflammatory effects, which in turn trigger the Wnt10b/β-catenin pathway to promote the growth of hair.

Due to the research gap concerning different wavelengths of LED light in combination with microneedle patches, this study aims to investigate the photobiomodulation effects of green LED light in comparison to previous studies on red LED light for stimulating hair growth. Low-level light therapy (LLLT) and microneedling will be combined for a photobiomodulation effect that can reduce inflammation, hasten the mitosis of keratinocyte and fibroblasts, stop nitric oxide synthesis, and ultimately promote the growth of hair (Atiyeh, Abou Ghanem, & Chahine, 2021; Cohen, & Elbuluk, 2016). Furthermore, microneedling enhances transdermal light delivery and makes it easier to create micropunctures on the skin to encourage wound healing and reduce inflammation (Hou, Cohen, Haimovic, & Elbuluk, 2017). This study compares the effectiveness and safety of green LED microneedle patches on the development of hair in patients with AGA. In this study, the best therapeutic success for patients with AGA is achieved by using microneedle patches in conjunction with LLLT.

2. Objectives

To evaluate the efficacy of green LED light in combination with the microneedle procedure on hair growth in AGA patients.

3. Materials and Methods

This study was conducted from July 2023 to September 2023 at the Dermatology OPD, Benchakitti Park Hospital and enrolled 8 participants aged between 18 to 60 years old who were diagnosed with AGA. Disease severity is usually classified using the Hamilton-Norwood classification, which is divided into I-VII main stages. Male participants presenting recession of the frontal hairline, particularly in a triangular pattern with Hamilton-Norwood Stages between III to IV (including Type III vertex), were enrolled. Female pattern hair loss usually presents with a diffuse thinning of the middle to lateral region with preservation of the frontal hairline, commonly using the Ludwig scale to classify. Female participants were enrolled with a Ludwig scale of I-II.

No participants were provided systemic medication (Finasteride within 12 months or Dutasteride within 18 months) or received topical treatment within the six months prior to the study. The standard treatment of AGA is well-known as oral finasteride and topical minoxidil. Additionally, none of the individuals had used any hair treatments or taken any supplements intended to stimulate hair growth for the three months before the trial as any recent treatments from patients could alter the efficacy and accuracy of the results in the study. Moreover, patients with a history of hair transplantation or restoration surgery were excluded. Systemic diseases like cancer, syphilis, HIV, hypertension, diabetes mellitus, malnourishment, autoimmune diseases, and immunocompromised diseases would also be disqualifying factors. All patients who met the inclusion and exclusion requirements were enrolled to take part in this study.

An LED helmet was used to emit different wavelengths of light: Green light was emitted at 513 nm, and red light was emitted at 629 nm with an energy dose of 0.2 J/cm^2, which was connected to a 20-minute timer. The microneedle patch measured 900 micrometers in length and 105 needles per centimeter in thickness. To promote hair development, an optical microneedle provides full LED energy down to the hair follicles. The green LED light in combination with microneedle patches on the right frontal lobe and the red LED light in combination with microneedle patches on the left frontal lobe will be used for the experiments in both frontal recession zones. Typically, the process requires 20 minutes for each weekly session over a three-month period. Each month, clinical photos were taken and gathered for comparison to the baseline. Every week at each appointment, any potential side effects or complications such as edema, erythema, infection, or allergy would also be assessed.

The clinical outcomes would be evaluated by one blinded dermatologist and participants using 7-point rating scale scores from the clinical photography. For results analysis, the Wilcoxon signed-rank test was used for a non-parametric statistical hypothesis test to compare with the baseline; a *p*-value <0.05 was considered statistically significant.

4. Results and Discussion

This study was conducted in the outpatient section of the Department of Dermatology, Benchakitti Park Hospital. A total of 8 participants, comprising five males and three females, met the inclusion criteria and were enrolled in this study. A few other participants who received previous treatments related to hair growth were excluded. The five male participants mainly had Hamilton-Norwood Stage grades 2 and 3 with frontal recession of the hairline, while two of three females had FPHL Ludwig type 2 with thinning of the centroparietal hairline. No patients withdrew from the study. The demographic data are shown in Table 1.

Table 1 Demographic characteristics of participants

Sex	AGA/FPHL Grading	n	Percent (%)
Female	1	1	33.3%
	2	2	66.7%
Male	1	1	20.0%
	2	2	40.0%
	3	2	40.0%

For the evaluation of clinical improvement using 7-point rating scale scores ranging from -3 to +3 based on satisfaction with hair growth, the scale includes scores of -3 significantly decreased, -2 moderately decreased, -1 slightly decreased, 0 no change, +1 slightly increased, +2 moderately increased and +3 significantly increased.

Table 2 Wilcoxon Signed Ranks Test with a 7-point rating scale for clinical evaluation

	Score	Patient satisfaction	*p*-value	Doctor satisfaction	*p*-value
Baseline	0	8 (100%)	Reference	8 (100%)	Reference
	1	0 (0%)		0 (0%)	
	2	0 (0%)		0 (0%)	
	3	0 (0%)		0 (0%)	
Month 1	0	3 (37.5%)	0.025*	7 (87.5%)	0.317
	1	5 (62.5%)		1 (12.5%)	
	2	0 (0%)		0 (0%)	
	3	0 (0%)		0 (0%)	
Month 2	0	1 (12.5%)	0.011*	6 (75%)	0.157
	1	6 (75%)		2 (25%)	
	2	1 (12.5%)		0 (0%)	
	3	0 (0%)		0 (0%)	
Month 3	0	0 (0%)	0.008*	2 (25%)	0.020*
	1	1 (12.5%)		5 (62.5%)	
	2	6 (75%)		1 (12.5%)	
	3	1 (12.5%)		0 (0%)	

The clinical evaluation analyzed patients' and dermatologists' satisfaction using 7-point rating scale scores. Patient satisfaction indicates that green LED light in combination with microneedle patches stimulates hair growth in the first month, accounting for 62.5%. Significantly, hair growth is slightly increased compared to the baseline with a *p*-value of 0.025. Moving on to patient satisfaction in the second month, the evaluation also indicates that green LED light in combination with microneedle patches slightly stimulates hair growth, accounting for 75%, with a *p*-value of 0.011, which is statistically significant. Lastly, patient satisfaction in the third month of the study indicates that green LED light in combination with microneedle patches moderately stimulates hair growth, accounting for 75%. The increase in hair growth from the combination of green LED light and microneedle patches is statistically significant compared to the baseline with a *p*-value of 0.008, as illustrated in Table 2 and Figure 1.

Clinical evaluation by a dermatologist in the first month of hair growth from green LED light in combination with microneedle patches shows no significant difference statistically from the baseline, accounting for 87.5% with a *p*-value of 0.317. In the second month, hair growth from green LED light with microneedle patches showed a statistically significant increase in hair growth, accounting for 75% with a *p*-value of 0.157. Lastly, the combination of green LED light with microneedle patches in the third month of treatment indicates slightly increased hair growth, accounting for 62.5% with a *p*-value of 0.02, which was statistically significant.

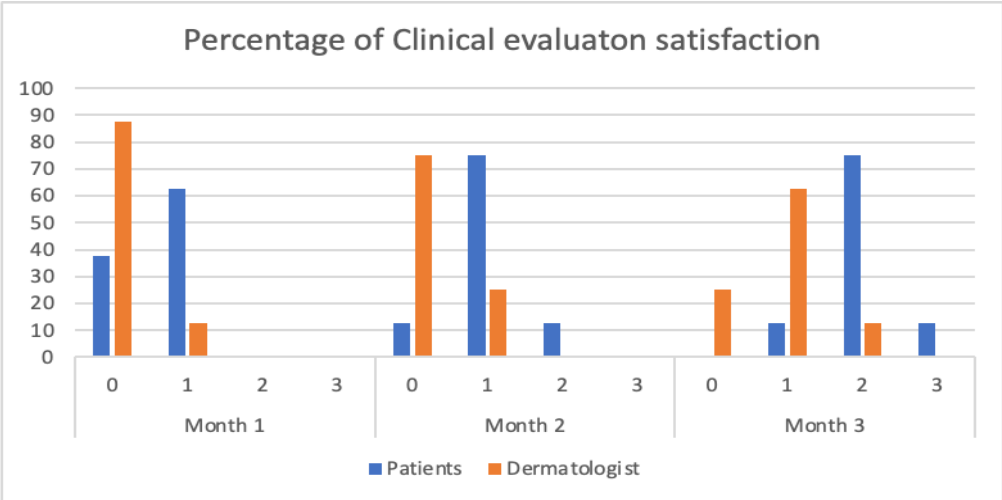

Figure 1 Percentage of clinical evaluation satisfaction on a 7-point rating scale

Figure 2 Progression of hair growth from green LED light in combination with microneedle patches

5. Conclusion

Androgenetic alopecia (AGA) is the most common non-scarring form of progressive hair loss nowadays. LLLT devices are FDA-approved and demonstrate safety as well as effectiveness in patients diagnosed with AGA and FPHL.

LLLT can increase the rate of mitosis, activate follicular keratinocytes or stimulate hair follicle stem cells, change cell metabolism, and reduce inflammation. Microneedling is another intriguing approach that can promote the creation of growth factors, collagen, and neovascularization. To get the best possible therapeutic effect, this study developed a unique LED microneedle patch that combines these two modalities. The photobiomodulation effects of low-level laser therapy (LLLT) lead to improvements in local blood circulation, immunity, anti-inflammation, pain management, wound healing, anti-edema, and antibiosis (Babapour, Glassberg, & Lask, 1995; Basford, 1995; Conlan, Rapley, & Cobb, 1996) Moreover, LLLT may promote hair follicle stem cells, facilitate mitosis, and activate follicular keratinocytes (Lubart et al., 2005). Inhibitory nitric oxide (NO) is photodissociated from cytochrome c oxidase (CCO) by LLLT, which affects the mitochondria, modifies reactive oxygen species (ROS) and increases ATP synthesis (Guo et al., 2021). The biological reactions of hair follicle cells and perifollicular cells during LLLT are triggered by these activated molecules through redox-related signaling pathways. Additionally, the light lowers levels of prostaglandin E-2 and other proinflammatory cytokines like TNF-α and IL-1β (de Lima et al., 2010; Sakurai, Yamaguchi, & Abiko, 2000), but raises levels of anti-inflammatory cytokines such as TGF-β1 and IL-10 (de Lima et al., 2011; Arany et al., 2007). By initiating the Wnt10b/β-catenin pathway, LLLT can cause hair follicles to enter the anagen phase (Zhang et al., 2017). Ultimately, these activities lead to an increase in hair diameter and density as well as the regeneration of hair follicles.

Microneedling or percutaneous collagen induction creates multiple micropunctures on the skin surface. It has been shown that microneedling promotes hair development from the wound healing process, which releases growth factors such as Wnt3a and Wnt10b, platelet-derived growth factor, and epidermal growth factors and activates the hair bulge (Fertig et al., 2018). It has been demonstrated in the study that patients experiencing hair loss can increase their hair growth by combining LLLT with microneedling.

The results of the study show that green LED light in combination with microneedle patches could stimulate hair growth over 3 months based on patients' as well as dermatologists' satisfaction levels. The increase in hair growth from green LED light demonstrates an accumulative trend over a 3-month period, as shown in Figure 2. Regarding the safety and adverse effects of LED light and microneedle patches, no reports have been made of any adverse reactions.

This study has a few limitations, including a small sample size and the limited follow-up period of the study. Obstacles in finding participants that fulfilled the inclusion criteria of the study and the willingness of each participant led to a small sample size in the study. Further study that recruits a larger sample size and a longer treatment duration is needed to confirm the positive effects of photobiomodulation using the green light LED and microneedle patches. Moreover, any potential long-term adverse effects should also be observed. Another potential bias that occurred in the study was the objectivity of scores from patients' and dermatologists' satisfaction on a 7-point rating scale concerning hair growth. In order to demonstrate more precise and accurate results, hair count and hair shaft diameter should also be measured along with the 7-point rating scale score in further study.

According to the findings in this study, the novel effects of photobiomodulation from the combination of green LED and microneedle patches demonstrate effective outcomes in stimulating hair growth. The combining of green LED light with microneedling can be applied for further treatment approaches in clinical practices as well as for interventions related to hair growth stimulation in AGA patients.

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7. References

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